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Approaches to Appropriate Drug Prescribing for the Older Adult

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Persons over age 65 years represent the largest consumers of medications. Results of the Slone Epidemiologic Survey suggest that 94% of women over age 65 years living in the community take at least 1 medication and 12% take 10 or more medications [1]. This observation combined with the general aging of the population, the increased number of available medications, and the increased marketing of medications challenges the primary care physician's efforts to craft the optimal drug regimen for each older adult seen in the office. Chief among these challenges is achieving a balance between prescribing an untenable number of medications to address the many chronic conditions prevalent in this population and avoiding a sense of therapeutic nihilism and consequent denial of efficacious medications to elderly patients. To fully appreciate the enormity of this task, the physician must understand the

- Pharmacodynamic and pharmacokinetic changes that occur with age
- Rate of adverse reactions and drug–drug interactions in the elderly
- Evidence for use of particular medications in an elderly population
- Medications that have been deemed harmful to most older adults
- Use of over-the-counter medications and herbal preparations
- Financial constraints particular to this population that affect compliance

Pharmacokinetic and pharmacodynamic changes in the elderly

The pharmacokinetics of an orally administered drug refers to the rate at which it is absorbed, distributed, metabolized, and eliminated from the body. Aging has little effect on the absorption of most drugs, although there

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may be a change in the rate of absorption in older persons taking many medications. Absorption of many floroquinolones, for example, can be impaired if taken concomitantly with iron.

Unlike absorption, drug distribution changes with age because of associated changes in body composition—namely, an increase in fat stores and a decrease in total body water [2]. As such, drugs that are water soluble (or hydrophilic) such as ethanol or lithium have a lower volume of distribution, whereas fat-soluble drugs (or lipohilic drugs) such as diazepam and trazadone have a larger volume of distribution. Practically speaking, this means that in an older population, hydrophilic drugs reach steady state quicker and are eliminated more expeditiously compared with lipophilic medications that require more time to reach steady state and are eliminated at a slower rate. Moreover, drugs that are highly protein bound, such as digoxin, often have a higher proportion of unbound, pharmacologically active drug in older persons because of decreases in albumin that can occur in association with many of the chronic conditions prevalent in an older population [2].

Metabolism of medications is affected by age because of an age-related decrease in hepatic blood flow and liver size. As such, drugs that undergo phase I reactions in the liver and are converted to active metabolites often accumulate in older persons. With a few exceptions, drugs that are conjugated in the liver and converted to inactive metabolites by way of phase II reactions involving glucuronidation and sulfate conjugation are thus preferred in this population. Examples of medicines undergoing phase I reactions include valium and amitriptyline; medicines undergoing phase II reactions include lorazepam and oxazepam. Drug elimination is also often reduced in the geriatric population because of reductions in renal blood flow, kidney size, and glomerular filtration that accompany many chronic conditions. It is important to recognize that serum creatinine is not an accurate reflection of creatinine clearance in this population. Because of the decrease in lean muscle mass and attendant decrease in creatinine production, normal serum creatinine values may be associated with a significant decline in renal function. As such, it is always prudent to estimate creatinine clearance by using the Cockroft-Gault equation or the modified diet in renal disease equation shown in Box 1.

The pharmacodynamics of a drug refers to the time course and intensity of the drug's effect. The pharmacodynamics of some drugs changes with age, with a tendency for older persons to experience a heightened effect. This increased sensitivity may be due to changes in the drug–receptor interactions, postreceptor events, or organ pathology that results from various chronic diseases that may accompany aging. The possible effects that aging may have on the pharmacodynamics of a few common drugs are listed in Table 1. Ultimately, the changes in pharmacodynamics and pharmacokinetics support the adage of "start low and go slow." It is prudent to initiate drugs at a low dosage and to titrate slowly to achieve the desired therapeutic benefit. For some medications (eg, lithium, digoxin, and

Box 1. Estimation of creatinine clearance

Cockroft-Gault equation for estimating creatinine clearance (Cr Cl):

$$\text{Cr Cl in milliliters per minute}^{a} = \frac{(140 - \text{age in years})(\text{weight in kilograms})}{72(\text{serum creatinine in milligrams per deciliter})}$$

[a]For women, this number should be multiplied by 0.85.

Modified diet in renal disease equation for estimating creatinine clearance:

$$\text{Cr Cl in milliliters per minute}^{b} = \exp(5.228 - 1.154 \times \log[\text{serum creatinine}]) - (0.203 \times \log[\text{age}])$$

[b]For women, this number should be multiplied by 0.742; for African Americans, this number should be multiplied by 1.21.

From Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461–70; with permission.

some anticonvulsants), dosages for the older adult will remain low and still prove effective because of the aforementioned changes in pharmacokinetics and pharmacodynamics, whereas for other medications (eg, angiotensin-converting enzyme inhibitors and some serotonin selective reuptake inhibitor antidepressants), slow titration to doses typically used in a younger population may be more appropriate [2].

Adverse drug reactions, drug–drug interactions, and drug–disease interactions in the elderly

Adverse drug reactions are common primarily because of the age-associated alterations in pharmacokinetics and pharmacodynamics and the sheer number of medications prescribed for older persons. Recent estimates suggest that 35% of ambulatory older adults experience an adverse drug reaction on a yearly basis and 29% require evaluation by a physician or evaluation in the emergency room/hospital for the adverse reaction. If ranked as a disease, adverse drug reactions would be the fifth leading cause

Table 1
Effects of aging on selected medications: changes in pharmacodynamics

Drug	Action	Effect of aging
Morphine	Acute analgesic effect	Increase
Albuterol	Bronchodilation	Decrease
Glyburide	Chronic hypoglycemic effect	No change
Diazepam	Sedation	Increase
Furosemide	Latency and size of peak diuretic response	Decrease
Nitroglycerin	Venodilation	No change

Data from Beers M, Berkow R. The Merck manual of geriatrics: clinical pharmacology. 3rd edition. Whitehouse Station (NJ): Merck Research Laboratory; 2000.

of death in America. Costs of medication-related problems in the ambulatory setting alone are estimated to surpass $75 billion [3].

Although much has been published about these reactions in the long-term care and acute care setting, little has been known until recently about the types of adverse drug reactions common in the outpatient setting. In 2003, Gurwitz and colleagues published a review of the frequency and potential prevention of adverse drug reactions in an outpatient population receiving care through a Medicare choice plan [4]. In a 1-year period in which 27,617 enrollees were followed, 1523 adverse drug events were identified. Of these events, 38% were categorized as serious, life-threatening, or fatal; 27% were considered preventable. Unlike the long-term care setting in which psychotropic medications have been identified as prime culprits, most preventable events in this outpatient population were related to cardiovascular medications followed by diuretics, nonopioid analgesics, hypoglycemics, and anticoagulants. The investigators concluded that the generalization of their results to the current population of Medicare enrollees translates into 1.9 million adverse drug events each year and approximately 180,000 life-threatening adverse drug reactions per year, of which about 50% would be preventable [4].

How can providers reduce the number of adverse drug reactions? The study by Gurwitz and colleagues [4] suggested that the largest number of preventable adverse reactions occurred at the prescribing or monitoring stages. Prescribing errors included wrong drug choices, wrong dose choices, inadequate patient education, and prescription of a drug for which there was a well-established, clinically important interaction with another drug. Monitoring errors included inadequate laboratory evaluation of drug therapies and failure to respond to signs, symptoms, or laboratory evidence of drug toxicity. Moreover, this failure to respond to evidence of drug toxicity may have been underestimated by the study, considering that such signs and symptoms may be atypical in older persons or poorly reported in those suffering from chronic cognitive impairments. Ultimately, the investigators postulated that in addition to physician education, health care systems need to respond to this problem by (1) making information on

adverse drug reactions more accessible to patients, (2) enhancing the surveillance and reporting of adverse drug reactions, and (3) using computerized physician order entry, which could alert providers of possible drug–drug interactions, inappropriate doses, and the need for laboratory monitoring with particular drugs [4].

Another way to prevent adverse drug reactions in the older population is to make providers conscious of the prescribing cascade. This cascade is often initiated by an adverse drug reaction that is misinterpreted by the provider as a new medical condition. Such a misdiagnosis may result in a prescription for an additional and unnecessary medication, thus increasing the risk for further adverse drug reactions and drug–drug interactions [5]. Examples of such cascades include the use of dopamine agonists to treat neuroleptic-induced parkinsonism and the prescription of antihypertensive medications to treat elevations in blood pressure caused by nonsteroidal anti-inflammatory drugs [6]. Results of a case-control study of geriatric patients enrolled in the New Jersey Medicaid program support this notion. The study showed that elderly patients using nonsteroidal anti-inflammatory drugs had an odds ratio of 1.66 for being placed on an antihypertensive compared with those not using these analgesics. Even more impressive, the odds ratio of being placed on a medication for parkinsonism was 5.2 for those who were prescribed 20 mg or more of metoclopramide compared with those not receiving this medication [5].

A final important concept in relation to adverse drug reactions in the elderly is the notion of drug–disease interactions. Because the burden of chronic illnesses increases with age, persons over age 65 years are at higher risk for experiencing such drug–disease interactions. Examples of such interactions include increased sensitivity or paradoxic reactions to psychotropic medications in persons who have dementia or worsening of urinary retention in men who have benign prostatic hypertrophy when an anticholinergic medication is prescribed (Table 2). In addition, the consequences of adverse drug reactions may be more serious in older persons because of the burden of their comorbidities. A younger person who falls due to excess sedation from a medication is less likely to have a hip fracture, whereas an older woman with osteoporosis is at substantial risk for this untoward outcome [7].

Zhan and colleagues [8] suggested in their recently published article on potentially harmful drug–drug and drug–disease interactions that prescribers may not fully attend to these issues. Using data obtained from the National Ambulatory Medical Care Survey and the National Hospital Medical Care Survey from 1995 to 2000, these investigators found that for visits in which two or more prescriptions were written, 0.76% of the visits resulted in inappropriate drug–drug combinations. Moreover, 2.58% of visits in which a prescription was written resulted in an inappropriate drug–disease combination. The most common inappropriate drug–drug interactions included those in which a medication that might interact negatively

Table 2
Selected drug–disease interactions in the elderly

Disease	Drug	Potential adverse outcome
Benign prostatic hypertrophy	α-agonists, anticholinergics	Urinary retention
Dementia	Anticholinergics, benzodiazepine	Increased confusion
Hypertension	Nonsteroidal anti-inflammatory drugs	Increased blood pressure
Parkinson's disease	Antipsychotics	Worsening of movement disorder
Osteoporosis	Corticosteroids	Fracture
Constipation	Anticholinergics, opiates, calcium channel blockers	Worsening of constipation
Diabetes	Corticosteroids	Hyperglycemia
Renal impairment	Nonsteroidal anti-inflammatory drugs, radiocontrast dye	Renal failure
Venous insufficiency	Dihydropyridine calcium channel blockers	Increased lower extremity edema

with warfarin was added to the medication regimen; the most common drug–disease interactions included the prescription of anticholinergic medications, bethanacol, or narcotics to men who had benign prostatic hypertrophy. The most significant predictor of having an inappropriate combination prescribed was the sheer number of medications prescribed, again underscoring the need to carefully weigh the risk/benefit ratio of each medication [8]. Examples of drug–drug interactions are listed in Table 3.

Elderly population and drug trials: toward an evidence-based geriatric practice

Although much has been written about adverse drug reactions in the elderly, there is a relative dearth of studies looking at the efficacy of medications in an older population, making it even more difficult for the clinician to intelligently weigh the potential benefit and risk of pharmacologic therapy. Despite the fact that older people represent the fastest growing segment of the population, they are often systematically excluded from clinical studies. Bugeja and colleagues [9], for example, reviewed all original research articles published in major British medical journals (including the *British Medical Journal*, *Gut*, *Lancet*, and *Thorax*) from 1996 to 1997 and found that roughly 33% of the articles excluded persons 75 years and older without justification. Lee and colleagues [10] reviewed the inclusion of persons 75 years and older in randomized controlled trials of cardiovascular interventions for acute coronary syndrome from 1966 to 2000 and found that this group was grossly under-represented. Between 1966 and 1990, this group accounted for only 2% of all patients enrolled. This number increased to only 13% in studies recruiting patients after 1995, despite the fact that this age

Table 3
Selected clinically important drug–drug interactions in the elderly

Drug	Interacting drug	Mechanism	Effect
Digoxin	Amiodarone	Decreased renal or nonrenal clearance of digoxin	Digitalis toxicity
	Verapamil Dilitiazem		
Warfarin	Metronidazole	Inhibition of drug metabolism	Increased anticoagulation
	Omeprazole Trimethoprim-sulafmethoxazole		
Levothyroxine	Calcium carbonate	Levothyroxine adsorbs calcium carbonate in an acidic environment	Reduced T_4 absorption
			Increased thyrotropin levels [29]
Diuretic	Nonsteroidal anti-inflammatory drugs	Decreased renal perfusion	Renal impairment
Acetylcholinesterase inhibitor	Anticholinergic medications	Decreased ability to favorably augment acetylcholine level	Potentially less effective as a therapy for dementia [30]

Data from Beers M, Berkow R. The Merck manual of geriatrics: clinical pharmacology. 3rd edition. Whitehouse Station (NJ): Merck Research Laboratory; 2000.

group represented approximately 37% of patients hospitalized for a myocardial infarction and about 60% of all deaths attributable to myocardial infarctions. Although there are many postulated underpinnings for this exclusion, including fears about adverse drug reactions, drug–drug and drug–disease interactions, and poor compliance, none seems to justify the current state of ageist exclusion. To help mitigate this problem, the Food and Drug Administration issued guidelines to enhance the participation of older persons in clinical trials in 1989 and, more recently in 1997, began requiring drug companies to include a separate geriatric-use section in their drug labeling [11]. The most recent legislation, however, falls short of requiring drug companies to perform additional studies in older persons and, thus, the ability of providers to truly embrace an evidenced-based approach in their prescribing patterns remains limited at best.

Faced with little direct evidence on the efficacy of medications in the older population, clinicians often extrapolate and apply the data obtained from studies performed in a younger cohort to their geriatric patients. This practice may result in significant iatrogenesis; for example, in the SHOCK (‘‘should we emergently revascularize occluded coronaries for cardiogenic shock?’’) trial, it was found that persons under age 70 years who were suffering from cardiogenic shock had a survival benefit if revascularization of the coronary arteries was pursued over a more conservative approach.

Applying these data to an older population over age 70 years, however, would not be clinically prudent because the trial also found that the older cohort seemed to fare better when the conservative approach was adopted over revascularization. Although treatment and medication regimens certainly need to be individualized, the current state of applying data from a younger population to older adults is fraught with problems [10].

Instead of applying data obtained from a younger cohort to older patients, clinicians may become overly cautious or even nihilistic and adopt a prescribing strategy that ignores potentially beneficial therapies in response to the lack of research applicable to this population. In the last decade, several studies have alleged that there is gross undertreatment of older persons with therapies that have been substantiated by the medical literature to improve outcomes [11]. Sloane and colleagues [12], for example, examined medication regimens of 2014 persons over age 65 years residing in assisted living facilities and found that 62% of persons who had congestive heart failure were not receiving an angiotensin-converting enzyme inhibitor, 51% of patients who had osteoporosis were not receiving calcium supplementation, and 37% were not receiving any antiplatelet or anticoagulant treatment despite a history of a cerebrovascular attack. Of the people who had a history of coronary artery disease, only 40% were receiving aspirin and only 34% were receiving a β-blocker. These numbers are comparable to the numbers found in studies enrolling community-dwelling seniors. Bungard and coworkers [13], for example, conducted a literature review of all studies examining the use of angiotensin-converting enzyme inhibitors in community-dwelling persons who had congestive heart failure and found that the two patient characteristics most associated with the lack of use of an angiotensin-converting enzyme inhibitor were female sex and older age. Andrade and colleagues [14] found that secondary prevention for osteoporotic fractures in a group of community-dwelling women was grossly underprescribed, with only 24% receiving any medication treatment in the year following the fracture. Of interest, increasing age was among the most robust predictors of not receiving such therapy.

Beers Criteria: applicability to an ambulatory population

Although recent critiques of provider prescribing styles have focused on the denial of potentially beneficial therapies, the earliest efforts at improving prescribing for a senior population focused on heightening provider awareness of the medications to avoid in an older population. The first of these publications appeared in 1991 and explicitly identified medications that were potentially inappropriate to use in frail older adults residing in nursing homes. This set of criteria, now known as the Beers Criteria, was agreed on by a consensus panel comprising experts from geriatric medicine, psychiatry, and pharmacology. Medications on this list were categorized as potentially inappropriate for use because of limited effectiveness or because

they posed a high risk for adverse effects. Among the drugs included were long half-life benzodiazepines and hypoglycemics, drugs with significant anticholinergic activity, and analgesic preparations containing propoxyphene [15]. This list was updated in 1997 and again in 2002 to (1) include new products and scientific information; (2) ascertain the generalizability of the list to all persons over age 65 years (regardless of functional level or place of residence); and (3) assign a relative rating of severity for potential adverse outcomes for each of the cited medications. The newest iteration of this list classifies medications into two broad headings, including 48 medications or medication classes that should generally be avoided in persons over age 65 years and 20 medications that should not be used in older persons known to have specific conditions (Table 4) [3].

In the years following the initial publication of the Beers Criteria, several studies were published that linked use of these medications to poor health outcomes [16]. Fick and colleagues [3], for example, found that ambulatory seniors who were prescribed a medication from the Beers Criteria list were more likely to be hospitalized or evaluated in an emergency room than those not taking such a medication. Chin and colleagues found poor control of pain and worse physical functioning in persons prescribed a medication from the list [16,17]. Despite these studies, Zhan and colleagues [18] found that the number of outpatient prescriptions for these medications remains unacceptably high. Using data from the 1996 Medical Expenditure Survey, these authors found that 21% of community-dwelling elderly persons were receiving a potentially inappropriate medication as defined by the Beers Criteria. Moreover, they noted that elderly women, persons who had poor health, and those with a lengthy medication list were the most likely recipients of these medications. It is unfortunate that the most recent data published by Goulding and coworkers in 2004 suggests that little has changed since 1996 [16]. Using data from the National Ambulatory Medical Care Survey and the National Hospital Medical Care Survey, these investigators examined the rate of inappropriate medication prescriptions to older persons from 1995 through 2000. They found that rates of prescription of inappropriate medications in the outpatient realm did not appreciably change over this period and noted that three drugs (propoxyphene, amitriptyline, and diazepam) represented the bulk of the inappropriate prescriptions. Like earlier studies, this study found that elderly women were more likely to receive these medications compared with their male counterparts [16].

Barriers to compliance

Further complicating the issue of drug prescribing in the elderly is compliance. Medication compliance in this population is influenced by a host of factors: the number of medications, common sensory impairments, cognitive impairments, functional impairments, and limitations in financial resources. This last factor may be a more important barrier than many

Table 4
2002 Criteria for potentially inappropriate medication use in older adults: independent of diagnoses or conditions

Drug	Concern	Severity rating (high or low)
Propoxyphene (Darvon) and combination products (Darvon with ASA, Darvon-N, and Darvocet-N)	Offers few analgesic advantages over acetaminophen, yet has the adverse effects of other narcotic drugs.	Low
Indomethacin (Indocin and Indocin SR)	Of all available nonsteroidal anti-inflammatory drugs, this drug produces the most CNS adverse effects.	High
Pentazocine (Talwin)	Narcotic analgesic that causes more CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs. Additionally, it is a mixed agonist and antagonist.	High
Trimethobenzamide (Tigan)	One of the least effective antiemetic drugs, yet it can cause extrapyramidal adverse effects.	High
Muscle relaxants and antispasmodics: methocarbamol (Robaxin), carisoprodol (Soma), chlorzoxazone (Paraflex), metaxalone (Skelaxin), cyclobenzaprine (Flexeril), and oxybutynin (Ditropan). Do not consider the extended-release Ditropan XL	Most muscle relaxants and antispasmodic drugs are poorly tolerated by elderly patients, since these cause anticholinergic adverse effects, sedation, and weakness. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.	High
Flurazepam (Dalmane)	This benzodiazepine hypnotic has an extremely long half-life in elderly patients (often days), producing prolonged sedation and increasing the incidence of falls and fracture. Medium-or short-acting benzodiazepines are preferable.	High
Amitriptyline (Elavil), chlordiazepoxide-amitriptyline (Limbitrol), and perphenazine-amitriptyline (Triavil)	Because of its strong anticholinergic and sedation properties, amitriptyline is rarely the antidepressant of choice for elderly patients.	High

Table 4 (*continued*)

Drug	Concern	Severity rating (high or low)
Doxepin (Sinequan)	Because of its strong anticholinergic and sedating properties, doxepin is rarely the antidepressant of choice for elderly patients.	High
Meprobamate (Miltown and Equanil)	This is a highly addictive and sedating anxiolytic. Those using meprobamate for prolonged periods may become addicted and may need to be withdrawn slowly.	High
Doses of short-acting benzodiazepines: doses greater than lorazepam (Ativan), 3 mg; oxazepam (Serax), 60 mg; alprazolam (Xanax), 2 mg; temazepam (Restoril), 15 mg; and triazolam (Halcion), 0.25 mg	Because of increased sensitivity to benzoadiazepines in elderly patients, smaller doses may be effective as well as safer. Total daily doses should rarely exceed the suggested maximums.	High
Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol) clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene)	These drugs have a long half-life in elderly patients (often several days), producing prolonged sedation and increasing the risk of falls and fractures. Short- and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.	High
Disopyramide (Norpace and Norpace CR)	Of all antiarrhythmic drugs, this is the most potent negative inotrape and therefore may induce heart failure in elderly patients. It is also strongly anticholinergic. Other antiarrhythmic drugs should be used.	High
Digoxin (Lanoxin) (should not exceed >0.125 mg/d except when treating atrial arrhythmias)	Decreased renal clearance may lead to increased risk of toxic effects.	Low
Short-acting dipyridamole (Persantine). Do not consider the long-acting dipyridamole (which has better properties than the short-acting in older adults) except with patients with artificial heart valves	May cause orthostatic hypotension.	Low

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Table 4 (*continued*)

Drug	Concern	Severity rating (high or low)
Methyldopa (Aldomet) and methyldopa-hydrochlorothiazide (Aldoril)	May cause bradycardia and exacerbate depression in elderly patients.	High
Reserpine at doses >0.25 mg	May induce depression, impotence, sedation, and orthostatic hypotension.	Low
Chlorpropamide (Diabinese)	It has a prolonged half-life in elderly patients and could cause prolonged hypoglycemia. Additionally, it is the only oral hypoglycemic agent that causes SIADH.	High
Gastrointestinal antispasmodic drugs: dicyclomine (Bentyl), hyoscyamine (Levsin and Levsinex), propantheline (Pro-Banthine), belladonna alkaloids (Donnatal and others), and clidinium-chlordiazepoxide (Librax)	GI antispasmodic drugs are highly anticholinergic and have uncertain effectiveness. These drugs should be avoided (especially for long-term use).	High
Anticholinergics and antihistamines: chlorpheniramine (Chlor-Trimeton), diphenhydramine (Benadryl), hydroxyzine (Vistaril and Atarax), cyproheptadine (Periactin), promethazine (Phenergan), tripelennamine, dexchlorpheniramine (Polaramine)	All nonprescription and many prescription antihistamines may have potent anticholinergic properties. Nonanticholinergic antihistamines are preferred in elderly patients when treating allergic reactions.	High
Diphenhydramine (Benadryl)	May cause confusion and sedation. Should not be used as a hypnotic, and when used to treat emergency allergic reactions, it should be used in the smallest possible dose.	High
Ergot mesyloids (Hydergine) and cyclandelate (Cyclospasmol)	Have not been shown to be effective in the doses studied.	Low
Ferrous sulfate >325 mg/d	Doses >325 mg/d do not dramatically increase the amount absorbed but greatly increase the incidence of constipation.	Low
All barbiturates (except phenobarbital) except when used to control seizures	Are highly addictive and cause more adverse effects than most sedative or hypnotic drugs in elderly patients.	High

Table 4 (*continued*)

Drug	Concern	Severity rating (high or low)
Meperidine (Demerol)	Not an effective oral analgesic in doses commonly used. May cause confusion and has many disadvantages to other narcotic drugs.	High
Ticlopidine (Ticlid)	Has been shown to be no better than aspirin in preventing clotting and may be considerably more toxic. Safer, more effective alternatives exist.	High
Ketorolac (Toradol)	Immediate and long-term use should be avoided in older persons, since a significant number have asymptomatic GI pathologic conditions.	High
Amphetamines and anorexic agents	These drugs have potential for causing dependence, hypertension, angina, and myocardial infarction.	High
Long-term use of full-dosage, longer half-life, non–COX-selective NSAIDs: naproxen (Naprosyn, Avaprox, and Aleve), oxaprozin (Daypro), and piroxicam (Feldene)	Have the potential to produce GI bleeding, renal failure, high blood pressure, and heart failure.	High
Daily fluoxetine (Prozac)	Long half-life of drug and risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation. Safer alternatives exist.	High
Long-term use of stimulant laxatives: bisacodyl (Dulcolax), cascara sagrada, and Neoloid except in the presence of opiate analgesic use	May exacerbate bowel dysfunction.	High
Amiodarone (Cordarone)	Associated with QT interval problems and risk of provoking torsades de pointes. Lack of efficacy in older adults.	High
Orphenadrine (Norflex)	Causes more sedation and anticholinergic adverse effects than safer alternatives.	High
Guanethidine (Ismelin)	May cause orthostatic hypotension. Safer alternatives exist.	High
Guanadrel (Hylorel)	May cause orthostatic hypotension.	High

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Table 4 (*continued*)

Drug	Concern	Severity rating (high or low)
Cyclandelate (Cyclospasmol)	Lack of efficacy.	Low
Isoxsurpine (Vasodilan)	Lack of efficacy.	Low
Nitrofurantoin (Macrodantin)	Potential for renal impairment. Safer alternatives available.	High
Doxazosin (Cardura)	Potential for hypotension, dry mouth, and urinary problems.	Low
Methyltestosterone (Android, Virilon, and Testrad)	Potential for prostatic hypertrophy and cardiac problems.	High
Thioridazine (Mellaril)	Greater potential for CNS and extrapyramidal adverse effects.	High
Mesoridazine (Serentil)	CNS and extrapyramidal adverse effects.	High
Short acting nifedipine (Procardia and Adalat)	Potential for hypotension and constipation.	High
Clonidine (Catapres)	Potential for orthostatic hypotension and CNS adverse effects.	Low
Mineral oil	Potential for aspiration and adverse effects. Safer alternatives available.	High
Cimetidine (Tagamet)	CNS adverse effects including confusion.	Low
Ethacrynic acid (Edecrin)	Potential for hypertension and fluid imbalances. Safer alternatives available.	Low
Desiccated thyroid	Concerns about cardiac effects. Safer alternatives available.	High
Amphetamines (excluding methylphenidate hydrochloride and anorexics)	CNS stimulant adverse effects.	High
Estrogens only (oral)	Evidence of the carcinogenic (breast and endometrial cancer) potential of these agents and lack of cardioprotective effect in older women.	Low

Abbreviations: CNS, central nervous system; COX, cyclooxygenase; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

From Fick DM, Cooper JW, Wade WE, et al. Updating the Beers Criteria for potentially inappropriate medication use in older adults. Results of a US Consensus Panel of Experts. Arch Intern Med 2003;163:2719–20; with permission.

prescribers appreciate. Presently, seniors pay 42% of the nation's bill for prescription drugs, and the congressional budget office estimates that the average Medicare beneficiary will spend $3155 in the year 2006 on prescription drugs [11]. This number is staggering when one considers that the median

household income for seniors is $23,000 [19]. The Medicare Prescription Drug Improvement and Modernization Act of 2003 was enacted in part to address the financial hurdle for older adults, yet opponents of the proposal warn that it may do little to change the significant financial barriers encountered by those over 65 years old. The act, which will take full effect in January 2006, represents the most sweeping change in Medicare legislation since its inception in 1965 [20]. It employs what many have termed a "doughnut design," providing 75% coverage for drug costs up to $2250 and paying 95% of costs over $5100. The "hole in the doughnut" refers to the lack of coverage for drug costs between these two dollar amounts for which beneficiaries will be responsible for 100% of the discounted cost. Thus, for an average beneficiary, there will be monthly premiums amounting to about $35, an annual deductible of $250, 25% of the next $2000 in drug costs, 100% of the next $2850, and 5% of costs over $5100. Low-income seniors are eligible for discounted premiums and will not be required to pay for drug costs falling in the "doughnut hole," but qualifying for this low-income status will require seniors to fall below 135% of the poverty level and possess less than $10,000 in assets. This coverage may represent a less substantial benefit than was previously available under state Medicaid programs for some low-income seniors, who will be required to forfeit this former benefit if they enroll in the Medicare program [20,21].

Leaving the debate about the relative value of the Medicare prescription plan aside, there is still much that prescribers can do to ease the financial burden incurred by this segment of the population. Remaining sensitive to financial constraints and choosing generic options are critical practices for clinicians who treat geriatric patients. A recent survey of primary care physicians in Massachusetts, however, suggests that there is significant room for improvement on both of these fronts. Glickman and colleagues [22] surveyed 132 primary care physicians to examine their awareness of the affordability of medications, the use of generic alternatives, and their level of understanding of drug costs. They found that although 85% of respondents reported that inability to afford medications was a problem for some of their patients, 20% did not believe generic brands were as safe or effective as their more expensive brand-name alternatives and 30% reported that they rarely or never accessed information on the cost of medications. An overwhelming majority of these physicians also underestimated the costs of most drugs. This apparent lack of knowledge about costs may not only adversely affect compliance on an individual-patient basis but also speaks to growing concerns about aggregate costs for drugs and health care at large.

Use of complementary medicine and over-the-counter medications in the elderly

As if overseeing prescription medications for an elderly population is not daunting enough, the clinician must also be mindful of older adults' use of

herbal preparations and over-the-counter medications. The last decade has seen an enormous increase in the use of complementary medicine including herbal supplements. Although early studies suggested that the use of such therapy was more common in younger persons, Astin [23] found that persons over age 65 years were just as likely to use complementary medicine as their younger counterparts. In a follow-up study of complementary medicine use exclusively in an older population enrolled in a managed Medicare program, these investigators found that 24% of seniors used an herbal medicine. *Ginkgo biloba* extract, garlic, and ginseng were among the most common herbs used. Also of great importance was the study's finding that a majority (58%) of those using herbal supplements did not report this use to their primary care physicians, raising the risk for drug–herb interactions such as the interactions of ginkgo and garlic with drugs that increase an individual's risk for bleeding (Table 5) [24,25].

Over-the-counter medications also complicate prescribing for older adults. Recent reviews suggest that the average number of over-the-counter medications taken by seniors on a daily basis is about 1.8, with the highest usage in white Midwestern women [26]. The most commonly used over-the-counter medications in the over-65-year-old population include analgesics, with about 20% to 30% of older persons using such medications on any given day [27]. More than 60% of older people cannot identify the active ingredient in the over-the-counter pain remedy that they are taking, and 40% believe that these medications are too weak to cause any real harm [27]. This notion often leads to an omission on the part of the senior in relaying their usage of over-the-counter medications. Thus, it is imperative that the physician query their older patient on their use of nonprescription drugs.

Table 5
Selected drug–herb interactions

Drug	Interaction
Warfarin	Garlic, ginkgo, ginger, and feverfew may augment the anticoagulant effect; ginseng may decrease the effectiveness of warfarin
Nonsteroidal anti-inflammatory drugs	Gossypol and uva-ursi may add to gastrointestinal irritation
Levothyroxine	Horseradish and kelp may suppress thyroid function
Iron	Chamomile, feverfew, and Saint-John's-wort may inhibit iron absorption
Diuretics	Dandelion and uva-ursi may offset the antihypertensive effects of diuretics; gossypol may exacerbate hypokalemia
Digoxin	Hawthorne may potentiate effects; Siberian ginseng may interfere with assay

Data from Miller LG. Herbal medicinals: selected clinical considerations. Focusing on known or potential drug–herb interactions. Arch Intern Med 1998;158(20):2200–11.

Practical strategies

Although there are numerous important considerations involved in prescribing for the elderly, there are some practical strategies that can help providers successfully address this difficult yet common task. Foremost is the forging of a partnership with patients to better understand their health care goals in the context of prognosis and advance care directives. The topic of shared decision making is addressed in more detail in an article by Brody elsewhere in this issue. For patients who have a poor prognosis, for example, efforts at primary prevention with costly medications may be much less important than simply focusing efforts on symptom relief. This aspect of prescribing is also covered in the article by Ogle and Hopper elsewhere in this issue. In persons with multiple comorbidities who would require a significant, perhaps untenable number of medications based on published guidelines, this partnership will enable appropriate prioritization of medications. The partnership would also enable physicians to introduce patients to the concept of a time-limited trial of a medication. Such a trial enables providers to discuss with their patients the anticipated benefits of a particular drug therapy, the possible harm associated with the drug, and a proposed timeline for reviewing whether the benefits have been achieved and whether the benefits are worth the potential risks. If no ostensible benefit has been noted or if the potential side effects are not deemed tolerable for the described benefit, then the medication can be discontinued or changed to an alternate therapy.

Although counting medications is clearly not the best strategy for dealing with the challenges inherent to prescribing for the elderly, reviewing the medication list at every visit is crucial. This practice enables the physician to alter the list based on changes in health status, the addition of other medications, and the outcomes of any time-limited trials. Reviewing the medication list also provides an opportunity to review drugs prescribed by other providers (and any over-the-counter or herbal preparations) and to entertain the notion of medication discontinuation in light of changes in health status. Common scenarios in which medication weaning may be appropriate are listed in Box 2. Finally, reviewing medication lists serves as a reminder to order laboratory testing to monitor drug therapy; to reconsider less expensive, generic alternatives; and to review potential drug–drug and drug–disease interactions.

Periodically, the older patient should also be asked to bring in all medication bottles rather than a simple list. Reviewing medications in this fashion may reveal previously unrecognized problems with medication compliance because the number of pills remaining in each container or in the pill box can be assessed. By having the older patient review how and why he or she takes each medication, the physician can also determine whether compliance is being restricted by functional limitations (eg, arthritic changes of the hands making it difficult to open the container), sensory impairments

Box 2. Common clinical scenarios in which medication weaning could be considered

1. Situations in which an exclusive comfort care approach has been adopted but the individual is still receiving medication aimed at primary and secondary prevention
2. ''Forgotten'' steroids in patients stabilized from a previous exacerbation of chronic obstructive pulmonary disease, rheumatoid arthritis, or a remote history of polymyalgia rheumatica
3. Proton pump inhibitors initiated as prophylaxis during an acute care admission in persons without another indication for continuation of these medicines
4. Oral hypoglycemics after a person has been initiated on insulin
5. Newly diagnosed adverse events including delirium, falls, or orthostatic hypotension
6. Longstanding psychoactive medication with unclear target symptoms

From Brazeau S. Polypharmacy and the elderly. Can J Cont Med Educ 2001;2: 85–95.

(eg, inability to see the label on pill container or hear physician or pharmacist instructions), or cognitive impairments (making it difficult to comply with the regimen without supervision or assistance).

When initiating a medication, the clinician should start with the lowest feasible dose to achieve the desired effect. The clinician should seek data to support the drug's efficacy in older adults, bearing in mind that advanced age in and of itself should never be seen as a contraindication to potentially beneficial therapy. Clinicians should be aware of the prescribing cascade mentioned earlier and be certain that the medication being considered is not in response to an adverse drug reaction, a drug–drug interaction, or a drug–disease interaction.

Ultimately, the prescriber may embrace the ''SEA-squared'' model (Box 3). The safety of the medication should be considered by reviewing untoward outcomes revealed in drug trials and postmarketing clinical experience. The soundness of the proposed treatment should be considered in the context of the patient's prognosis and expressed goals for care. The efficacy or discernible benefit of the medication should be considered in the context of a structured scientific study, and more important, the putative effectiveness or the benefit of the medication should be assessed in the context of the patient's total environment. The appropriateness of the

Box 3. The SEA-squared model for evaluating prudent prescribing

Safety: is the medication safe based on clinical trials and clinical experience?
Soundness: is the medication in keeping with the patient's goals for care?
Effective: has the medication been shown to have a positive outcome in clinical trials?
Efficacious: will the medication prove beneficial in the ''real world''?
Appropriate: is the medication approved for this indication? Would its use be consistent with the current standard of care?
Affordability: can the patient afford the medication?

medication should carefully be reviewed, taking into account regulatory approval by the Food and Drug Administration, scientific research, and the current standard of care. Finally, the affordability of the medication should be considered.

On a larger scale, the health care system should evolve in a manner that makes the challenge of prescribing for this age group less daunting. Demanding further research on particular therapies in this population, evaluating drug regimens over longer periods, and designing drug trials that include quality of life and functional outcomes will collectively attenuate the current challenge. Integrating possible drug–drug interactions in a unified, easily accessible database; working consistently in multidisciplinary teams in which a pharmacist can give real-time advice to prescribers; and computerized entry, which can immediately warn of problematic prescribing, will also significantly ease the prescriber's burden. Ultimately, prescribing medications for an older population may require a paradigm shift in how clinicians approach medical care. Optimal prescribing may require us to abandon the disease model, given its inherent tendency to cause the clinician to perceive patients as collections of maladies, each of which obligates a list of medications. In older persons, this model often leads to the prescription of an untenable number of medications that, in aggregate, have a dubious impact on the total well-being of the person or, worse yet, completely ignore the primary concerns of the patient, harm the patient, or force the patient to abandon beneficial therapies. In place of the disease model, we should adopt what Tinetti and Fried [28] have termed the *integrated individually tailored model of care*, whereby patients' priorities for their health care are paramount and medications are prescribed after careful consideration in accordance with these directives.

Summary

When prescribing for the older adult, the office-based physician walks the fine line between introducing the drugs that are considered best practices for each disease that the person has and acknowledging that as the number of drugs increases, the risks of adverse drug reactions, drug–drug interactions, or drug–disease interactions increase considerably. Establishing the clinician–patient partnership to develop goals of care is the first step in the process. Avoiding drugs that are likely to be associated with adverse outcomes (the Beers Criteria list) is an important next step, as is awareness of the prescribing cascade. It is also important, however, to not be overly pessimistic. Quality of care and quality of life may be greatly enhanced by careful use of prescription and over-the-counter medications in the older adult.

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