Therapeutic Considerations in the Elderly

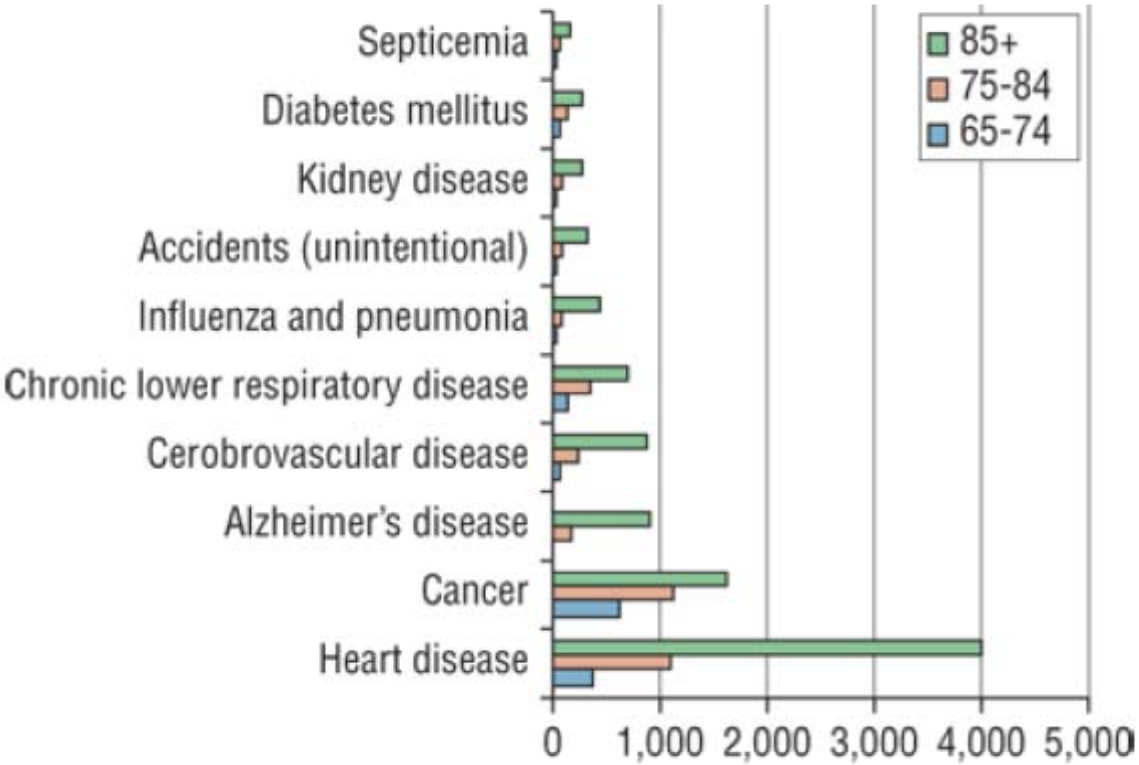
Therapeutic Considerations in the Elderly

- Elderly patients are those 65 years of age and older.
- The health characteristics of those 65-74 years of age are different from those who are 85 years of age and older.
- Institutionalized individuals are also different from those living in the community.
- Age-related changes in physiology can affect the pharmacokinetics and pharmacodynamics of drugs.

Therapeutic Considerations in the Elderly

- **Drug-related problems in older adults are common and cause significant morbidity.**
- **Common medical conditions in the elderly include: hypertension, diabetes mellitus, bronchial asthma, COPD, cancer, arthritis, heart diseases, Alzheimer's disease and cognitive dysfunction, and stroke.**
- **The most common sensory impairments are: difficulties in hearing and vision.**

Leading Causes of Deaths in Older Adults: 2013; Rates per 100,000 Reference 11 pertains to this figure.



Source: J.T. DiPiro, R.L. Talbert, G.C. Yee, G.R. Matzke, B.G. Wells, L.M. Posey: Pharmacotherapy: A Pathophysiologic Approach, 10th Edition, www.accesspharmacy.com

Therapeutic Considerations in the Elderly

- **Older adults use more health resources than any other group, including prescription medications.**

Human Aging & Changes in Drug Pharmacokinetics and Pharmacodynamics

Clinical manifestations of normal aging include:

1. **Changes in biochemical makeup of tissues.**
2. **Reduced capacity of body systems.**
3. **Reduced ability to adapt to physiological stress.**
4. **Increased vulnerability to disease.**

Human Aging & Changes in Drug Pharmacokinetics and Pharmacodynamics

5. **Frailty (a syndrome associated with advanced age – weakness, fatigue, weight loss and functional decline) – may be more important than chronological age as a risk factor for altered pharmacokinetics and pharmacodynamics of drugs.**

- **Individuals experience aging at different rates.**

Common Physiological Changes Associated with Aging

Organ System	Manifestation
Balance and gait	↓ Stride length and slower gait ↓ Arm swing ↑ Body sway when standing
Body composition	↓ Total body water ↓ Lean body mass ↑ Body fat ↔ or ↓ Serum albumin ↑ α_1-Acid glycoprotein (↔ or ↑ by several disease states)
Cardiovascular	↓ Cardiovascular response to stress ↓ Baroreceptor activity leading to ↑ orthostatic hypotension ↓ Cardiac output ↑ Systemic vascular resistance with loss of arterial elasticity and dysfunction of systems maintaining vascular tone ↓ Resting and maximal heart rate

Common Physiological Changes Associated with Aging

Central nervous system	↓ Size of the hippocampus and frontal and temporal lobes ↓ Number of receptors of all types and ↑ sensitivity of remaining receptors ↓ Short-term memory, coding and retrieval, and executive function Altered sleep patterns
Endocrine	↓ Estrogen, testosterone, TSH, and DHEA-S levels Altered insulin signaling
Gastrointestinal	↓ Motility of the large intestine ↓ Vitamin absorption by active transport mechanisms ↓ Splanchnic blood flow ↓ Bowel surface area
Genitourinary	Atrophy of the vagina with decreased estrogen Prostatic hypertrophy with androgenic hormonal changes Detrusor hyperactivity may predispose to incontinence

Common Physiological Changes Associated with Aging

Hepatic	↓ Hepatic size ↓ Hepatic blood flow ↓ Phase I (oxidation, reduction, hydrolysis) metabolism
Immune	↓ Antibody production in response to antigen ↑ Autoimmunity
Oral	Altered dentition ↓ Ability to taste salt, bitter, sweet, and sour
Pulmonary	↓ Respiratory muscle strength ↓ Chest wall compliance ↓ Arterial oxygenation and impaired carbon dioxide elimination ↓ Vital capacity ↓ Maximal breathing capacity ↑ Residual volume

Common Physiological Changes Associated with Aging

Renal	↓ GFR ↓ Renal blood flow ↓ Filtration fraction ↓ Tubular secretory function ↓ Renal mass
Sensory	Presbyopia (diminished ability to focus on near objects) ↓ Night vision Presbycusis (high-pitch, high-frequency hearing loss) ↓ Sensation of smell and taste
Skeletal	↓ Skeletal bone mass (osteopenia) Joint stiffening caused by reduced water content in tendons, ligaments, and cartilage
Skin/hair	Thinning of stratum corneum ↓ Langerhans cells, melanocytes, and mast cells ↓ Depth and extent of the subcutaneous fat layer Thinning and graying of hair caused by more hairs in the resting phase and shortening of the growth phase as well as changes in follicular melanocytes

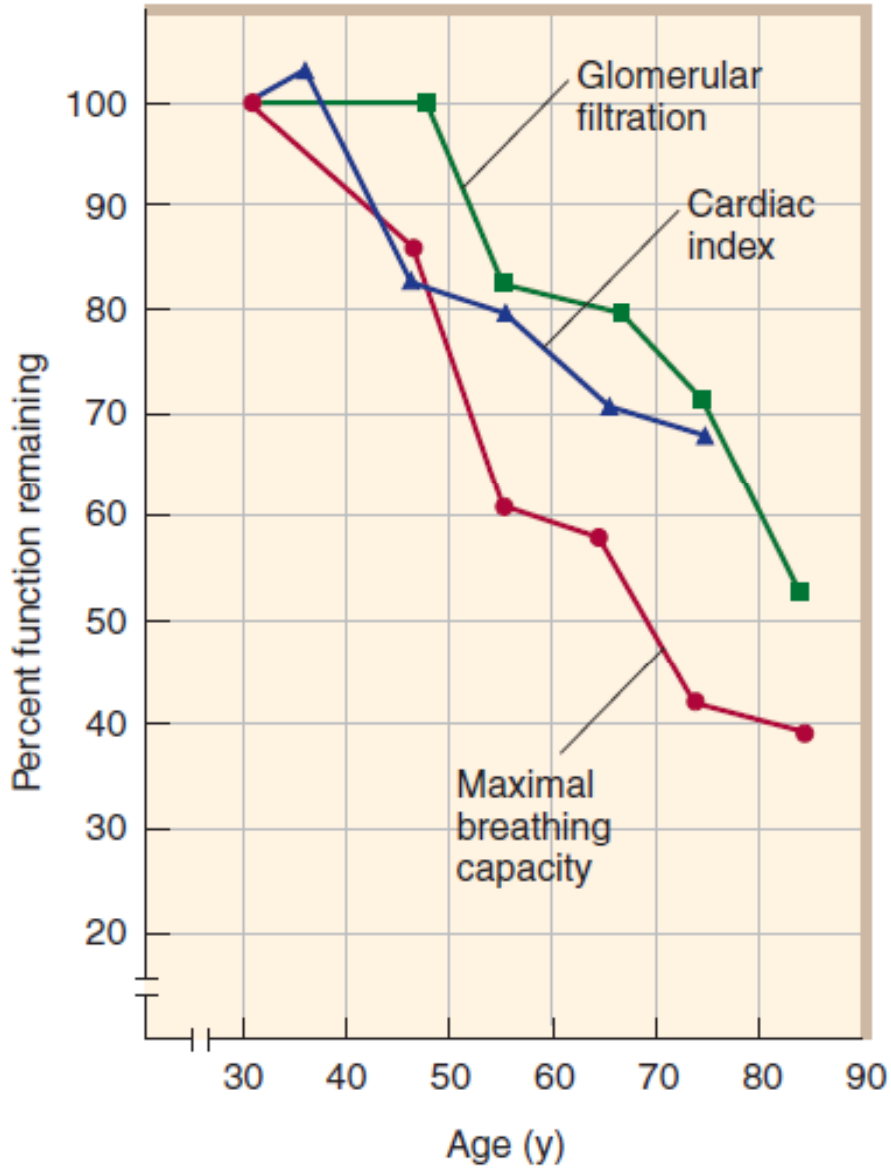


FIGURE 60–1 Effect of age on some physiologic functions.

(Modified and reproduced, with permission, from Kohn RR: *Principles of Mammalian Aging*. Prentice-Hall, 1978.)

TABLE 60–1 Some changes related to aging that affect pharmacokinetics of drugs.

Variable	Young Adults (20–30 years)	Older Adults (60–80 years)
Body water (% of body weight)	61	53
Lean body mass (% of body weight)	19	12
Body fat (% of body weight)	26–33 (women)	38–45
	18–20 (men)	36–38
Serum albumin (g/dL)	4.7	3.8
Kidney weight (% of young adult)	(100)	80
Hepatic blood flow (% of young adult)	(100)	55–60

Common Physiological Changes Associated with Aging

- **These changes may be associated with reduced functional reserve capacity and reduced ability to maintain homeostasis, making them susceptible to de-compensation in stressful situations.**
- **Examples of such impaired homeostatic mechanisms: postural or gait stability, orthostatic blood pressure responses, thermoregulation, cognitive reserve, and bowel or bladder function.**

Age-Related Altered Drug Pharmacokinetics

Pharmacokinetic Phase	Pharmacokinetic Parameters
Gastrointestinal absorption	Unchanged passive diffusion and no change in bioavailability for most drugs ↓ Active transport and ↓ bioavailability for some drugs ↓ First-pass metabolism, ↑ bioavailability for some drugs, and ↓ bioavailability for some prodrugs
Distribution	↓Volume of distribution and ↑ plasma concentration of water-soluble drugs ↑ Volume of distribution and ↑ terminal disposition half-life ($t_{1/2}$) for lipid-soluble drugs
Hepatic metabolism	↓ Clearance and ↑ $t_{1/2}$ for some drugs with poor hepatic extraction (capacity-limited metabolism); phase I metabolism may be affected more than phase II ↓ Clearance and ↑ $t_{1/2}$ for drugs with high hepatic extraction ratios (flow-limited metabolism)
Renal excretion	↓ Clearance and ↑ $t_{1/2}$ for renally eliminated drugs and active metabolites

Age-Related Altered Drug Pharmacokinetics

Absorption:

- **Absorption of drugs may be affected by age-related changes in GIT physiology.**
- **Drug-food interactions, concurrent medication use, and co-morbidities affecting GI function must be considered.**
- **The bioavailability of drugs absorbed by passive diffusion is Not affected significantly.**

Age-Related Altered Drug Pharmacokinetics

- **Nutrients absorbed by active transport such as vitamin B_{12}, calcium, iron, magnesium, leucine may have impaired absorption.**
- **First-pass effect is decreased, bioavailability and plasma concentration are increased for drugs such as propranolol and labetolol. There is reduced bioavailability of pro-drugs such as enalapril and codeine.**

Age-Related Altered Drug Pharmacokinetics

- **Elderly patients with atrophic gastritis, or those taking gastric acid-lowering agents may have reduced extent of absorption of drugs that require an acidic environment for absorption, such as ketoconazole, iron, digoxin, and atazanavir.**

Age-Related Altered Drug Pharmacokinetics

Distribution:

- **The distribution of drugs in the body depends on blood flow, body composition and protein binding.**
- **The volume of distribution of water-soluble drugs (ethanol, gentamicin, digoxin, and cimetidine) is reduced.**
- **Lipophilic drugs (benzodiazepines, metronidazole, and rifampin) exhibit an increased volume of distribution.**

Age-Related Altered Drug Pharmacokinetics

- **Changes in the volume of distribution have an impact on loading doses of drugs.**
- **Reduction of tissue perfusion with aging slows the distribution of dugs to their site of action.**
- **Decreased serum albumin and increased α_1-acid glycoprotein with aging may affect the distribution of dugs that have high hepatic extraction ratio, extensive protein binding, especially when administered intravenously.**

Age-Related Altered Drug Pharmacokinetics

- **The brain of elderly patients may be exposed to higher concentrations of drugs and toxins because of age-related changes in the blood-brain-barrier.**

Age-Related Altered Drug Pharmacokinetics

Metabolism:

- Hepatic metabolism of drugs depends on liver perfusion, activity and capacity of drug metabolizing enzymes, and protein binding.
- All of these factors are affected by the aging process.
- For drugs that have high intrinsic clearance (high hepatic extraction ratio), hepatic clearance depends on hepatic blood flow (flow-limited metabolism).

Age-Related Altered Drug Pharmacokinetics

- **For drugs that have low intrinsic clearance (low hepatic extraction ratio), clearance depends on hepatic enzyme activity (capacity-limited metabolism).**
- **Age-related decreases in hepatic blood flow (20-50%) can decrease significantly the metabolism of high extraction ratio drugs (propranolol, amitriptyline, diltiazem, lidocaine, metoptolol, morphine and verapamil).**

Age-Related Altered Drug Pharmacokinetics

- Interpretation of the effect of age on drugs that undergo capacity-limited metabolism is more complex. Metabolism for such drugs depends also on the fraction of the drug unbound to plasma proteins.
- Generally, liver size and its enzyme content are reduced in the elderly.
- Hepatic metabolism of warfarin, piroxicam and lorazepam is reduced with aging.

Age-Related Altered Drug Pharmacokinetics

- Metabolism of phenytoin, ibuprofen, and naproxen is increased with aging.
- Metabolism of diazepam, temazepam, and valproic acid is not affected with aging.
- Serum albumin concentration declines with age.
- For capacity-limited drugs with extensive protein binding, the fraction of the drug unbound will increase, leading to increased total hepatic clearance (naproxen).

Age-Related Altered Drug Pharmacokinetics

- **Generally, phase II drug metabolism, in contrast to phase I, is preserved in the elderly.**
- **Frail older adults may experience reduced phase II drug metabolism as well.**

Age-Related Altered Drug Pharmacokinetics

Elimination:

- Age-related reductions in GFR are well documented.
- Serum creatinine is a poor indicator of renal function in the elderly. Creatinine is produced by muscles and there may be reduction in muscle mass in the elderly. (i.e. reduced creatinine production).

Age-Related Altered Drug Pharmacokinetics

- **Therefore, it is recommended to use Cockcroft and Gault equation to calculate creatinine clearance:**

$$\text{Creatinine clearance} = \frac{(140 - \text{Age})\,(\text{Actual body weight})}{72\,(\text{Serum creatinine concentration})}$$

Multiply the result by 0.85 for females.

However, you should attempt measuring CLcr accurately when you plan dose adjustment in patients with reduced renal function.

Age-Related Altered Drug Pharmacokinetics

- **Dosing guidelines of drugs that are eliminated by the kidney are based on creatinine clearance.**
- **Drugs that should be avoided when CLcr < 30 mL/min: colchicine, co-trimoxazole, glyburide, nitrofurantoin, probenecid, spironolactone, triamterene.**
- **Drugs that need dose reduction in reduced renal function: acyclovir, amantadine, ciprofloxacin, gabapentin, ranitidine.**

Age-Related Altered Drug Pharmacodynamics

- **Less understood than altered pharmacokinetics.**
- **Proposed changes include:**

1. **Changes in drug concentration at the receptor.**
2. **Changes in receptor numbers.**
3. **Changes in receptor affinity.**
4. **Post-receptor changes.**
5. **Age-related changes in homeostatic mechanisms.**

Age-Related Altered Drug Pharmacodynamics

- **Older adults are sensitive to the CNS effects of drugs:**

1. **Changes in size and weight of brain.**
2. **Changes in the neurotransmitter systems.**
3. **Drugs penetrate CNS easier than in young adults.**

- **For example, in elderly there is decreased levels of dopamine transporters, decreased number of dopaminergic neurons, and decreased density of dopamine receptors; leading to increased sensitivity to the adverse effects of antipsychotic drugs.**

Age-Related Altered Drug Pharmacodynamics

- There is also increased sensitivity to benzodiazepines, opioids, general anesthtecis. Antipsychotics, lithium and anticholinergic drugs.
- The elderly are more likely to develop orthostatic hypotension as an adverse effect of some drugs.
- There is increased hypotensive and bradycardic effect to calcium channel blockers.

Age-Related Altered Drug Pharmacodynamics

- Reduced blood pressure response to β-blockers.
- Reduced effectiveness of diuretics.
- Increased risk of bleeding with warafarin.

Some Problems in the Elderly

Immobility	Instability
Isolation	Intellectual impairment
Incontinence	Impotence
Infection	Immunodeficiency
Inanition (malnutrition)	Insomnia
Impaction	Iatrogenesis
Impaired senses	

Atypical Disease Presentation in the Elderly

Disease	Presentation
Acute myocardial infarction	Only ~50% present with chest pain. In general, older adults present with weakness, confusion, syncope, and abdominal pain; however, electrocardiographic findings are similar to those in younger patients.
Congestive heart failure	Instead of dyspnea, older patients may present with hypoxic symptoms, lethargy, restlessness, and confusion.
Gastrointestinal bleed	Although the mortality rate is ~10%, presenting symptoms are nonspecific, ranging from altered mental status to syncope with hemodynamic collapse. Abdominal pain often is absent.
Upper respiratory infection	Older patients typically present with lethargy, confusion, anorexia, and decompensation of a preexisting medical condition. Fever, chills, and a productive cough may or may not be present.
Urinary tract infection	Dysuria, fever, and flank pain may be absent. More commonly, older adults present with incontinence, confusion, abdominal pain, nausea or vomiting, and azotemia.

Drug-Related Problems in the Elderly

- **Three important, potentially preventable, negative outcomes caused by drug-related problems are:**

1. **Adverse drug withdrawal events.**
2. **Therapeutic failure.**
3. **Adverse drug reactions.**

Drug-Related Problems in the Elderly

Risk Factors:

1. **Polypharmacy including prescription and non-prescription drugs and herbal medicines and supplements and unnecessary drugs.**

- **Polypharmacy has been strongly associated with ADRs, risk of geriatric syndromes (falls, cognitive impairment), nonadherance, diminished functional status, and increased health care costs.**

Drug-Related Problems in the Elderly

2. **Inappropriate Prescribing:**

- **Which is prescribing outside the bounds of acceptable medical standards.**
- **Examples include:**

a. **Wrong dose and duration**
b. **Duplication**
c. **Drug interaction problem**
d. **Prescription of drugs that should be avoided in the elderly.**

Drug-Related Problems in the Elderly

3. **Underuse:**

- **Omission of drug therapy that is indicated in prevention or treatment of disease.**

4. **Medication non-adherence:**

Causes:

a. **Adverse effects.**

b. **Complex regimens.**

Drug-Related Problems in the Elderly

c. Misunderstanding of information about prescribed medications.
d. Cost.
e. Dys-mobiliy (arthritis, ..).
f. Social factors (living alone).
g. Dementia.

Assessing and Monitoring Drug Therapy

1. **Compare the patient's problem list with drug list:**

A drug may be considered unnecessary if:

a. **It does not have indication per the problem list.**
b. **Is not effective.**
c. **The risk of its use outweigh the benefits.**
d. **There is therapeutic duplication.**

Assessing and Monitoring Drug Therapy

2. **Determine if the patient is having a chronic condition but is not receiving an evidence-based medication to improve outcome.**
3. **Monitor efficacy and toxicity of drugs by clinical assessment and lab tests.**

Examples for Monitoring of Medication Use in Older Long Term Care Facility Patients

Drug	Monitoring	Monitoring Interval (in mo)
Amiodarone	Hepatic function tests, TSH level	6
Antiepileptic agents (carbamazepine, phenobarbital, phenytoin, primidone, and valproate)	Drug levels	3-6
Angiotensin-converting enzyme inhibitors or angiotensin I receptor blockers	Potassium levels	6
Antipsychotic agents	Extrapyramidal side effects, fasting serum glucose, serum lipid panel	6
Appetite stimulants	Weight, appetite	*a*
Digoxin	Serum blood urea nitrogen, creatinine, trough drug level	6
Diuretics	Serum sodium and potassium levels	3

Erythropoiesis stimulants	Blood pressure, iron and ferritin levels, CBC	1
Fibrates	Hepatic function test, CBC	6
Hypoglycemic agents	Fasting serum glucose level or glycated hemoglobin level	6
Iron	Iron and ferritin levels, CBC	*a*
Lithium	Trough serum drug levels	3
Niacin	Blood sugar levels, hepatic function tests	6
Theophylline	Trough serum drug levels	3
Thyroid replacement	TSH level	6
Warfarin	Prothrombin time or international normalized ratio	1

Medication Appropriateness Index

Questions to Ask About Each Individual Medication

1. Is there an indication for the medication?
2. Is the medication effective for the condition?
3. Is the dosage correct?
4. Are the directions correct?
5. Are the directions practical?
6. Are there clinically significant drug–drug interactions?
7. Are there clinically significant drug–disease or drug–condition interactions?
8. Is there unnecessary duplication with other medication(s)?
9. Is the duration of therapy acceptable?
10. Is this medication the least expensive alternative compared with others of equal utility?

Examples of Clinically Important Drug–Disease Interactions Determined by Expert Panel Consensus[61]

Drug	Disease
Acetylcholinesterase inhibitors	Syncope
α-Adrenergic blockers, peripheral	Syncope Urinary incontinence in women
Anticholinergic agents	Benign prostatic hyperplasia/lower urinary tract symptoms Dementia or cognitive impairment/delirium
Antipsychotics	History of falls or fracture Parkinson's disease
Aspirin (>325 mg/day)	Peptic ulcer disease
Benzodiazepine receptor agonists	Dementia or cognitive impairment/delirium History of falls or fracture

Bupropion	Chronic seizures or epilepsy
Calcium channel blockers (nondihydropyridine)	Heart failure (systolic dysfunction with reduced ejection fraction)
Chlorpromazine	Chronic seizures or epilepsy
Cilostazol	Heart failure
Corticosteroids	Delirium Peptic ulcer
Decongestants (oral)	Insomnia
Dronedarone	Heart failure (severe or recently decompensated
Estrogen (oral)	Urinary incontinence (women)
Histamine-2 receptor blockers	Delirium

Drug	Disease
Non-aspirin nonsteroidal anti-inflammatory drugs	Chronic kidney disease Heart failure Peptic ulcer disease
Olanzapine	Chronic seizures or epilepsy
Pioglitazone	Heart failure
Selective serotonin reuptake inhibitors	History of falls or fracture
Thioridazine	Syncope
Tricyclic antidepressants	History of falls and fractures
Tramadol	Chronic seizures or epilepsy

Assessing and Monitoring Drug Therapy

4. **Documenting problems and Formulating a Therapeutic Plan:**

- **Keep in mind that a reasonable outcome for a 40-year-old patient may not be reasonable for an 80-year-old patient.**
- **Take into account remaining life expectancy, time until therapeutic benefit, treatment target, medication regimen complexity, and goals of care when deciding on prescribing rationale.**

Assessing and Monitoring Drug Therapy

5. **Implement a team-based management approach and develop strategies to avoid prescribing errors.**
6. **Take measures to enhance adherence to medications:**

a. **Modify medication schedule to fit patient's life-style.**
b. **Prescribe generic agents to reduce cost.**
c. **Offer easy-to-open bottles.**
d. **Offer easy-to-swallow dosage forms.**
e. **Provide both written and oral drug information.**
f. **Involve caregivers stressing the importance of adherence.**

Table 2. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System, Therapeutic Category, Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation	Evidence
Anticholinergics					
First-generation antihistamines: Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Cyproheptadine Dexbrompheniramine Dexchlorpheniramine Dimenhydrinate Diphenhydramine (oral) Doxylamine Hydroxyzine Meclizine Promethazine Triprolidine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate	Avoid	Moderate	Strong	2015 Criteria: Duran 2013 Fox 2014 Kalisch Ellet 2014 From previous criteria: Agostini 2001 Boustani 2007 Guaiana 2010 Han 2001 Rudolph 2008
Antiparkinsonian agents Benztropine (oral) Trihexyphenidyl	Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more-effective agents available for treatment of Parkinson disease	Avoid	Moderate	Strong	Rudolph 2008
Antispasmodics: Atropine (excludes ophthalmic) Belladonna alkaloids Clidinium-	Highly anticholinergic, uncertain effectiveness	Avoid	Moderate	Strong	Lechevallier-Michel 2005 Rudolph 2008

Chlordiazepoxide Dicyclomine Hyoscyamine Propantheline Scopolamine					
Antithrombotics					
Dipyridamole, oral short-acting (does not apply to the extended-release combination with aspirin)	May cause orthostatic hypotension; more effective alternatives available; IV form acceptable for use in cardiac stress testing	Avoid	Moderate	Strong	De Schryver 2010 Dipyridamole package insert
Ticlopidine	Safer, effective alternatives available	Avoid	Moderate	Strong	Ticlopidine package insert
Anti-infective					
Nitrofurantoin	Potential for pulmonary toxicity, hepatoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available	Avoid in individuals with creatinine clearance <30 mL/min or for long-term suppression	Low	Strong	2015 Criteria: Bains 2009 Geerts 2013 From previous criteria: Felts 1971 Hardak 2010 Holmberg 1980
Cardiovascular					
Peripheral 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	ALLHAT 2000 Aronow 2011
Central alpha blockers Clonidine Guanabenz Guanfacine Methyldopa	High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension	Avoid clonidine as first-line antihypertensive. Avoid others as	Low	Strong	Aronow 2011 Methyldopa package insert Reserpine package insert

Reserpine (>0.1 mg/d)		listed			
Disopyramide	Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred	Avoid	Low	Strong	Fuster 2006 Disopyramide package insert
Dronedarone	Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or severe or recently decompensated heart failure	Avoid in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure	High	Strong	Connolly 2011 FDA Drug Safety 2011 Hohnloser 2009 Korber 2008 Dronedarone packageinsert – revised
Digoxin	Use in atrial fibrillation: should not be used as a first-line agent in atrial fibrillation, because more-effective alternatives exist and it may be associated with increased mortality Use in heart failure: questionable effects on risk of hospitalization and may be associated with increased mortality in older adults with heart failure; in heart failure, higher dosages not associated with additional benefit and may increase risk of toxicity Decreased renal clearance of	Avoid as first-line therapy for atrial fibrillation Avoid as first-line therapy for heart failure If used for atrial fibrillation or heart failure, avoid dosages >0.125 mg/d	Atrial fibrillation: moderate Heart failure: low Dosage >0.125 mg/d: moderate	Atrial fibrillation: strong Heart failure: strong Dosage >0.125 mg/d: strong	2015 Criteria: Use in atrial fibrillation: Al-Khatib 2013 Turakhia 2014 Whitbeck 2013 Gheorghiade2013a Gheorghiade2013b Friberg 2010 Mulder 2014 Ambrosy 2014 National PBM Bulletin 2014 Use in heart failure: Freeman 2013 From previous

	digoxin may lead to increased risk of toxic effects; further dose reduction may be necessary in those with Stage 4 or 5 chronic kidney disease.				criteria: Adams 2002 Ahmed 2007 Rathore 2003
Nifedipine, immediate release	Potential for hypotension; risk of precipitating myocardial ischemia	Avoid	High	Strong	Furberg 1995 Nifedipine package insert Pahor1995 Psaty1995a Psaty1995b
Amiodarone	Amiodarone is effective for maintaining sinus rhythm but has greater toxicities than other antiarrhythmics used in atrial fibrillation; it may be reasonable first-line therapy in patients with concomitant heart failure or substantial left ventricular hypertrophy if rhythm control is preferred over rate control	Avoid amiodarone as first-line therapy for atrial fibrillation unless the patient has heart failure or substantial left ventricular hypertrophy	High	Strong	Fuster 2006 ACC/AHA 2006 guideline
Central nervous system					
Antidepressants, alone or in combination Amitriptyline Amoxapine Clomipramine Desipramine Doxepin >6 mg/d Imipramine Nortriptyline Paroxetine Protriptyline	Highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low-dose doxepin (≤6 mg/d) comparable with that of placebo	Avoid	High	Strong	Coupland 2011 Nelson 2011 Scharf 2008

Trimipramine					
Antipsychotics, first- (conventional) and second- (atypical) generation	Increased risk of cerebrovascular accident (stroke) and greater rate of cognitive decline and mortality in persons with dementia Avoid antipsychotics for behavioral problems of dementia and/or delirium unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible ***and*** the older adult is threatening substantial harm to self or others	Avoid, except for schizophrenia, bipolar disorder, or short-term use as antiemetic during chemotherapy	Moderate	Strong	2015 Criteria: Hwang 2014 Langballe 2014 From previous criteria: Dore 2009 Maher 2011 Schneider 2005 Schneider 2006a Schneider 2006b Vigen 2011
Barbiturates Amobarbital Butabarbital Butalbital Mephobarbital Pentobarbital Phenobarbital Secobarbital	High rate of physical dependence, tolerance to sleep benefits, greater risk of overdose at low dosages	Avoid	High	Strong	Cumbo 2010 McLean 2000 Messina 2005
Benzodiazepines *Short- and intermediate- acting:* Alprazolam Estazolam Lorazepam Oxazepam Temazepam Triazolam	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults May be appropriate for seizure	Avoid	Moderate	Strong	2015 Criteria: Breitbart 1996 de Gage 2012 de Vries 2013 Gallacher 2012 Tannenbaum 2012 From previous criteria: Allain 2005

Long-acting: Clorazepate Chlordiazepoxide (alone or in combination with amitriptyline or clidinium) Clonazepam Diazepam Flurazepam Quazepam	disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia				Cotroneo 2007 Finkle 2011 Paterniti 2002
Meprobamate	High rate of physical dependence; very sedating	Avoid	Moderate	Strong	Keston 1974 Rhalimi 2009
Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone Zolpidem Zaleplon	Benzodiazepine-receptor agonists have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); increased emergency room visits/hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration	Avoid	Moderate	Strong	2015 Criteria: Berry 2013 Hampton 2014 From previous criteria: Allain 2005 Cotroneo 2007 Finkle 2011 McCrae 2007 Orriols 2011 Rhalimi 2009 Wang 2001b Yang 2011
Ergoloid mesylates (dehydrogenated ergot alkaloids) Isoxsuprine	Lack of efficacy	Avoid	High	Strong	Isoxsuprine package insert
Endocrine					
Androgens Methyltestosterone	Potential for cardiac problems; contraindicated in men with	Avoid unless indicated for	Moderate	Weak	2015 Criteria: Basaria 2013

Testosterone	prostate cancer	confirmed hypogonadism with clinical symptoms			Vigen 2013 Hildreth 2013 From previous criteria: Basaria 2010 Jones 2011
Desiccated thyroid	Concerns about cardiac effects; safer alternatives available	Avoid	Low	Strong	Baskin 2002 Rees-Jones 1977 Rees-Jones1980 Sawin1978 Sawin1989
Estrogens with or without progestins	Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women. Evidence indicates that vaginal estrogens for the treatment of vaginal dryness are safe and effective; women with a history of breast cancer who do not respond to nonhormonal therapies are advised to discuss the risk and benefits of low-dose vaginal estrogen (dosages of estradiol <25 mcg twice weekly) with their health care provider	Avoid oral and topical patch Vaginal cream or tablets: acceptable to use low-dose intravaginal estrogen for management of dyspareunia, lower urinary tract infections, and other vaginal symptoms	Oral and patch: high Vaginal cream or tablets: moderate	Oral and patch: strong Topical vaginal cream or tablets: weak	2015 Criteria: Chlebowski 2013 Nelson 2012 Manson 2013 Majoribanks 2012 Oskarsson 2014 From previous criteria: Bath 2005 Cho 2005 Epp 2010 Hendrix 2005 Perrotta 2008 Sare 2008
Growth hormone	Impact on body composition is	Avoid, except as	High	Strong	Liu 2007

	small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose	hormone replacement following pituitary gland removal			
Insulin, sliding scale	Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting; refers to sole use of short- or rapid-acting insulins to manage or avoid hyperglycemia in absence of basal or long-acting insulin; does not apply to titration of basal insulin or use of additional short- or rapid-acting insulin in conjunction with scheduled insulin (ie, "correction insulin")	Avoid	Moderate	Strong	2015 Criteria: AGS ADA 2012 ADA Diabetes Care 2014 Pandya 2013 From previous criteria: Queale 1997
Megestrol	Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults	Avoid	Moderate	Strong	2015 Criteria: Ruiz Garcia 2013 From previous criteria: Bodenner 2007 Reuben 2005 Simmons 2005 Yeh 2000
Sulfonylureas, long-duration Chlorpropamide Glyburide	Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes SIADH Glyburide: higher risk of severe prolonged hypoglycemia in older	Avoid	High	Strong	Clarke 1975 Gangji 2007 Shorr 1996

	adults				
Gastrointestinal					
Metoclopramide	Can cause extrapyramidal effects, including tardive dyskinesia; risk may be greater in frail older adults	Avoid, unless for gastroparesis	Moderate	Strong	Bateman 1985 Ganzini 1993 Miller 1989
Mineral oil, given orally	Potential for aspiration and adverse effects; safer alternatives available	Avoid	Moderate	Strong	Marchiori 2010a Marchiori 2010b Meltzer 2006 Simmons 2007
Proton-pump inhibitors	Risk of *C difficile* infection and bone loss and fractures	Avoid scheduled use for >8 weeks unless for high-risk patients (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment (e.g., due to failure of drug discontinuation trial or H_2 blockers)	High	Strong	2015 Criteria: Deshpande 2012 Janarthanan 2012 Adams 2014 Maggio 2013 Fraser 2013 Targownik 2012 Yu 2011(MASR) Targownik 2010 (Neg. Study) Cea Soriano 2014 Ding 2014 Abrahamsen 2013 Lee 2013 Cea Soriano 2013 Khalili 2012 Ye 2011 (MASR) Ngamruengphong 2011 Eom 2011 Pouwels 2011 Prieto-Alhambra 2014

					Chiu 2010 Teramura-Gronblad 2010
Pain medications					
Meperidine	Not effective oral analgesic in dosages commonly used; may have higher risk of neurotoxicity, including delirium, than other opioids; safer alternatives available	Avoid, especially in those with chronic kidney disease	Moderate	Strong	2015 Criteria: Marcantonio 1994b Kaiko 1983 Szeto 1977 From previous criteria: Kaiko 1982 Szeto 1977 Meperidine package insert
Non-cyclooxygenase-selective NSAIDs, oral: Aspirin >325 mg/d Diclofenac Diflunisal Etodolac Fenoprofen Ibuprofen Ketoprofen Meclofenamate Mefenamic acid Meloxicam Nabumetone Naproxen Oxaprozin Piroxicam	Increased risk of gastrointestinal bleeding or peptic ulcer disease in high-risk groups, including those aged >75 or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents; use of proton-pump inhibitor or misoprostol reduces but does not eliminate risk. Upper gastrointestinal ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months and in ~2–4% of patients treated for 1 year; these trends continue with longer duration of use	Avoid chronic use, unless other alternatives are not effective and patient can take gastroprotective agent (proton-pump inhibitor or misoprostol)	Moderate	Strong	2015 Criteria: Derry 2012 Medlock 2013 O'Neil 2012 Roth 2012 From previous criteria: AGS Pain Guideline 2009 Langman 1994 Lanas 2006 Llorente Melero 2002 Pilotto 2003 Piper 1991

Sulindac Tolmetin					
Indomethacin Ketorolac, includes parenteral	Indomethacin is more likely than other NSAIDs to have adverse CNS effects. Of all the NSAIDs, indomethacin has the most adverse effects. Increased risk of gastrointestinal bleeding/peptic ulcer disease, and acute kidney injury in older adults	Avoid	Moderate	Strong	2015 Criteria: Strom 1996 Ketorolac package insert From previous criteria: Onder2004 Lanas 2006 Llorente Melero 2002
Pentazocine	Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other opioid analgesic drugs; is also a mixed agonist and antagonist; safer alternatives available	Avoid	Low	Strong	AGS Pain Guideline 2009 Pentazocine package insert
Skeletal muscle relaxants Carisoprodol Chlorzoxazone Cyclobenzaprine Metaxalone Methocarbamol Orphenadrine	Most muscle relaxants poorly tolerated by older adults because some have anticholinergic adverse effects, sedation, increased risk of fractures; effectiveness at dosages tolerated by older adults questionable	Avoid	Moderate	Strong	2015 Criteria: Richards 2012 Spence 2013 From previous criteria: Billups2011 Rudolph 2008
Genitourinary					
Desmopressin	High risk of hyponatremia; safer alternative treatments	Avoid for treatment of nocturia or nocturnal	Moderate	Strong	2015 Criteria: Juul 2011 Sand 2013 Weiss 2013

		polyuria			Rembratt 2006 Weatherall 2004

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CNS=central nervous system; NSAIDs=nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone.

Table 3. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug–Disease or Drug–Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation	Evidence
Cardiovascular						
Heart failure	NSAIDs and COX-2 inhibitors Nondihydropyridine CCBs (diltiazem, verapamil)—avoid only for heart failure with reduced ejection fraction Thiazolidinediones (pioglitazone, rosiglitazone) Cilostazol Dronedarone (severe or recently decompensated heart failure)	Potential to promote fluid retention and/or exacerbate heart failure	Avoid	NSAIDs: moderate CCBs: moderate Thiazolidinediones: high Cilostazol: low Dronedarone: high	Strong	Cilostazol package insert Connolly 2011 Dronedarone package insert – revised Dec2011 Heerdink 1998 Goldstein 1991 Jessup 2009 Korber 2009 Loke 2011 Pioglitazone package insert Rosiglitazone package insert
Syncope	Acetylcholinesterase inhibitors (AChEIs) Peripheral alpha-1 blockers Doxazosin	Increases risk of orthostatic hypotension or bradycardia	Avoid	Peripheral alpha-1 blockers: high TCAs, AChEIs, antipsychotics: moderate	AChEIs, TCAs: strong Peripheral alpha-1 blockers, antipsychotics:	2015 Criteria: Russ 2012 From previous criteria: Bordier 2005 Davidson1989

	Prazosin Terazosin Tertiary TCAs Chlorpromazine Thioridazine Olanzapine				weak	French 2006 Gaggioli1997 Gill 2009 Kim 2011 Litvinenko 2008 Nickel 2008 Schneider 2006a Schneider 2006b Wild 2010
Central nervous system						
Chronic seizures or epilepsy	Bupropion Chlorpromazine Clozapine Maprotiline Olanzapine Thioridazine Thiothixene Tramadol	Lowers seizure threshold; may be acceptable in individuals with well-controlled seizures in whom alternative agents have not been effective	Avoid	Low	Strong	2015 Criteria: Hughes 2015 Lertxundi 2013 From previous criteria: Pisani 2002
Delirium	Anticholinergics (see Table 7 for full list) Antipsychotics Benzodiazepines Chlorpromazine Corticosteroids[a] H_2-receptor antagonists Cimetidine Famotidine Nizatidine Ranitidine Meperidine	Avoid in older adults with or at high risk of delirium because of potential of inducing or worsening delirium Avoid antipsychotics for behavioral problems of dementia and/or delirium unless	Avoid	Moderate	Strong	From 2015 Criteria: Aparasu 2012 Chavant 2011 Citrome 2013 Hampton 2014 Han 2004 Rigler 2013 From previous criteria: Clegg 2011 Gaudreau 2005 Laurila 2008 Marcantonio 1994a

	Sedative hypnotics [a]excludes inhaled and topical forms. Oral and parenteral corticosteroids may be required for conditions such as exacerbations of COPD but should be prescribed in the lowest effective dose and for the shortest possible duration.	nonpharmacological options (e.g., behavioral interventions) have failed or are not possible ***and*** the older adult is threatening substantial harm to self or others. Antipsychotics are associated with increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia				Moore 1999 Morrison 2003 Ozbolt 2008 Panharipande 2006 Rudolph 2008 Stockl 2010
Dementia or cognitive impairment	Anticholinergics (see Table 7 for full list) Benzodiazepines H_2-receptor antagonists Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone Zolpidem	Avoid due to adverse CNS effects Avoid antipsychotics for behavioral problems of dementia and/or delirium unless nonpharmacological options (e.g., behavioral interventions) have failed or are not possible ***and*** the	Avoid	Moderate	Strong	2015 Criteria: Chavant 2011 Kalicsh Ellet 2014 From previous criteria: Boustani 2007 Hanlon2004 Finkle 2011 Frey 2011 Paterniti 2002 Rasmussen 1999 Rudolph 2008 Schneider 2005 Schneider 2006a

	Zaleplon Antipsychotics, chronic and as-needed use	older adult is threatening substantial harm to self or others. Antipsychotics are associated with increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia				Schneider 2006b Seitz 2011 Vigen 2011 Wright 2009
History of falls or fractures	Anticonvulsants Antipsychotics Benzodiazepines Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics Eszopiclone Zaleplon Zolpidem TCAs SSRIs Opioids	May cause ataxia, impaired psychomotor function, syncope, additional falls; shorter-acting benzodiazepines are not safer than long-acting ones If one of the drugs must be used, consider reducing use of other CNS-active medications that increase risk of falls and fractures (ie, anticonvulsants, opioid-receptor agonists, antipsychotics,	Avoid unless safer alternatives are not available; avoid anticonvulsants except for seizure and mood disorders Opioids: avoid, excludes pain management due to recent fractures or joint replacement	High Opioids: moderate	Strong Opioids: strong	2015 Criteria For Falls/Fractures: Rolita 2013 Soderberg 2013 For Opioids: Rolita 2013 Soderberg 2013 From previous criteria: Allain 2005 Berdot 2009 Deandrea 2010 Ensrud 2003 Hartikainen 2007 Jalbert 2010

		antidepressants, benzodiazepine-receptor agonists, other sedatives/hypnotics) and implement other strategies to reduce fall risk				Liperoti 2007 Mets 2010 Sterke 2008 Turner 2011 van der Hooft 2008 Vestergaard 2008 Wagner 2004 Wang 2001a Wang 2001b Zint 2010
Insomnia	Oral decongestants Pseudoephedrine Phenylephrine Stimulants Amphetamine Armodafinil Methylphenidate Modafinil Theobromines Theophylline Caffeine	CNS stimulant effects	Avoid	Moderate	Strong	Foral 2011
Parkinson disease	All antipsychotics (except aripiprazole, quetiapine, clozapine) Antiemetics Metoclopramide Prochlorperazine Promethazine	Dopamine-receptor antagonists with potential to worsen parkinsonian symptoms Quetiapine, aripiprazole, clozapine appear to be less likely to precipitate	Avoid	Moderate	Strong	2015 Criteria: Leung 2011 Maher 2011 From previous criteria: Bateman 1985 Dore 2009 Ganzini 1993 Morgan 2005 Thanvi 2009

		worsening of Parkinson disease				
Gastrointestinal						
History of gastric or duodenal ulcers	Aspirin (>325 mg/d) Non-COX-2 selective NSAIDs	May exacerbate existing ulcers or cause new/additional ulcers	Avoid unless other alternatives are not effective and patient can take gastroprotective agent (ie, proton-pump inhibitor or misoprostol)	Moderate	Strong	2015 Criteria: O'Neil 2012 From previous criteria: Gabriel 1991 Laine 2010
Kidney/Urinary tract						
Chronic kidney disease Stages IV or less (creatinine clearance <30 mL/min)	NSAIDs (non-COX and COX-selective, oral and parenteral)	May increase risk of acute kidney injury and further decline of renal function	Avoid	Moderate	Strong	Gooch 2007 Griffin 2000 Lafrance 2009 Murray 1995 Schneider 2006 Winkelmayer 2008
Urinary incontinence (all types) in women	Estrogen oral and transdermal (excludes intravaginal estrogen) Alpha-1 blockers, peripheral Doxazosin Prazosin Terazosin	Aggravation of incontinence	Avoid in women	Estrogen: high Peripheral alpha-1 blockers: moderate	Estrogen: strong Peripheral alpha-1 blockers: strong	2015 Criteria: Cody 2012 Northington 2012 Peron 2012 Shamilyan 2012 From previous criteria: Dew 2003 Epp 2010 Grodstein 2004 Hartmann 2009

						Hendrix 2005 Marshall 1996 Perrotta 2008 Ruby 2010
Lower urinary tract symptoms, benign prostatic hyperplasia	Strongly anticholinergic drugs, except antimuscarinics for urinary incontinence (see Table 7 for complete list).	May decrease urinary flow and cause urinary retention	Avoid in men	Moderate	Strong	2015 Criteria: Vande Griend 2012 Ozbilen 2012 From previous criteria: Afonso 2011 Athanasopoulos 2003 Barkin 2004 Blake-James 2006 Chapple 2005 Griebling 2009 Kaplan 2006 Kraus 2010 Malone-Lee 2001 Martin Merino 2009 Spigset 1999 Uher 2009 Verhamme 2008 Wuerstle 2011

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CCB=calcium channel blocker; AChEI=acetylcholinesterase inhibitor; CNS=central nervous system; COX=cyclooxygenase; NSAIDs=nonsteroidal antiinflammatory drug; TCAs=tricyclic antidepressant.

Table 4. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution in Older Adults

Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation	Evidence
Aspirin for primary prevention of cardiac events	Lack of evidence of benefit versus risk in adults ≥80 years old	Use with caution in adults ≥80 years old	Low	Strong	2015 Criteria: FDA2014b From previous criteria: McQuaid 2006 Wolff 2009
Dabigatran	Increased risk of gastrointestinal bleeding compared with warfarin and reported rates with other target-specific oral anticoagulants in adults ≥75 years old; lack of evidence of efficacy and safety in individuals with CrCl <30 mL/min	Use with caution in in adults ≥75 years old and in patients with CrCl <30 mL/min	Moderate	Strong	
Prasugrel	Increased risk of bleeding in older adults; benefit in highest-risk older adults (e.g., those with prior myocardial infarction or diabetes mellitus) may offset risk	Use with caution in adults aged ≥75	Moderate	Weak	Hochholzer 2011 Wiviott 2007 Prasugrel package insert
Antipsychotics Diuretics Carbamazepine Carboplatin Cyclophosphamide Cisplatin Mirtazapine Oxcarbazepine SNRIs	May exacerbate or cause SIADH or hyponatremia; monitor sodium level closely when starting or changing dosages in older adults	Use with caution	Moderate	Strong	2015 Criteria: Arampatzis 2013 From previous criteria: Bouman 1998 Coupland 2011 Liamis

SSRIs TCAs Vincristine					2008 Liu 1996
Vasodilators	May exacerbate episodes of syncope in individuals with history of syncope	Use with caution.	Moderate	Weak	Davidson1989 Gaggioli1997

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CrCl= creatinine clearance; SNRIs = Serotonin-nonrepinephrine reuptake inhitibors; SSRIs = Selective serotonin reuptake inhitibors; TCA=tricyclic antidepressant.

Table 5. 2015 American Geriatrics Society Beers Criteria for Potentially Clinically Important Non-anti-infective Drug–Drug Interactions That Should Be Avoided in Older Adults

Object Drug and Class	Interacting Drug and Class	Risk Rationale	Recommendation	Quality of Evidence	Strength of Recommendation	Evidence
ACEIs	Amiloride or triamterene	Increased risk of hyperkalemia	Avoid routine use; reserve for patients with demonstrated hypokalemia while taking an ACEI	Moderate	Strong	Juurlink 2003
Anticholinergic	Anticholinergic	Increased risk of cognitive decline	Avoid, minimize number of anticholinergic drugs (Table 7)	Moderate	Strong	Cai 2013 Pasina 2013
Antidepressants (ie, TCAs and SSRIs)	≥2 other CNS-active drugs[a]	Increased risk of falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS-active drugs	Moderate	Strong	Weiner 1998 Hanlon 2009a
Antipsychotics	≥2 other CNS-active drugs[a]	Increased risk of falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS active drugs	Moderate	Strong	Weiner 1998 Hanlon 2009a
Benzodiazepines and nonbenzodiazepine, benzodiazepine receptor agonist hypnotics	≥2 other CNS-active drugs[a]	Increased risk of falls and fractures	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS active drugs	High	Strong	Weiner 1998 Hanlon 2009a Zint 2010
Corticosteroids, oral or parenteral	NSAIDs	Increased risk of peptic ulcer	Avoid; if not possible, provide	Moderate	Strong	Piper 1991

		disease or gastrointestinal bleeding	gastrointestinal protection			
Lithium	ACEIs	Increased risk of lithium toxicity	Avoid, monitor lithium concentrations	Moderate	Strong	Juurlink 2004b
Lithium	Loop diuretics	Increased risk of lithium toxicity	Avoid, monitor lithium concentrations	Moderate	Strong	Juurlink 2004b
Opioid receptor agonist analgesics	≥2 other CNS-active drugs[a]	Increased risk of falls	Avoid total of ≥3 CNS-active drugs[a]; minimize number of CNS drugs	High	Strong	Weiner, 1998 Hanlon 2009a Nurminen, 2013
Peripheral, Alpha-1 blockers	Loop diuretics	Increased risk of urinary incontinence in older women	Avoid in older women, unless conditions warrant both drugs	Moderate	Strong	Peron 2012
Theophylline	Cimetidine	Increased risk of theophylline toxicity	Avoid.	Moderate	Strong	Vestal 1987 Loi 1997
Warfarin	Amiodarone	Increased risk of bleeding	Avoid when possible; monitor INR closely	Moderate	Strong	Lam 2013
Warfarin	NSAIDs	Increased risk of bleeding	Avoid when possible; if used together, monitor for bleeding closely	High	Strong	Battistella 2005 Shorr 1993 de Abajo 2013

[a]Central nervous system (CNS)-active drugs: antipsychotics; benzodiazepines; nonbenzodiazepine, benzodiazepine receptor agonist hypnotics; tricyclic antidepressants (TCAs); selective serotonin reuptake inhibitors (SSRIs); and opioids.

ACEI = angiotensin-converting enzyme inhibitor; NSAID=nonsteroidal antiinflammatory drug.

Table 6. 2015 American Geriatrics Society Beers Criteria for Non-Anti-Infective Medications That Should Be Avoided or Have Their Dosage Reduced with Varying Levels of Kidney Function in Older Adults

Medication Class and Medication	Creatinine Clearance, mL/min, at Which Action Required	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation	Evidence
Cardiovascular or hemostasis						
Amiloride	<30	Increased potassium and decreased sodium	Avoid	Moderate	Strong	Somogyi 1990
Apixaban	<25	Increased risk of bleeding	Avoid	Moderate	Strong	Leil 2010
Dabigatran	<30	Increased risk of bleeding	Avoid	Moderate	Strong	Lehr2012 Stangier 2010 Stangier 2012
Edoxaban	30–50 <30 or >95	Increased risk of bleeding	Reduce dose Avoid	Moderate	Strong	Buller 2013 Salazaar 2012 Guigliano 2013 Parasrampuria 2015
Enoxaparin	<30	Increased risk of bleeding	Reduce dose	Moderate	Strong	Collet 2001
Fondaparinux	<30	Increased risk of bleeding	Avoid	Moderate	Strong	Fox 2007 Turpie 2009
Rivaroxaban	30–50 <30	Increased risk of bleeding	Reduce dose Avoid	Moderate	Strong	Kubitz 2010
Spironolactone	<30	Increased potassium	Avoid	Moderate	Strong	Juurlink 2003 Lee 2013 Edwards 2012

						Hanlon 2009b
Triamterene	<30	Increased potassium and decreased sodium	Avoid	Moderate	Strong	Favre 1982 Perazella 1999 Sica 1989 Hanlon 2009b
Central nervous system and analgesics						
Duloxetine	<30	Increased gastrointestinal adverse effects (nausea, diarrhea)	Avoid	Moderate	Weak	Lobo 2010 Skinner 2003
Gabapentin	<60	CNS adverse effects	Reduce dose	Moderate	Strong	Hanlon 2009b Wong 1995 Rowan 2005
Levetiracetam	≤80	CNS adverse effects	Reduce dose	Moderate	Strong	Contin 2010 Hirsch 2007
Pregabalin	<60	CNS adverse effects	Reduce dose	Moderate	Strong	May 2007 Randinitis 2003
Tramadol	<30	CNS adverse effects	Immediate release: reduce dose Extended release: avoid	Low	Weak	Likar 2006 Tramadol package insert
Gastrointestinal						
Cimetidine	<50	Mental status changes	Reduce dose	Moderate	Strong	Schentag, 1979; Larsson, 1982 Manlucu 2005
Famotidine	<50	Mental status changes	Reduce dose	Moderate	Strong	Inotsume, 1989 Manlucu 2005
Nizatidine	<50	Mental status changes	Reduce dose	Moderate	Strong	Aronoff, 1988 Manlucu 2005
Ranitidine	<50	Mental status changes	Reduce dose	Moderate	Strong	Manlucu 2005 McFadyen

						1983 Hanlon 2009b
Hyperuricemia						
Colchicine	<30	Gastrointestinal, neuromuscular, bone marrow toxicity	Reduce dose; monitor for adverse effects	Moderate	Strong	Mikuls 2004 Hanlon 2009b; Wason 2014 Solak 2014
Probenecid	<30	Loss of effectiveness	Avoid	Moderate	Strong	Mikuls 2004 Hanlon 2009b Pui 2013

CNS=central nervous system.