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IS YOUR PATIENT TAKING TOO MANY PILLS?

Before you prescribe another drug, consider whether new symptoms might be caused by the medications the patient is already taking.

PRACTICE RECOMMENDATIONS

- ▶ Consider the possibility that an adverse drug effect—rather than a new condition—is at play when a patient taking multiple medications develops a new symptom. **(C)**
- ▶ Use an online interaction checker, which can be accessed via a smart phone or tablet, to check for potential drug-drug interactions in patients on multiple medications. **(C)**
- ▶ Cross-check patients' medications with a list of their medical problems, with the goal of discontinuing any drug that duplicates the action of another or is age-inappropriate, ineffective, or not indicated for the condition for which it was prescribed. **(C)**

Strength of recommendation (SOR)

- (A)** Good-quality patient-oriented evidence
- (B)** Inconsistent or limited-quality patient-oriented evidence
- (C)** Consensus, usual practice, opinion, disease-oriented evidence, case series

Older adults are taking more medications than ever before. Nearly 9 out of 10 US residents who are 60 years of age or older take at least one prescription drug, more than a third take 5 to 9 medications, and 12% take 10 or more.¹

The increase is largely driven by newer medications to effectively treat a variety of medical conditions, and by practice guidelines that often recommend multidrug regimens.² As a result, the term “polypharmacy,” which once referred to a specific number of medications, is now used more broadly to mean “a large number” of drugs.

From a safety standpoint, the number of medications a patient takes matters. The risk of adverse drug effects and dangerous drug-drug interactions increases significantly when an individual takes ≥ 5 medications.³

More than 4.5 million adverse drug effects occur each year in the United States, and nearly three quarters of them are initially evaluated in outpatient settings.⁴ Research suggests that about 80% of the time, these adverse effects are not recognized as such by the patient's physician. So instead of discontinuing the offending medication, physicians treat the drug-related symptoms by adding yet another medication—a phenomenon known as “the prescribing cascade.”⁵

This review can help you safeguard older patients taking multiple medications by recognizing and responding to drug-related problems, identifying drugs that can be safely eliminated (or, in some cases, drugs that should be added), and checking regularly to ensure that the medication regimen is appropriate and up to date.

CASE ▶ Mrs. R, a 79-year-old woman who recently moved to town, is brought to your office by her daughter and son-in-law.

The patient has a hard time reporting her medical history, but her daughter tells you her mother has chronic obstructive pulmonary disease (COPD), heart failure, type 2 diabetes, and mild urinary incontinence, and was recently diagnosed with early dementia.

Mrs. R's daughter has brought in a bagful of medications, but she's not sure which ones her mother takes regularly. The medications are an albuterol inhaler, alprazolam, digoxin, diphenhydramine, donepezil, furosemide, glargine insulin, guaifenesin, levothyroxine, metformin, extended-release metoprolol, naproxen, omeprazole, simvastatin, tolterodine, and zolpidem—a total of 16 different drugs.

If Mrs. R were your patient, how would you manage her multidrug regimen?

Start with a medication review

The first step in evaluating a patient's medication regimen is to find out whether the drugs in the patient's possession and/or in the medical record are the ones he or she is actually taking. Ask older patients who haven't brought in their medications, or the caregiver of a confused patient, to bring them to the next visit.

The next step: Determine whether the medication regimen is right for the patient.

Polypharmacy may be indicated

Despite the risks associated with polypharmacy, do not assume that it is inappropriate. For some conditions, multiple medications are routinely recommended. Patients with heart failure, for example, have been shown to have better outcomes when they take 3 to 5 medications, including beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and diuretics.²

Some treatment guidelines also call for multiple medications. Achieving the more stringent blood pressure goals recommended in the Seventh Report of the Joint National Committee on Prevention, for instance, often requires 2 or more antihypertensive agents.⁶ In many cases, however, patients end up taking more drugs than necessary.

Is the patient taking the right drugs?

Medication reconciliation (determining whether the treatment regimen is appropriate

for the patient's diagnoses) is the way to find out.

The most widely recommended approach to medication reconciliation is to create a table and do a systematic review.⁷ List all the patient's medical conditions in the first column and all current medications in the second column. Use the third column to note whether each medication is one the patient should be on, based not only on his or her medical conditions and other drugs being taken but also on current renal and hepatic function and body size, and contraindications.

■ **A medication may be inappropriate** if it duplicates, cancels out the action of, or otherwise interacts with another drug the patient is taking; is contraindicated in older patients; or is ineffective for the condition for which it was prescribed. In one key study of nearly 200 patients 65 years and older who took 5 or more medications, more than half had been prescribed at least one drug that was ineffective for the patient's condition or that duplicated the action of another medication.⁸

In addition to finding drugs that the patient should not be taking, medication reconciliation may also reveal that the patient is not receiving optimal therapy and that one or more drugs should be *added* to his or her treatment regimen.

■ **Check meds after transitions.** A move from home to hospital, from emergency department to home, or any other transition relating to patient care should prompt a medication reconciliation. Medications are often added or inadvertently discontinued at such times,^{9,10} and instructions relating to medication are often misunderstood.¹¹ In one study of 384 frail elderly patients being discharged from a hospital, for example, 44% were found to have been given at least one unnecessary prescription—most commonly for a medication that was neither indicated nor effective for any of the patient's medical problems.¹² It was also common for patients to be given drugs that duplicated the action of others they were already taking.

Even in the absence of such transitions, medication reconciliation should occur at regular intervals. Many physicians do a medication reconciliation at every visit to ensure



For more on polypharmacy, see this month's editorial on page 645.

TABLE 1

START criteria: Drug therapy that should be given to older patients¹³⁻¹⁷

<p>Cardiovascular</p> <ul style="list-style-type: none"> • Anticoagulation or antiplatelet therapy for atrial fibrillation • Antiplatelet therapy for patients with known coronary, cerebral, or peripheral vascular disease • Antihypertensive therapy for systolic BP >160 mm Hg • Statins for secondary prevention in patients with coronary, cerebral, or peripheral vascular disease (with life expectancy >5 years) • ACE inhibitor for heart failure or after MI • Beta-blocker for chronic stable angina
<p>Endocrine</p> <ul style="list-style-type: none"> • Metformin for type 2 diabetes • ACE inhibitor for patients with diabetes and nephropathy • Antiplatelet and statin therapy for patients with diabetes and CVD risk factors
<p>Gastrointestinal</p> <ul style="list-style-type: none"> • PPI for severe GI reflux or esophageal stricture • Fiber supplement for chronic symptomatic diverticular disease
<p>Musculoskeletal</p> <ul style="list-style-type: none"> • Antirheumatic drugs for moderate-to-severe chronic rheumatoid disease • Bisphosphonates for patients taking chronic oral steroids • Calcium and vitamin D for osteoporosis
<p>Nervous system</p> <ul style="list-style-type: none"> • Levodopa for Parkinson's disease with functional impairment • Antidepressant for moderate-to-severe depression lasting >3 months
<p>Respiratory</p> <ul style="list-style-type: none"> • Daily inhaled beta-agonist or anticholinergic agent for asthma or COPD • Daily inhaled steroid for asthma or COPD with FEV1 <50% of predicted value • Continuous home oxygen for chronic hypoxemic respiratory failure

ACE, angiotensin-converting enzyme; BP, blood pressure; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; FEV1, forced expiratory volume in 1 second; GI, gastrointestinal; MI, myocardial infarction; PPI, proton-pump inhibitor; START, Screening Tool to Alert doctors to Right Treatment.

that the medical record is accurate and the patient's medication regimen is optimal.

Managing polypharmacy: These resources can help

Numerous tools are available to help you evaluate and monitor patients' medication regimens, including some that were developed specifically for older patients.

■ **START** (Screening Tool to Alert doctors to Right Treatment) identifies drugs and drug classes that are underused with older patients.¹³ START criteria (**TABLE 1**)¹³⁻¹⁷ focus on medica-

tions that should be used yet are often omitted in older patients who have the appropriate indications.

In using START or any other drug-related tool, it is important to keep in mind that therapy should be individualized. Not all the medications in the START criteria are appropriate for every patient, and a medication that is indicated for a given medical condition may or may not provide real benefit for a particular patient. That would depend on the individual's overall health and life expectancy, the goals of treatment, and how long it would take for the patient to realize any ben-

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TABLE 2

Calculating your patient's "real" age¹⁹

Actual age (y)	Physiologic age (y)							
	Self-reported health							
	Excellent		Good		Fair		Poor	
	Male	Female	Male	Female	Male	Female	Male	Female
65	58	60	64	64	68	66	73	72
70	62	65	69	69	73	71	78	77
75	67	70	74	74	78	76	83	82
80	72	75	79	79	83	81	85+	85+

>
A medication reconciliation is needed when transitions of care occur—for example, from home to hospital or emergency department to home.

efit from the drug in question.¹⁸ A vigorous 79-year-old might benefit from statin therapy for prevention of cardiovascular events, for instance, while a patient like Mrs. R, who is also 79 but has dementia and multiple other medical problems, would be unlikely to live long enough to realize such a benefit.

■ **"Age" assessment tool.** One criterion in deciding whether medication(s) are appropriate for an older patient is his or her "physiologic age"—calculated on the basis of the individual's chronological age and self-reported health status (TABLE 2).¹⁹

Flagging drugs that may be inappropriate
Several tools have been developed to aid clinicians in identifying medications that are potentially inappropriate for older adults, although here, too, decisions about their use must be individualized. Two of the most widely used tools are the Beers criteria and STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions).

■ **Beers criteria** were developed by Mark Beers et al in 1991²⁰ and have been updated at regular intervals, most recently by the American Geriatrics Society in 2012.²¹ The drugs and drug classes included in the Beers criteria should not be prescribed for older patients in most cases, either because the risk of using them outweighs the benefit or because safer alternatives are available. Key components are listed in TABLE 3.²¹

One limitation of the Beers criteria has been its all-or-nothing approach, with many

of the medications on the list deemed inappropriate for all older adults regardless of their circumstances. The 2012 update does a better job of individualizing recommendations: Medications are now categorized as those that should be avoided in older patients regardless of their diseases or conditions, those that should be avoided only in patients with certain diseases or conditions, and those that may be used for this patient population but require caution.²¹

■ **STOPP** is similar to the Beers criteria, but uses a different approach: Most medications on this list are considered in the context of specific medical problems.²² While the Beers criteria classify digoxin >0.125 mg/d as generally inappropriate for older adults, for example, STOPP criteria state that long-term dosing at that level is inappropriate only for those with impaired renal function.²² A list of medications identified by STOPP as contributing to hospitalization due to adverse drug effects is available at <http://ageing.oxfordjournals.org/content/37/6/673>.

■ **Both tools address this drug category.** Cumulative anticholinergic burden is a concept applied to the use of anticholinergic medications, which are included in both the Beers and STOPP criteria. Although isolated short-term exposure to a drug with anticholinergic properties may be tolerated by a healthy and cognitively intact older patient, repetitive exposure to such drugs, even if separated in time, has negative effects.

TABLE 3

Beers criteria:* Drug classes that may be inappropriate for older adults²¹

Drug class	Concern
Alpha-blockers with peripheral activity	Orthostatic hypotension
Anticholinergics	Cognitive impairment, urinary retention
Antipsychotics	Increased death rate when used for behavior control in patients with dementia
NSAIDs	Renal dysfunction, GI bleeding, fluid retention, exacerbation of heart failure
Sedative hypnotics	Cognitive impairment, delirium
Tricyclic antidepressants	Cognitive impairment, delirium, urinary retention

GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs.

*The full Beers criteria contains 53 drugs and drug classes that are generally inappropriate for older adults. The full list is available from the American Geriatrics Society at: www.americangeriatrics.org/files/documents/beers/2012BeersCriteria_JAGS.pdf.

One study evaluated more than 500 community-dwelling older adults and found that the more exposure an individual had to anticholinergic medications over the course of a year, the greater the impairment in short-term memory and activities of daily living.²³ Another study, this one involving more than 13,000 community-dwelling and institutionalized patients, showed that the longer an older patient takes an anticholinergic medication, the more likely there is to be a measurable decline in performance on the Mini-Mental State Examination.²⁴

Programs that flag potential interactions

Drug-drug interactions are a key concern of polypharmacy, and electronic medical records and prescribing systems that flag potential drug-drug interactions when a new medication is ordered are designed to help physicians avoid them. Unfortunately, clinicians only react to 3% to 9% of such notifications, overriding them because computerized systems often fail to distinguish between important and unimportant interactions.²⁵⁻²⁷ Thus, clinicians often must decide whether to react to or override warnings, an often difficult decision with patient safety and medicolegal implications. The best advice we can offer is to carefully evaluate drug interaction warnings using common sense, and seek consultation with a clinical pharmacist when

uncertainty exists. This approach should prevent prescribing medications that have potentially harmful interactions with drugs the patient is already taking.

For physicians who do not have access to an electronic prescribing system that provides such notification, several online resources are available, some by subscription (eg, Lexicomp, www.lexi.com; Micromedex, www.micromedex.com/index.html; and PEPID, www.pepid.com) and others with free access (eg, AARP, healthtools.aarp.org/drug-interactions; Drugs.com (www.drugs.com/drug_interactions.php); and HealthLine, www.healthline.com/druginteractions).

CASE ► After doing a medication reconciliation for Mrs. R, you find that she is taking tolterodine, an anticholinergic medication for urge urinary incontinence, and donepezil, a procholinergic medication for dementia. This type of drug-drug interaction, in which the action of one drug effectively cancels out the effect of another, should not be ignored.

Overall, you identify 8 of her medications that could be discontinued: The list includes guaifenesin (a nonessential medication of questionable efficacy); naproxen (inappropriate per Beers criteria; inappropriate in patients with heart failure, according to STOPP); alprazolam, zolpidem, and diphenhydramine (duplicate medications that are all on the



A patient's physiologic age—estimated from his or her chronological age and self-reported health status—is an important consideration in assessing the benefits and risks of many drugs.

TABLE 4

Recommendations for discontinuing hard-to-stop drugs

Medication or drug class	Discontinuation regimen	Comments
Benzodiazepines ³⁰	Taper dose by 25% q 2 wk	No withdrawal symptoms reported with this taper regimen. Subtle cognitive improvement noted over a period of months
Guaifenesin ³¹	Can be discontinued without tapering if not combined with opioids or other medications. Elimination half-life is approximately 1 hour	Guaifenesin is often marketed as a combination product with opioids; such combination products require tapering
PPIs ³²⁻³⁴	Decrease dose by 50% q 2 wk; supplement with H2 blocker if needed, but tapering of H2 blocker may be required	Abrupt discontinuation after long-term use causes rebound gastric acid hypersecretion and lowers rate of success. Higher success rates with taper regimen and in patients who do not have documented GERD
NSAIDs ³⁵	No taper required	Short-term use (<3 mo) acceptable for patients with no contraindications
SSRIs ^{36,37}	Gradual reduction in dose over 6-8 wk	Highest rate of success in patients without a clear diagnosis of depression

GERD, gastroesophageal reflux disease; NSAIDs, nonsteroidal anti-inflammatory drugs; PPIs, proton-pump inhibitors; SSRIs, selective serotonin reuptake inhibitors.

Beers criteria as inappropriate for chronic use and ill-advised in patients with cognitive impairment); and omeprazole and levothyroxine (for which nothing in the patient's history suggests a need), as well as tolterodine. Depending on dose, digoxin is yet another candidate for discontinuation.

Discontinuing medications: Proceed carefully

Physicians are often reluctant to discontinue chronic medications in older patients—even in those with advanced disease who are not likely to benefit from treatment. Focus groups have identified a number of reasons for their hesitation, including:

- the assumption that patients have no problem taking large numbers of drugs
- the fear that patients may misinterpret a plan to discontinue medications as evidence that the physician is giving up on them
- the belief that physicians must comply with practice guidelines that recommend multiple drug treatments
- concern that proposing discontinuation of medications often leads to a discussion of life expectancy and end-of-life care.²⁸

Physicians may also fear that discontinuation of certain drugs will increase the risk of adverse outcomes. More than 30 studies have evaluated discontinuation of chronic medications in older adults, however, and found that drugs as diverse as antihypertensives, antipsychotics, benzodiazepines, and selective serotonin reuptake inhibitors (SSRIs) can often be discontinued without adverse outcomes. In many cases, improvement in patient function results.²⁹ Medications that present the most difficulty are those that patients often become physically or psychologically dependent on, such as benzodiazepines, guaifenesin, proton-pump inhibitors, nonsteroidal anti-inflammatory drugs, and SSRIs. Some (eg, benzodiazepines, SSRIs) require a gradual reduction; for others, no taper is required (TABLE 4).³⁰⁻³⁷

CASE ► You trim down Mrs. R's regimen by discontinuing each of the 8 drugs, one at a time, and carefully monitor the patient during the withdrawal period. Because she had been taking alprazolam daily, the dose is tapered slowly to avoid withdrawal. Omeprazole also requires a gradual taper to avoid rebound hyperacidity.³

After confirming that Mrs. R has heart

failure and COPD, you identify 2 medications that should be *added* to her drug regimen—an ACE inhibitor for heart failure and an inhaled anticholinergic for COPD.

Going from 16 medications to 10 saves money, decreases the likelihood of adverse events and drug-drug interactions, and helps

with adherence. Mrs. R's new drug regimen is expected to lead to improvements in memory and overall quality of life, as well.

JFP

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➤ **Short-term exposure to a drug with anticholinergic properties may be tolerated by a healthy and cognitively intact older patient, but repetitive exposure may have negative effects.**



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