Abstract and Introduction

Abstract

The population of older adult patients in the United States is growing each year. Appropriate pharmacotherapy has allowed many older patients to live longer and maintain healthy lives. Unfortunately, the inappropriate utilization of medications can be harmful to older adult patients. Inappropriate pharmacotherapy may lead to overusing medications and polypharmacy. Polypharmacy can contribute to a higher incidence of adverse effects, increase the risk of dangerous drug interactions, cause noncompliance with appropriate medication use, and significantly increase the cost of health care. The polypharmacy issue with geriatric patients has been described as an epidemic and this issue must be addressed. This review provides objective rules that may help prevent polypharmacy. Consideration of these rules when prescribing, dispensing, and caring for older adult patients will improve the overall pharmacotherapy regimens instituted by healthcare providers.

Introduction

Various publications have clearly documented the growing problem of medication use in the geriatric population. In the last 100 years, the life span for humans has improved dramatically. This can be attributed to various discoveries and events, not the least of which has been the proliferation of various medications and treatment modalities that can be used to treat a wide variety of both acute and chronic conditions. As patients live longer, they are likely to be diagnosed as having a multitude of different medical conditions that will need to be treated by many different physicians, each of whom may prescribe a variety of medications, thus leading to the possibility of polypharmacy. Improvements in pharmacology are sometimes a double-edged sword. They have greatly improved health care in many individuals, but too much pharmacology may be dangerous for certain patient populations. One such population is older adults.

Some authors have defined polypharmacy as the utilization of a specific number of medications (eg, >10) in a single patient. It may be more appropriate to simply define polypharmacy as taking multiple unnecessary medications. This is important because many patients with a number of treatable conditions may be prescribed a multitude of different medications. This therapy regimen may be appropriate. Polypharmacy, then, is drug therapy that is unnecessary or that may do more harm than good.

The polypharmacy problem can be caused by many factors, including multiple physicians, multiple pharmacies, drug interactions, excessive over-the-counter drug use, and the use of unproven or dangerous herbal therapies or supplements. Quantifying the “polypharmacy problem” is challenging because clearly delineating which medications are appropriate and which are not for individual patients can be difficult. Epidemiologic data illustrate the average number of medications that patients older than 65 years consume each day. Unfortunately, even with the data to document the problem, polypharmacy is difficult to correct. The number of older adult patients admitted to hospitals or nursing facilities who are receiving medications for no documented reason is increasing, as is the number of adverse drug reactions and deaths caused by inappropriate medication use. Because polypharmacy can cause confusion for patients and their caregivers, it may increase the risk of noncompliance with appropriate medical therapy. Finally, polypharmacy can increase the cost of health care to patients and society as a whole.

The solution to polypharmacy is not an easy one. It is too early to know whether the Patient Protection and Affordable Care Act (PL 111–148) will have any effect on polypharmacy in older adults. There is much media attention focused on pharmaceutical treatments for numerous ailments, and many patients are quick to demand a prescription when they see a physician or other prescriber, or they self-diagnose and make inappropriate treatment decisions and use over-the-counter drugs or herbal therapies, causing polypharmacy. Prescribers must be cognizant of a potential polypharmacy problem in an older adult patient before any drug is prescribed, dispensed, or administered.

With all of this in mind, rules/guidelines should be established and adhered to by all healthcare providers so that the polypharmacy epidemic can be stopped and older adult patients can lead better lives. This article provides practitioners with specific rules/guidelines that they can use when prescribing medications for their older adult patients. These rules/guidelines could be printed and posted where prescribers could easily and readily be reminded of these important objective concerns. Following these
rules would greatly enhance the pharmacotherapy plan for all older patients, prevent potential adverse drug effects, reduce healthcare costs, and allow patients to lead happier and healthier, productive lives.

**Rule 1: Know the Patient and Use the Patient's Most Current Medical Record**

The designation "older adult patient" must be defined. Many organizations, including the US Food and Drug Administration, and authors define older adult as a person aged 65 years or older. Furthermore, some entities have designated patients in the age range of 65 to 74 years as being "early" older adult and those older than 75 years as being "late" older adult. This age distinction is objective, but it does not describe the overall health of specific individuals; there probably are many "late" older adults who are much healthier than those who are described as early older adult. These distinctions are important when researching this population and can be used to describe specific groups that may affect treatment regimens and recommendations.\[6,7\]

Being defined in this way informs the practitioner that the patient has undergone physiologic changes that are common to aging. These changes can have a major influence on the pharmacology of many medications. These specific changes are discussed later in the article, but the ability to identify patients who warrant special pharmacologic care enables the practitioner to make informed care decisions using the best evidence available.

Unless it is an emergency, practitioners should not make healthcare decisions based on limited information about the patient. Healthcare providers must have access to patients' pertinent medical information before they can make informed and effective medical decisions regarding the patient. The practitioner or the patient's caregivers or family must have autonomy to make an informed healthcare decision in conjunction with medical professionals. This will help ensure that the healthcare decisions established by the practitioner are the same as those desired by the patient or the person making decisions for the patient. These decisions must be made a part of the patient's healthcare record.\[13,14\]

The so-called digital age has made it much easier to review patients' healthcare information, but having current, accurate information and taking the time to find and access it are key. This is extremely important for older adults because their physiological differences mean that even minor decisions on or minute changes in medications can result in significant issues. Digitized data, however, cannot replace familiarity with patients. Many practitioners are responsible for patients with whom they do not have much history or understanding. A current and complete physical examination should be available to the practitioner before medical decision making for that patient is necessary. If not, a thorough examination is necessary, with an accurate collection of medical information pertinent to that patient's care. This may be both time consuming and difficult because older adult patients may have cognitive impairments that can make data collection arduous.\[14–16\]

An accurate medical record also means an accurate, current, and complete medication list. Unfortunately, some patients do not know their pharmacotherapy regimen and they do not maintain a medication list. Patients also may have several healthcare providers involved in their care, which can make it difficult to maintain a current medication list. An incomplete, inappropriate, outdated, or possibly mismanaged medication profile can lead to polypharmacy. In general, older adult patients who are cared for in a healthcare facility (eg, long-term care facility, skilled nursing facility) have a more consistent list of current medications; however, if a skilled practitioner is not reviewing the list on a regular basis, the medication profile could become inappropriate and possibly dangerous. The following provides guidelines about how to obtain current pharmacotherapy information from an older adult patient:\[15,16\]

- Use proper communication skills when interviewing an older adult patient or the patient's caregiver.
  - Allow extra time for older patients (do not be in a hurry)
  - Avoid distractions (eg, quiet room)
  - Sit face to face
  - Maintain proper eye contact
  - Listen
  - Assess patient's hearing and speak slowly, clearly, and loudly
  - Use language and terms that the patient or caregiver can understand
  - Stick to one topic at a time and do not change topics until each issue is addressed
- Write down instructions and make sure the patient understands
- Obtain interpreter if necessary
- Do not be judgmental

- Provide patient examples/pictures of different drugs
- Have the patient bring all prescription bottles to each office visit ("brown bag approach")
- Contact each of the patient's pharmacies to assess medication use
- Interview family members if necessary
- Assess compliance

An up-to-date medication list must include all medications that the patient takes on a regular basis, both scheduled or as needed. A complete list should include not only prescription medications but also over-the-counter medications, vitamins and/or supplements, and any herbal or natural products (Fig.). The practitioner should never assume that a patient understands what a complete medication list entails, so inquiries must be made of the patient or the patient's caregiver regarding every type of product the patient may use. Patients may not understand what "over-the-counter" or "herbal therapy" means, so providing the patient or caregiver with specific examples (eg, ibuprofen/Advil, cough syrup/Robitussin) can be helpful. Patients may not remember or may not be as forthcoming regarding some agents (eg, herbal or natural products), so the practitioner must be specific with his or her questions.[2,3,15–19]
An effective medical record means being cognizant of the other healthcare providers involved in a patient's care. These providers also may include pharmacists/pharmacies, nursing personnel, dentists, optometrists, and insurance companies. Multiple caregivers can mean several different and sometimes conflicting recommendations for a patient's health care.

To combat the issue of multiple practitioners, it is helpful when one practitioner is in charge of a patient's healthcare needs. Other physicians and healthcare providers then can work with this primary healthcare provider to ensure that the best decisions are made on behalf of the patient. The primary provider can ensure that the patient is receiving only the essential medications or services that have been screened and approved by both the patient and the primary provider. Such a system is effective in reducing polypharmacy. A drawback to this system is that some providers are reluctant to take on the role of primary provider. Many physicians feel uncomfortable altering or questioning the advice, recommendations, decisions, or prescriptions of other practitioners. Some patients create problems by seeking out other healthcare professionals to advise, prescribe, or contradict the decisions of others. Proper communication skills and willingness to cooperate among the members of the healthcare team help patients' healthcare needs to be addressed and improved.

### Rule 2: Follow the Tenets of Evidence-based Medicine, but Understand the Limitations of the Evidence

Sackett and colleagues defined evidence-based medicine "as the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients."[20] The best evidence comes from high-quality randomized controlled trials, which assess specific treatment modalities in particular patient populations. Practitioners then attempt to apply the information to the care of their patients.
The basic concepts of evidence-based practice are as follows:[21–23]

1. Formulate answerable clinical questions
2. Find the evidence (effective search strategy)
3. Appraise the evidence
4. Apply the evidence
5. Evaluate performance

For the most part, applying these principles to pharmacotherapy selection is not difficult and can ensure that appropriate and timely therapy is being used to treat particular conditions in particular patient populations.[22,23]

The older adult population presents unique challenges in the utilization of evidence-based medicine. Because many elderly patients have several comorbid conditions and often take more than one medication for them, finding older adult subjects to fit a specific inclusion criteria for most studies can be difficult. The information gleaned from most studies generally does not fit perfectly with the condition(s) being manifested.[23,24]

When reviewing new treatment guidelines and deciding whether these guidelines apply to his or her geriatric patients, the practitioner must ask some important questions:

1. How does the population that was studied fit with the population being cared for?
   - Is the study population similar enough to the practitioner's patient population that the results of the study can be used by the practitioner to treat his or her patients?
2. What is the quality of the evidence?
   - Does the information come from a well-done randomized controlled trial?
   - If evidence-based guidelines are being used, are those guidelines supported by a national organization (eg, the American Geriatrics Society)?
3. Will the statistical changes (eg, improvements, safety) supported by the study translate into meaningful clinical differences in the practitioner's patient population? (This question may be difficult to answer until the practitioner has applied the new guidelines to several patients.)
4. If the guidelines deal with specific pharmacotherapy, do the doses recommended by the guidelines need to be tailored to fit the pharmacokinetic profile(s) of the practitioner's patients?
   - Do doses need to be altered based on renal or hepatic changes?
5. Can benefits and risks from a particular therapy be easily monitored in the practitioner's patients?
6. Will insurance or Medicare pay for the new treatments established by the guidelines?
7. Can the patient comply easily with the new treatment dictated by the guidelines?

Rule 3: Understand the Potential Pharmacokinetic and Pharmacodynamic Changes That can Occur in Older Adult Patients and use This Specific Patient Information to Make Prudent Prescribing Decisions

All healthcare providers who prescribe, dispense, administer, or recommend drugs must comprehend how the physiological process of aging affects the pharmacotherapy that many older adult patients receive (ie, the process of pharmacokinetics). Practitioners also must realize that these drugs may have different effects or actions on geriatric patients compared with the general population (ie, the process of pharmacodynamics).[2,3,25,26] The pharmacokinetic parameters that can be influenced by aging include the following:
• Absorption. The aging process can reduce gastrointestinal motility and certain gastric secretions, and these can affect absorption of drugs via the gastrointestinal tract. The degree of these changes varies from individual to individual. Drugs affected by first-pass metabolism also may have altered pharmacokinetics in older adults. Because liver blood flow may be reduced as the body ages, first-pass metabolism is reduced, which means higher drug levels for certain medications following absorption.

• Distribution. The distribution of drugs throughout the body following absorption also may be altered by aging. Many factors can affect distribution, including protein binding and fat solubility. Individuals older than 65 years tend to make less protein (e.g., albumin), which can bind certain drugs in the bloodstream. Then, as protein binding is reduced, more "free drug" is available to exact an effect. Older adults also tend to have reduced muscle mass and greater fat content, so highly lipophilic drugs have greater distribution.

• Metabolism. As is to be expected, hepatic metabolism is generally reduced for most drugs in older adults. Hepatic blood flow is decreased, as is hepatic enzyme induction. The net result of these actions is generally greater blood levels for hepatically metabolized drugs.

• Elimination. Drugs eliminated via the kidney are also affected by aging. Renal blood flow and glomerular filtration rate (GFR) are reduced and can lead to higher blood concentrations for renally cleared drugs.

Pharmacodynamics also can be altered by aging. Receptor sensitivity can change for certain drugs, which can alter the effectiveness of certain medications. The net effect of all of these changes can be minimal or they can be highly significant because these alterations vary considerably from individual to individual as well as from drug to drug.\[27–31\]

Using this information effectively means that the practitioner must have a good understanding of a drug's pharmacology profile before he or she can prescribe it safely. This understanding is even more important regarding older adults because they are at much greater risk than younger individuals for developing adverse effects to drugs. This helps to ensure appropriate medication use and limit the hazards of pharmacotherapy. The following pharmacologic information is essential:

• Knowing the drug's mechanism of action

• Knowing precisely what the drug has been approved by the Food and Drug Administration to treat or whether there is sufficient evidence to support its use

• Understanding the pertinent pharmacokinetic parameters associated with the drug being prescribed

• Knowing the drug's major adverse effects

• Knowing the major contraindications associated with use of the drug

• Understanding how the drug is dosed in patients with normal hepatic/renal function and in patients with hepatic or renal dysfunction

Understanding pertinent laboratory values also is necessary before a drug can be prescribed safely. Reviewing this patient-specific data and understanding the pharmacotherapy being considered takes significant knowledge, experience, and clinical skill. Assessing a patient's renal function is more comprehensive than simply obtaining a patient's serum creatinine (SCr) or blood urea nitrogen. An SCr measurement in an older adult patient is not an effective way to assess renal function because these patients generally have lower muscle mass than younger patients; therefore, lower SCr can be falsely interpreted as normal renal function. Using various formulas may provide the practitioner with a reasonable estimation of a patient's GFR.\[30–33\]

The most common formulas used today are listed in . Numerous Web sites and applications make the calculation of a patient's GFR simple, and studies have documented which formula provides the best data. The Chronic Kidney Disease Epidemiology Collaboration equation has stood up to rigorous review and is believed to provide the best estimate of GFR; however, this calculation provides only an estimate of a patient's renal function at a specific time. Older adult patients' GFR can vary widely and can be further pronounced with certain medications and/or disease states.\[2,3,32,33\]

Table 1. Equations for estimating GFR

<table>
<thead>
<tr>
<th>Source</th>
<th>Equation</th>
<th>Variables</th>
<th>Comments</th>
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</thead>
</table>

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<table>
<thead>
<tr>
<th>Method</th>
<th>Formula</th>
<th>Parameters</th>
<th>Dosage adjustment recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cockcroft-Gault</td>
<td>CCR = [(140 − age) × weight]/(72 × SCr)</td>
<td>Age, weight,</td>
<td>Dosage adjustment recommendations are generally based on pharmacokinetic studies using this equation; several variations of the original equation overestimates GFR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>sex, serum creatinine level</td>
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<tr>
<td></td>
<td>• ×0.85 (if patient is female)</td>
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<tr>
<td></td>
<td>• CCR: creatinine clearance, mL/min</td>
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<tr>
<td></td>
<td>• Age: y</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Weight: kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• SCr: serum creatinine, mg/dL</td>
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<tr>
<td>Modification of Diet in Renal Disease</td>
<td>Estimated GFR (mL/min/1.73 m$^2$ = 186 × (PCr$^{1.154}$ × (age)$^{0.203}$)</td>
<td>Age, sex, race, serum creatinine level</td>
<td>Underestimates GFR when GFR &gt;60 mL/min/1.73 m$^2$</td>
</tr>
<tr>
<td></td>
<td>• ×0.742 (if patient is female)</td>
<td></td>
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<tr>
<td></td>
<td>• ×1.21 (if patient is African American)</td>
<td></td>
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<tr>
<td></td>
<td>• Age: y</td>
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</tr>
<tr>
<td></td>
<td>• SCr: serum creatinine, mg/dL</td>
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<tr>
<td>CKD-EPI</td>
<td>Expressed as a single equation: GFR = 141 × min (SCr/k, 1)$^A$ × max (SCr/k, 1)$^{-1.209}$ × 0.993$^\text{Age}$</td>
<td>Age, sex, race, serum creatinine level</td>
<td>More accurate than MDRD for estimating GFR in patients with normal kidney function, stage 1 and 2 CKD</td>
</tr>
<tr>
<td></td>
<td>• ×1.018 [if female] × 1.159 [if African American]</td>
<td></td>
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<tr>
<td></td>
<td>• SCr: serum creatinine, mg/dL</td>
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<td></td>
<td>• K: 0.7 for females and 0.9 for males</td>
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</tr>
<tr>
<td></td>
<td>• A: −0.329 for females and −0.411 for males</td>
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</tr>
<tr>
<td></td>
<td>• Min: minimum of SCr/k or 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Max: maximum of SCr/k or 1</td>
<td></td>
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<tr>
<td>Online calculators</td>
<td><a href="http://www.pharmacologyweekly.com/app/medical-calculators/glomerular-filtration-rate-gfr-calculator">Online calculators</a></td>
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<td><a href="http://www.davita.com/gfr-calculator">Online calculators</a></td>
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<td><a href="http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm">Online calculators</a></td>
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</tbody>
</table>

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease Study.

These formulas should be used to guide the practitioner in assessing a patient's renal function and for dosing medications that are excreted renally. The Food and Drug Administration mandates that pharmaceutical companies provide pharmacokinetic data on new drugs, which guide the practitioner in dosing the drug in various patient populations.[37–40]

Estimating a patient's hepatic function is much more difficult. There is no effective formula that uses endogenous markers to provide a clear estimate of hepatic function. For the most part, alterations in the standard hepatic panel used by most practitioners to assess hepatic function (aspartate aminotransferase, alanine aminotransferase, bilirubin) indicate only that the liver may be inflamed or damaged in some way. Elevated liver enzymes (aspartate aminotransferase or alanine aminotransferase) may indicate...
drug-induced liver toxicity, but they are not helpful in predicting hepatic drug clearance, which can be used in estimating drug doses in the setting of hepatic dysfunction. To assess the metabolic function of the liver, a patient's albumin or clotting factors can be measured. Each of these laboratory parameters is only a guide and usually is unreliable as a way to dose medications.

The aging process slows hepatic function, but the degree to which this takes place can vary greatly from patient to patient. In general, the physiology of aging results in reduced blood flow in the liver such that drugs that have a high extraction ratio on first pass through the liver (eg, amitriptyline, verapamil, lidocaine) will be at higher blood levels because of increased bioavailability. Also, phase 1 reactions in the liver, which typically involve cytochrome P450 monooxygenase enzymes, are in general affected much more by the aging process than phase 2 reactions. The cytochrome P450 monooxygenase system is where many drug–drug interactions take place. Both inducer and inhibitor drugs can cause numerous drug interactions. Because the older adult patient population is prescribed a greater number of medications compared with other patient populations, hepatic drug interactions are much more common in and must be monitored closely.

Dosing recommendations for heptically metabolized drugs in older adult patients are somewhat unclear. It is prudent to start with much lower doses than those recommended (eg, reduce the initial dose by 50%) and slowly titrate the dose up or down based on efficacy and tolerability. Patients should be monitored closely for adverse effects and should be monitored when possible for therapeutic and/or toxic blood levels.

Rule 4: Recognize and Investigate Patient Factors That may Contribute to Medication Problems

Older adult patients may exhibit certain characteristics that put them at a higher risk for polypharmacy or drug-related problems. These problems can be prevented by the ability to recognize and address these characteristics, such as the following:

- More than one healthcare provider
- Use of more than one pharmacy
- Several different comorbidities
- Number of medications that an individual is taking (whether prescribed medications, over-the-counter medications, vitamins, supplements, herbal therapies) is directly related to the risk of medication problems and polypharmacy
- Memory/cognitive issues in patient and/or caregiver
- Vision difficulties
- Hearing difficulties
- Reading difficulties
- Communication issues (eg, language barriers)
- Dexterity issues (eg, difficulty opening medicine bottles, pressing certain inhalers)
- Swallowing issues
- Scheduling issues—logistical problems with taking various medications
- Monetary issues and difficulty paying for medications
- Certain drugs causing adverse effects
- Poor understanding of why certain drugs are prescribed

Knowing a patient's comorbidities is extremely important for safe and effective patient care, particularly in reducing the risk of potential drug interactions and drug–disease interactions. The practitioner should discern how each of these conditions is being treated and whether any newly prescribed therapies could interact or interfere with the patient's pharmacotherapy regimen. lists drug–disease interactions that are common in older adults.

Table 2. Potential drug–disease interactions in older adults
### Rule 5: Avoid the Prescribing Cascade, if Possible

Many medications are prescribed to treat the observed or anticipated adverse effects caused by other medications that a patient is taking. This is the prescribing cascade ( ), and it can quickly lead to polypharmacy[2,3,5–7] The prescribing cascade is an extremely common problem in older adults, which can arise because the patient's medication list has not been properly reviewed, the prescriber is not familiar with the drugs being prescribed for the patient, or the patient has more than one healthcare provider.

### Table 3. Examples of the prescribing cascade

<table>
<thead>
<tr>
<th>Initial drug/drug class</th>
<th>Added drug because of effects from initial drug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid analgesics (eg, morphine, codeine)</td>
<td>Laxatives</td>
<td>Necessary because of opiate-induced constipation</td>
</tr>
<tr>
<td>β-Adrenergic blockers (eg, propranolol, metoprolol, carvedilol)</td>
<td>Sildenafil</td>
<td>Beta-blockers can cause erectile dysfunction</td>
</tr>
<tr>
<td>Other gastrointestinal drugs (metoclopramide)</td>
<td>Benztropine</td>
<td>Metoclopramide is a dopamine receptor antagonist and can induce movement disorder (Parkinson-like symptoms)</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors (eg, lisinopril, enalapril, captopril)</td>
<td>Guaifenesin (Robitussin)</td>
<td>Guaifenesin is prescribed to treat a dry, nonproductive cough caused by the angiotensin-converting enzyme inhibitor lisinopril</td>
</tr>
<tr>
<td>Calcium channel blockers (eg, amlodipine, verapamil)</td>
<td>Furosemide</td>
<td>The diuretic furosemide is prescribed to treat lower-extremity edema caused by amlodipine</td>
</tr>
</tbody>
</table>

### Conclusions

Polypharmacy has become such an important healthcare issue that enacting rules or guidelines that healthcare providers can use when making pharmacotherapy decisions for geriatric patients has become a necessity. Rules 1 through 5 provide reasonable recommendations that can improve patient care, limit drug-induced problems in older patients, and can save healthcare dollars. These rules cannot prevent all adverse medication effects in the geriatric population, but they can help to ensure that all patients are treated consistently and thoughtfully. This goes a long way toward improving pharmacotherapy to older individuals.

### Sidebar

**Key Points**

- Polypharmacy in the geriatric population is an important issue.
- Older adult patients undergo physiologic changes that can alter a drug's pharmacokinetics and pharmacodynamics.
- Practitioners must take great care when prescribing medications to older adult patients to ensure that every drug prescribed is appropriately assessed and monitored.

### References


43. Dose adjustment of drugs with high hepatic extraction are required in patients with severe liver disease. Drugs Ther Perspect 2006;22:23–26.