Using Medications Appropriately in Older Adults

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Older Americans comprise 13 percent of the population, but they consume an average of 30 percent of all prescription drugs. Every day, physicians are faced with issues surrounding appropriate prescribing to older patients. Polypharmacy, use of supplements, adherence issues, and the potential for adverse drug events all pose challenges to effective prescribing. Knowledge of the interplay between aging physiology, chronic diseases, and drugs will help the physician avoid potential adverse drug events as well as drug-drug and drug-disease interactions. Evidence is now available showing that older patients may be underprescribed useful drugs, including aspirin for secondary prevention in high-risk patients, beta blockers following myocardial infarction, and warfarin for nonvalvular atrial fibrillation. There is also evidence that many older adults receive medications that could potentially cause more harm than good. Finding the right balance between too few and too many drugs will help ensure increased longevity, improved overall health, and enhanced functioning and quality of life for the aging population. (Am Fam Physician 2002;66:1917-24. Copyright© 2002 American Academy of Family Physicians.)

See page 1856 for definitions of strength-of-evidence levels.

The U.S. population is aging. Patients 65 years and older represent approximately 13 percent of the population, but they consume about 30 percent of all prescription medications.[1] Older American consumers spend an average total of $3 billion annually on prescription medications.[2] Sixty-one percent of older people seeing a physician are taking at least one prescription medication,[3] and most older Americans take an average of three to five medications.[4,5] These data do not include the use of over-the-counter medications or herbal therapies. An estimated 40 percent of older Americans have used some form of dietary supplement within the past year[6] *(Table 1)*.[7]

The physician who cares for aging patients with numerous chronic medical conditions must make daily decisions about appropriate drug therapy. More than 60 percent of all physician visits include a prescription for medication.[8] The multiple medications and complex drug schedules may be justified for older persons with complex medical problems. However, the use of too many medications can pose problems of serious adverse drug events and drug-drug interactions, and often can contribute to nonadherence *(Table 2)*.[9]

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Adherence and Adverse Drug Events

Many factors influence the efficacy, safety, and success of drug therapy with older patients. These factors include not only the effects of aging on the pharmacokinetics and pharmacodynamics of medications but also patient characteristics *(Table 3)*[10] and other issues, including atypical presentation of illness, the use of multiple health care professionals, and adherence to drug regimens *(Table 4)*.[11,12]

Adherence or compliance with drug therapy is essential to successful medical management. Noncompliance or nonadherence with drug therapy in older patient populations ranges from 21 to 55 percent.[13,14] The reasons for nonadherence include more medication use (total number of pills taken per day), forgetting or confusion about dosage schedule, intentional nonadherence because of medica-

TABLE 1
Common Herbs Taken by Older Adults and Drug Interactions

Herb (uses)	*Drug*	*Adverse events*
Ginkgo biloba (Alzheimer's and vascular dementia; peripheral vascular disease, erectile dysfunction, and tinnitus)	Aspirin Warfarin (Coumadin) Thiazide diuretic Acetaminophen and ergotamine/caffeine	Spontaneous hyphema Intracerebral hemorrhage Hypertension Subdural hematoma
St. John's wort (mild depression)	Protease inhibitors, cyclosporine (Sandimmune), theophylline, warfarin Digoxin (Lanoxin) Selective serotonin-reuptake inhibitors	Induction of CYP450 3A4 system with decreased levels of drugs available Decreased drug absorption from the gut Lethargy/incoherence/mild serotonin syndrome
Saw palmetto (benign prostatic hypertrophy)	No specific drug interactions	Headaches, GI upset
Ginseng (cure-all herb)	Warfarin Alcohol Phenelzine (Nardil); MAOI)	Decreased INR Increased alcohol clearance Headache, tremor, mania
Yohimbine (sexual dysfunction)	Tricyclic antidepressants	Hypertension
Senna, cascara (laxative)	Possible interference with any intestinally absorbed drug	Decreased drug availability

CYP450 = cytochrome P-450; GI = gastrointestinal; INR = International Normalized Ratio; MAOI = monoamine oxidase inhibitor.

Information from Fugh-Berman A. Herb-drug interactions. Lancet 2000;355:134-8.

tion side effects, and increased sensitivity to drugs leading to toxicity and adverse events.[12] Older patients may intentionally take too much of a medication, thinking it will help speed their recovery, while others, who cannot afford the medications, may undermedicate or simply not take any of the medication. Simple interventions by the health care team, such as reinforcing the importance of taking the prescribed dose and encouraging use of pill calendar boxes, can improve adherence and overall compliance with drug therapy *(Table 5)*.[11]

One study[15] revealed that adverse drug events in older patients led to hospitalizations in 25 percent of patients 80 years and older. Adverse drug reactions are a common cause of iatrogenic illness in this age group, with psychotropic and cardiovascular drugs accounting for many of these.[11] Many drugs can cause distressing and potentially disabling or life-threatening reactions *(Table 6)*.[11] A basic understanding of how drugs affect the aging body is needed to appreciate the risk inherent in prescribing to older adults.

How Do Drugs Interact with the Aging Body?

Pharmacokinetics includes absorption, distribution, metabolism, and excretion. Of the four, absorption is least affected by aging.[16] In older persons, absorption is generally complete, just slower. In addition to age-related changes, common medical conditions such as heart failure may reduce the rate and extent of absorption. Distribution of most medications is related to body weight and composition changes that occur with aging (decreased lean muscle mass, increased fat mass, and decreased total body water). Drug dosage recommendations may have to be modified based on estimates of lean body mass. Loading doses of drugs may be lowered because of decreased total body water. Fat-soluble drugs may have to be administered in lower dosages because of the potential for accumulation in fatty tissues and a longer duration of action.[16]

Pharmacokinetics includes absorption, distribution, metabolism, and excretion. Of the four, absorption is least affected by the aging process.

TABLE 2
Factors Associated with Medication-Related Problems

Wrong or unnecessary drugs being prescribed
Unmet need for new or additional medications
Wrong medication (contraindications, inappropriate for condition being treated)
Dosage too low or too high
Adverse drug reaction or event
Nonadherence or noncompliance (failure to take drugs properly, cost, prescribing errors)

Information from Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. Am J Hosp Pharm 1990;47:533-43.

TABLE 3
Common Characteristics of Older Adults with Medication-Related Problems

85 years and older
More than six active chronic medical diagnoses
Decreased kidney function (estimated creatinine clearance < 50 mL per minute [0.83 mL per second])
Low body weight or body-mass index
Nine or more medications
More than 12 doses of medication per day
Previous adverse drug reaction

Information from Fouts M, Hanlon J, Pieper C, Perfetto E, Feinberg J. Identification of elderly nursing facility residents at high risk for drug-related problems. Consult Pharm 1997;12:1103-11.

How a drug is cleared, through hepatic metabolism or renal clearance, dramatically changes with aging. Hepatic metabolism is variable and depends on age, genotype, lifestyle, hepatic blood flow, hepatic diseases, and interactions with other medications.[16] Hepatic metabolism occurs through one of two biotransformation systems. Phase I reactions (oxidation, reduction, demethylation, or hydrolysis) via the cytochrome P450 system (CYP450) can produce biologically active metabolites. Phase I reactions tend to occur more slowly in older adults, which often leads to less than optimal drug metabolism. In contrast, phase II metabolism, including acetylation, sulfonation, conjugation, and glucuronidation, is little changed with aging *(Table 7)*.[16] Cigarette smoking, alcohol use, and caffeine use may also affect hepatic metabolism of medications.[16]

Renal excretion of drugs is affected by aging, although there is great interindividual variation. Drug elimination is correlated with creatinine clearance, which declines by 50 percent between 25 and 85 years of age.[16] Because lean body mass decreases with aging, the serum creatinine level is a poor indicator of (and tends to overestimate) the creatinine clearance in older adults. The Cockroft-Gault formula[17] should be used to estimate creatinine clearance in older adults:

$$\text{Creatinine clearance} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{72 \times \text{serum creatinine } (\times\ 0.85 \text{ for women})}$$

For example, a 25-year-old man and an 85-year-old man, each weighing 72 kg (158.4 lb) and having a serum creatinine value of 1 mg per dL (76 µmol per L), would have different estimated creatinine clearance even though their serum creatinine value is the same. The younger man would have an estimated creatinine clearance of 115 mL per minute (1.92 mL per second), while the older man's would be 55 mL per minute (0.92 mL per second). This difference is especially important with drugs that have a low therapeutic index and appreciable renal excretion (aminoglycosides, lithium, digoxin, procainamide [Pronestyl], vancomycin [Vancocin]).[2]

Pharmacodynamics relates to how sensitive tissues are to drugs. Sensitivity to drugs may increase or decrease with aging, and these full effects are poorly understood as a

TABLE 4
Factors That Interfere with Safe and Successful Drug Therapy

Impediments to the recognition of the need to obtain care (cultural, economic, physical, psychologic)
Atypical presentation of illness
Multiple illnesses
Dementia
Diminished vision or hearing
Impairments to adherence (cultural, economic, physical, psychologic)
Polypharmacy
Increased susceptibility to adverse drug events
Age-related changes in pharmacology (absorption, distribution, metabolism, excretion)

Information from references 11 and 12.

TABLE 5
Strategies to Enhance Adherence to Drug Therapy

1. Use once- or twice-daily dosing schedules.
2. Time doses to correspond with daily routine (meals or bedtime).
3. Instruct caregivers concerning drug regimen and potential side effects.
4. Enlist the aid of pharmacists or home health aides to ensure compliance.
5. Provide or use aids such as pill boxes, large-type labeling, easy-to-open pill containers, and pill calendars.
6. Make sure the patient can afford and obtain the medications.
7. Keep updated medication records.
8. Continue to educate patients about their medications.
9. Consider over-the-counter medications as a potential source of noncompliance with prescribed medications.
10. Evaluate for dementia and depression as possible contributors to a drug regimen.

Adapted with permission from Kane RL, Ouslander JG, Abrass IB. Essentials of clinical geriatrics. 4th ed. New York: McGraw-Hill, 1999:383.

Drug elimination correlates with creatinine clearance, which declines by 50 percent between 25 and 85 years of age.

TABLE 6
Common Adverse Drug Events and Clinical Outcomes

Drug/drug class	*Common adverse reactions*	*Common clinical outcomes*
Anti-inflammatory agents	Gastric irritation, ulcers, chronic blood loss, nephrotoxicity	Hemorrhage, anemia, sodium retention, renal failure, may decrease effectiveness of antihypertensive drugs
Aminoglycosides	Renal failure	Increased serum concentration of medications; dialysis
Anticholinergics	Dry mouth, decreased gut motility, bladder hypotonia, decreased cognition, sedation, orthostatic hypotension, blurry vision	Constipation, urinary retention, confusion, instability and falls
Anticoagulants	Bleeding complications	Hemorrhage
Antidepressants (tricyclics)	Anticholinergic effects, heart block	Falls, confusion, urinary retention
Antipsychotics	Sedation, tardive dyskinesia, dystonia, anticholinergic effects, hypotension	Falls, hip fractures, confusion, social disability
Beta blockers	Decreased myocardial contractility, decreased cardiac conduction, mild sedation, orthostatic hypotension	Bradycardia, heart failure, possible confusion, falls
Digoxin	Decreased cardiac conduction, gastrointestinal disturbances	Arrhythmias, nausea, anorexia
Insulin, sulfonylureas, acarbose (Precose)	Hypoglycemia	Falls, confusion, brain injury
Narcotics	Decreased gut motility, sedation	Confusion, constipation
Sedative hypnotics	Excessive sedation, cognitive impairment, gait disturbances, impaired psychomotor performance	Falls and fractures, confusion

Information from Kane RL, Ouslander JG, Abrass IB. Essentials of clinical geriatrics. 4th ed. New York: McGraw-Hill, 1999.

component of the aging process.[16] Pharmacodynamic changes may be related to changes in receptor binding, decreased receptor number, or altered translation of a receptor-initiated cellular response. For older adults, complete elimination of a drug from body tissues, including the brain, can take weeks because of a combination of pharmacokinetic and pharmacodynamic effects.

How Many Drugs Are Too Many?

Polypharmacy is simply the use of many medications at the same time. Other definitions include prescribing more medication than is clinically indicated, a medical regimen that includes at least one unnecessary medication, or the empiric use of five or more medications.[18] Polypharmacy is particularly harmful when the patient receives too many medications for too long and in too high a dosage. The major concern about polypharmacy is the potential for adverse drug reactions and interactions. It has been estimated that for every dollar spent on pharmaceuticals in nursing homes, another dollar is spent treating the iatrogenic illnesses attributed to the medications.[19] Drug-induced adverse events can mimic other geriatric syndromes or precipitate confusion, falls, and incontinence *(Table 6)*,[11] possibly causing the physician to prescribe yet another drug. This prescribing cascade[20,21] is a preventable problem that requires the physician to be certain that all medications being taken by the patient are appropriately indicated, safe, and effective.

To prevent an iatrogenic illness caused by overprescribing, it is important to consider any new signs and symptoms in an older patient to be a possible consequence of current drug therapy.[20] A 10-step approach to help reduce polypharmacy has been described *(Table 8)*.[22] Another way to avoid adverse drug events is to use lower dosages for older patients. Many popular drugs do not have effective lower-dosage recommendations from the manufacturers. Physicians should remember to start low and go slow. Starting with one third to one half of the recommended dosage may help eliminate potential harmful effects.[22]

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TABLE 7
Drugs with Decreased Clearance in Older Adults

Route of clearance	*Representative drug*
Renal	All aminoglycosides, vancomycin (Vancocin), ciprofloxacin (Cipro), levofloxacin (Levaquin), ofloxacin (Floxin), sparfloxacin (Zagam), imipenem (Primaxin), penicillins, digoxin (Lanoxin), procainamide (Pronestyl), lithium, enalapril (Vasotec), lisinopril (Zestril), quinapril (Accupril), ramipril (Altace), sotalol (Betapace), atenolol (Tenormin), nadolol (Corgard), dofetilide (Tikosyn), cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid), ranitidine (Zantac), acetohexamide (Dymelor), chlorpropamide (Diabinese), glyburide (Micronase), tolazamide (Tolinase)
Phase I hepatic biotransformation via cytochrome P450 system	Alprazolam (Xanax), midazolam (Versed), triazolam (Halcion), verapamil (Calan), diltiazem (Cardizem), dihydropyridine calcium channel blockers, lidocaine (Xylocaine), diazepam (Valium), phenytoin (Dilantin), celecoxib (Celebrex), theophylline, imipramine (Tofranil), desipramine (Norpramin), trazodone (Desyrel), flurazepam (Dalmane)
Phase II hepatic biotransformation	Lorazepam (Ativan), oxazepam (Serax), isoniazid (INH), procainamide

Information from Luisi AF, Owens NJ, Hume AL. Drugs and the elderly. In: Gallo JJ, Reichel W, eds. Reichel's Care of the elderly: clinical aspects of aging, 5th ed. Philadelphia: Williams & Wilkins, 1999:59-87.

What Medications Could Potentially Cause Trouble?

Drug-related problems including therapeutic failure, adverse drug reactions, and adverse drug withdrawal events are common in older patients.[23] To address this problem, a list of drugs that may be inappropriate to prescribe to older persons, especially the frail elderly, was developed through a consensus of experts in geriatric medicine and pharmacology.[24,25] This list, known as the Beers criteria, was originally targeted at nursing homes but has been expanded for community-dwelling seniors.[26]

A recent review[27] of the Beers criteria applied to various health care settings, from community-dwelling seniors to frail nursing home patients, found that between one in four and one in seven older patients received at least one inappropriate medication. The problematic drugs most often prescribed were long-acting benzodiazepines, dipyridamole (Persantine), propoxyphene (Darvon), and amitriptyline (Elavil).[27] When applying these criteria to a patient, it is important to remember that if a drug has been used for a long time without a serious adverse effect, it may not need to be discontinued. The physician should continually monitor a patient's drug list and carefully ascertain if any medication is causing harm. Physicians can address this issue by keeping a list of drugs that can cause serious adverse events when prescribed to older adults *(Table 9)*.[24,25] [References 24 and 25, Evidence level C: expert opinion/consensus]

What Medications Can Benefit Older Patients?

To avoid adverse drug events and polypharmacy, drugs that are beneficial in the treatment or prevention of serious diseases may not be prescribed to older adults.[27,28] For example, clinical evidence is now available showing that older adults benefit from beta-blocker therapy after myocardial infarction, adequate control of hypertension, and adequate treatment of hyperlipidemia. Other medications that have shown benefit in older adults, but are sometimes not prescribed, include angiotensin-converting enzyme inhibitors for heart failure and anticoagulants for nonvalvular atrial fibrillation *(Table 10)*.[29-39]

Prescribing medications for older adults requires main-

TABLE 8
10 Steps to Reducing Polypharmacy

1. Have patients "brown bag" all medications at each office visit, and keep an accurate record of all medications, including over-the-counter medications and herbs.
2. Get into the habit of identifying all drugs by generic name and drug class.
3. Make certain the drug being prescribed has a clinical indication.
4. Know the side-effect profile of the drugs being prescribed.
5. Understand how pharmacokinetics and pharmacodynamics of aging increase the risk of adverse drug events.
6. Stop any drug without known benefit.
7. Stop any drug without a clinical indication.
8. Attempt to substitute a less toxic drug.
9. Be aware of the prescribing cascade (treating an adverse drug reaction as an illness with another drug).
10. As much as possible, use the motto, "one disease, one drug, once-a-day."

Information from Carlson JE. Perils of polypharmacy: 10 steps to prudent prescribing. Geriatrics 1996;51;26-30,35.

TABLE 9

Inappropriate Medication/Medication Classes for Use in Older Adults

Medication/medication class	*Problematic use*
Antihistamines (chlorpheniramine [Extendryl], diphenhydramine [Benadryl], hydroxyzine [Atarax], cyproheptadine [Periactin], dexchlorpheniramine [Polaramine], promethazine [Phenergan], tripelennamine [PBZ])	Many of these are over-the-counter drugs used to treat the common cold with potent anticholinergic effects; many elderly persons use these drugs to induce sleep; if using to treat seasonal allergies, use lowest effective dose.
Blood products/modifiers/volume expanders (dipyridamole [Persantine], ticlopidine [Ticlid])	Platelet aggregation inhibitors are used to prevent blood from clotting in persons who have had strokes or myocardial infarction; ticlopidine has been shown to be no better than aspirin, and it is more toxic; dipyridamole is beneficial in patients with artifical valves.
Antihypertensives (methyldopa [Aldomet], reserpine [Serpasil])	Methyldopa can slow heart rate and exacerbate depression; reserpine causes depression, erectile dysfunction, sedation, and light-headedness.
Peripheral vasodilators (cyclandelate [Cyclospasmol], ergot mesyloids [Hydergine])	Used to treat dementia and migraines; not shown to be effective for either in doses studied
Antiarrhythmics (disopyramide [Norpace])	Potent negative inotrope, may induce heart failure; strongly anticholinergic
Narcotics (meperidine [Demerol], pentazocine [Talwin], propoxyphene [Darvon])	Meperidine is not an effective oral agent for pain and has many disadvantages over other narcotics; pentazocine causes more central nervous system effects, including confusion and hallucinations; propoxyphene offers no advantages over acetaminophen but has same side effects as other narcotic drugs.
Barbiturates (except phenobarbital) (butalbital [Fiorinal], pentobarbital [Nembutal], secobarbital [Seconal])	Highly addictive and cause more side effects than other sedative hypnotics; should not be started as new therapy except to treat seizures
Benzodiazepines (chlordiazepoxide [Librium],diazepam [Valium], flurazepam [Dalmane], triazolam [Halcion])	Long half-life benzodiazepines produce prolonged sedation and increase risk for falls and fractures; triazolam may cause cognitive and behavioral abnormalities.
Meprobamate (Miltown, Equanil)	Used to treat anxiety; highly addictive and sedating
Antidepressants (amitriptyline [Elavil], doxepin [Sinequan], imipramine [Tofranil], combination antidepressant/antipsychotics	Highly anticholinergic and sedating; amitriptyline is rarely the antidepressant of choice in the elderly.
Methylphenidate (Ritalin)	May cause agitation, stimulation of the central nervous system, and seizures.
Antiemetic (trimethobenzamide [Tigan])	Least effective, can cause extrapyramidal side effects
Gastrointestinal antispasmodics (Donnatal with belladonna, clidinium [Quarzan], dicyclomine [Bentyl], hyoscyamine [Levsin], propantheline [Pro-Banthine])	All are highly anticholinergic and generally produce substantial toxic effects; best avoided in the elderly; not for long-term use.
Antidiarrheals (diphenoxylate [Lomotil])	Drowsiness, cognitive impairment, and dependence; long-term use is not recommended.
Genitourinary-antispasmodic (oxybutynin [Ditropan])	Anticholinergic effects; use lowest effective dose.
Hypoglycemic agents (chlorpropamide [Diabinese])	Prolonged half-life with prolonged and serious hypoglycemia; can cause syndrome of inappropriate antidiuretic hormone.
NSAIDs (indomethacin [Indocin], phenylbutazone [Butazolidine], ketorolac [Toradol], mefenamic acid [Ponstel], piroxicam [Feldene])	Indomethacin produces serious central nervous system effects; phenylbutazone produces serious hematologic effects (bone marrow suppression); ketorolac, mefenamic acid, and piroxicam have greater risk of upper gastrointestinal bleeding than other NSAIDs.
Skeletal muscle relaxants (all)	Effectiveness questionable; anticholinergic effects, sedation, and weakness

NSAIDs = nonsteroidal anti-inflammatory drugs.

Information from references 24 and 25.

taining a balance between using too few and too little, and too many and too much.[40] Frequent follow-up visits, especially if a new drug has been introduced, allow the physician to assess for adverse drug events and possible drug-disease and drug-drug interactions. One recommended strategy is to verify at each patient visit if there is an indication for each drug, if it is effective in this case, if there is any unnecessary duplication with other drugs, and if this is the least expensive drug available compared with others of equal benefit. Before deciding that a medication is a therapeutic failure, the physician should make sure that an adequate dosage has been administered for an appropriate

TABLE 10
Drugs with Proven Benefits in Older Adults

Clinical indication	*Drug*	*Evidence*
Status post MI, CAD, transient ischemic attacks, stable and unstable angina, peripheral vascular disease, stroke prevention, and embolic stroke prevention in those unable to take warfarin (Coumadin)	Aspirin, 75 mg per day	Beneficial; most benefit seen for high-risk patients taking medium-dose aspirin for at least three years; should probably be used for life; no clear evidence of use in low-risk patients.[29] [Evidence level A, systematic review of RCTs]
Status post MI	Beta blockers	Beneficial; given within hours of infarction and continued for at least one year or until a complication contraindicates use; most benefit found for those older than 65 years and those who suffered large infarcts.[30,31] [Reference 30, Evidence level B, retrospective cohort study; Reference 31, Evidence level A, meta-analysis]
Hypertension Systolic hypertension Status post MI/CAD CHF/DM	 Thiazide diuretic Beta blocker ACE inhibitor	Any reduction in BP appears to confer benefit; treatment of BP reduces stroke, CHD, cardiovascular disease, heart failure, and mortality; treatment goal is BP < 140/90 mm Hg; however, an interim goal of systolic BP below 160 mm Hg may be needed in those with marked systolic hypertension; JNC VI recommends starting BP treatment with a low-dose thiazide diuretic or beta blockers in combination with thiazide diuretics.[32,33] [References 32 and 33, Evidence level A, meta-analyses]
Heart failure	ACE inhibitor (no significant difference between ACE inhibitors).[34]	Beneficial; reduction in mortality, admission to hospitals, and ischemic events.[34,35] [References 34 and 35, Evidence level A, meta-analyses]
	Spironolactone (Aldactone, 12.5 to 25.0 mg per day)[36]	Spironolactone additive effect in reduction of morbidity and death with severe heart failure (NYHA III-IV).[36] [Evidence level A, RCT]
Hypercholesterolemia	Statins Start with one half lowest recommended dose and titrate upward to target LDL level Baseline liver function tests with repeat test after six to 12 weeks of therapy, then twice yearly	Beneficial; consider treatment for patients 50 to 80 years of age without CAD who have serum LDL levels > 130 mg per dL (3.35 mmol per L) and serum HDL levels < 50 mg per dL (1.30 mmol per L) because older patients are at increased risk of CAD. Treat all men and women with CAD, previous stroke, DM, peripheral artery disease, extracranial carotid arterial disease, and abdominal aortic aneurysm to LDL level < 100 mg per dL (2.59 mmol per L). Active liver disease is a contraindication; a history of liver disease and alcohol use requires cautious use. Myopathy can be a problem; have patients report any unusual muscle tenderness.[37] [Evidence level A, systematic review of RCTs]
Chronic nonvalvular atrial fibrillation	Warfarin to maintain an INR between 2.0 and 3.0	Beneficial; as primary prevention, about 25 strokes and about 12 disabling fatal strokes would be prevented yearly for every 1,000 patients given oral anticoagulation therapy. Careful monitoring of INR required to offset potential hemorrhagic risk.[38,39] [References 38 and 39, Evidence level A, meta-analyses]

MI = myocardial infarction; CAD = coronary artery disease; RCT = randomized controlled trial; CHF = congestive heart failure; DM = diabetes mellitus; ACE = angiotensin-converting enzyme; BP = blood pressure; CHD = coronary heart disease; JNC VI = sixth report of the Joint National Committee; NYHA = New York Heart Association classes; LDL = low-density lipoprotein; HDL = high-density lipoprotein; INR = International Normalized Ratio.

Information from references 29 through 39.

length of time.[41] The goals in using drug therapy are to treat disease, alleviate pain and suffering, and prevent the life-threatening complications of many chronic diseases. Being successful with these goals requires a balance between benefit and risk to optimize prescribing for the aging population.

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