Quality Indicators for Appropriate Medication Use in Vulnerable Elders

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Medications are a centrally important aspect of the care of elderly patients, especially vulnerable elders, and are the final common pathway for most therapeutic decisions. While they make up only 14% of the U.S. population, persons 65 years of age and older consume more than 30% of all prescription drugs (1). Because they more often experience acute and chronic illnesses, elders are particularly likely to benefit from the therapeutic and preventive effects of pharmaceutical therapy. However, aspects of the aging process that occur in healthy elders and that are considerably magnified in vulnerable elderly patients increase their risk for drug side effects (2). These include impaired renal function in clearing drugs that are primarily excreted by the kidney; reduction in hepatic blood flow, liver size, and phase I degradative metabolic processes; increased body fat at the expense of lean body mass, which increases the volume of distribution for lipid-soluble drugs and extends their half-life; and aging-induced changes in receptor sensitivity, which can further complicate the prediction and assessment of drug effects.

Another important aspect of medication use in vulnerable elders is that the patient, caregivers, or even physician often mistake side effects for the onset of new illness, or worse, for aging itself. Such side effects include confusion, forgetfulness, gait instability, parkinsonian signs, incontinence, and fatigue. Because complex, frail elderly patients with multiple comorbid conditions are generally underrepresented in clinical trials of drugs, the effect of particular doses on such patients is more difficult to predict from the available clinical literature. This factor, in turn, contributes to therapeutic nihilism: Potentially life-saving medications, such as those that reduce serum cholesterol levels, may be underused because too few older adults were enrolled in key efficacy studies to allow conclusions on their use in this population—a kind of pharmacologic paradox. However, with few exceptions, as more studies begin to enroll adequate numbers of older patients, the benefits seen in younger patients are found to occur in this age group as well.

As a result, the central issue in considering drug misuse in the elderly is no longer just concern about drug-induced side effects. An additional area must now be assessed as well: underutilization of necessary medications to treat conditions such as depression, isolated systolic hypertension, or hyperlipidemia. Such underuse has joined overuse and misuse as indicators for assessing the prescribing of medications to older patients. Comprehensive programs to measure the quality of medication use in vulnerable elders should evaluate each of these domains to provide the most thorough measure of the appropriateness of drug use in such patients.

Methods

The methods for developing these quality indicators, including literature review and expert panel consideration, are detailed in a preceding paper (3). For medication use, the structured literature review identified 5171 titles, from which abstracts and articles relevant to this report were identified. On the basis of the literature and the authors' expertise, 16 potential quality indicators were proposed. The search terms and results of the literature review can be accessed at www.acponline.org/sci-policy/.

Results

Of the 16 potential quality indicators, 12 were judged to be valid by the expert panel process (see the quality indicators on pp 653-667), 1 was merged with an accepted indicator, and 3 were not accepted (www.acponline.org/sci-policy/). We summarize the literature reviews that support each indicator judged to be valid by the expert panel process.

Quality Indicator 1

Drug Indication

IF a vulnerable elder is prescribed a new drug, THEN the prescribed drug should have a clearly defined indication documented in the record BECAUSE the medication may have been prescribed for an indication that was unclear or transient.

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Supporting Evidence. Documenting the indication for a new prescription is such a basic axiom of good medical practice that no clinical trials have assessed it. Over time, older patients are particularly vulnerable to the addition of multiple medications to their regimen at a rate that is generally greater than the rate of medication reassessment and withdrawal. Through a lapse in communication or absence of reevaluation, medications begun for a transient problem may be inadvertently continued indefinitely. In the case of medications prescribed to treat behavioral symptoms, the absence of a specified, clear indication for the drug makes it difficult to assess whether the medication is indeed meeting the need for which it was prescribed (as described in indicator 4). Clear specification of an indication for each drug can facilitate evaluation of the effectiveness of the regimen, help the patient to better understand the regimen (as described in indicator 2), and assist in the continuity of care when physicians other than the patient's usual caregiver are responsible for care (for example, during an acute hospitalization).

For each medication in the active regimen, it is important to ascertain that its indication is still present; if the original indication is no longer present or if none can be found, a cautious trial of tapering may be appropriate.

Quality Indicator 2

Patient Education

IF a vulnerable elder is prescribed a new drug, THEN the patient (or, if incapable, a caregiver) should receive education about the purpose of the drug, how to take it, and the expected side effects or important adverse reactions BECAUSE such education may improve adherence and clinical outcomes and may alert patients or caregivers to potential adverse effects.

Supporting Evidence. The medication regimens of vulnerable elderly patients are generally more complex than those of healthier elderly or younger patients. Nevertheless, in routine practice clinicians rarely have additional time to explain the regimen to the patient or caregiver. This is particularly significant if the patient has cognitive impairment. Because the side effects of a drug may have no obvious connection to the indication for which it is being prescribed (for example, anorexia or nausea from digoxin or parkinsonian symptoms from haloperidol), such education may be the only way that a patient or caregiver can identify the origins of an adverse drug effect in its early stages. For preventive therapies that provide no symptomatic benefit, adequate explanation of the need for the therapy is often necessary to persuade the patient to continue taking the regimen as directed.

All patients who receive medication therapy should be educated about the purpose of any new medication, how to take the medication, and any expected side effects and possible important adverse effects. One of the goals of patient education is to improve adherence to therapy and, ultimately, improve clinical outcomes. A 1998 meta-analysis reviewed 153 studies published between 1994 and 1997 that evaluated methods to improve adherence (4). The authors found that one-on-one educational interventions significantly improved adherence measures and clinical outcomes. A randomized, controlled trial involving patients with hypertension showed that an educational intervention improved adherence to therapy and blood pressure control (5). A hospital-based educational intervention in older patients increased medication knowledge and improved adherence (6), and a multidisciplinary inpatient educational program for patients with congestive heart failure improved adherence to therapy after 30 days (7) as well as clinical outcomes. In a study of patients with chronic heart failure (8), an educational intervention improved adherence as well as clinical and functional outcomes.

Quality Indicator 3

Medication List

For ALL vulnerable elders, the outpatient medical record of every physician and the hospital medical record should contain an up-to-date medication list BECAUSE such a list can make it possible to identify and eliminate inappropriate duplication of therapies, correct potentially dangerous drug–drug or drug–disease interactions, and "streamline" the drug regimen to improve adherence.

Supporting Evidence. A significant portion of physician visits for older patients taking multiple medications consists of reviewing current medications. An up-to-date medication list that is readily available enables a physician to review the necessity of ongoing drug therapy and to evaluate any potential drug interactions. This medi-

cation list should also include over-the-counter medications because these medications can have significant interactions with prescription drugs. In addition, an allergy list also helps prevent prescribing errors that can cause allergic reaction. Computerization of medication lists can make feasible and efficient screening for inappropriate drug use, allergies, and interactions.

A recent cohort study (9) implemented a computer-based evaluation of prescription data to target drug–age interactions, excessive maximal daily dosages, and drug–disease interactions. Inappropriate prescribing triggered telephone calls to physicians by pharmacists with specific geriatric training. This intervention demonstrated a reduction in inappropriate drug use, inappropriate dosing, and potential drug–disease interactions. Although this study was not a randomized, controlled trial, it illustrates the potential for automated screening of medication lists to improve prescribing and supports the recommendation for comprehensive medication lists.

Quality Indicator 4

Response to Therapy

EVERY new drug that is prescribed to a vulnerable elder on an ongoing basis for a chronic medical condition should have a documentation of the response to therapy within 6 months BECAUSE such an approach can help to clarify whether a drug is meeting the therapeutic goal for which it was prescribed. This documentation can provide a rational basis for continuation of the regimen if it is effective, modification if it is ineffective, or discontinuation if the underlying indication is no longer present.

Supporting Evidence. One of the major roles of the clinician is to assess the safety and efficacy of a prescribed therapy to determine whether it may have caused unacceptable adverse effects and should be discontinued; may have been well tolerated but had no demonstrable benefit; or may have been somewhat effective but may require a change in dose to achieve greater benefit.

Identification of a target goal for the use of medications has application in a wide variety of prescribing situations, including the management of hypertension or diabetes mellitus and the use of psychoactive medications.

For example, multiple studies have demonstrated that treatment of hypertension in older patients reduces important adverse outcomes (10–12). However, only 27% of patients with hypertension are estimated to have good control with systolic blood pressure (<140 mm Hg) or diastolic blood pressure (<90 mm Hg) (13). Hypertension therapy provides an important illustration of how such follow-up documentation can provide a useful marker of quality of care to ensure that therapeutic goals are met.

Of course, the appropriate time for assessment of response to a new drug (or change in dose) may be as short as a day or two or as long as several months. The interval of 6 months was identified as a quality audit tool because it represents the upper limit of the time interval within which the effect of virtually any new therapy should be assessed.

Quality Indicator 5

Periodic Drug Regimen Review

ALL vulnerable elders should have a drug regimen review at least annually BECAUSE such a review provides an opportunity for the discontinuation of unnecessary medications as well as the addition of necessary drugs not currently prescribed.

Supporting Evidence. Multiple providers, acute hospitalizations, intercurrent illnesses, and over-the-counter preparations can all contribute to complicating the drug regimen of a vulnerable elder. When reviews are conducted, physicians often are surprised to discover that patients are taking medications of which the physicians are completely unaware or continuing to refill prescriptions (such as those for H_2-blockers or nonsteroidal anti-inflammatory drugs) that were originally intended for short-term use only. The periodic drug regimen review also provides an opportunity to act on emerging data concerning the efficacy of preventive regimens in specific at-risk patients. This category includes drugs often underprescribed in the elderly: antidepressants for patients with depression, angiotensin-converting enzyme inhibitors for patients with systolic dysfunction and congestive heart failure or for patients with diabetic nephropathy, antihypertensive agents for patients with isolated systolic hypertension or poorly controlled diastolic pressure, lipid-lowering drugs for patients who have hypercholesterolemia or who have had a myocardial infarction, and osteoporosis prophylaxis.

Inappropriate prescribing in community-dwelling

elders is common. By using criteria developed by Beers and colleagues (14), investigators found that at least 23.5% of community-dwelling patients at least 65 years of age received potentially inappropriate medications (15). Similar findings have been obtained in nursing homes (16). However, despite the prevalence in nursing homes of polypharmacy and multiple potential drug interactions in older patients with many comorbid illnesses, few rigorous studies have examined the efficacy of drug regimen reviews in this setting. One randomized, controlled trial (17) of a clinical pharmacy review of drug regimens for older patients who were using five or more medications on a long-term basis reported that inappropriate prescribing decreased by 24% in the intervention group compared with 6% in the controls ($P < 0.001$) after 3 months; this difference was sustained after 1 year.

Several projects sponsored by the Health Care Financing Administration have evaluated computer-based review of drug use (18). The most effective strategies have been targeted retrospective drug-use review (RDUR) programs. However, most of the evidence from these studies indicates that, in general, routine use of automated computer screening of prescription-drug regimens does not result in demonstrable changes in health status, morbidity, or mortality.

Quality Indicator 6

Monitoring Warfarin Therapy

IF a vulnerable elder is prescribed warfarin, THEN an international normalized ratio (INR) should be determined within 4 days after initiation of therapy and at least every 6 weeks BECAUSE vulnerable elderly patients are at particularly high risk for drug toxicity, which can be identified earlier if appropriate assays are performed for agents with a narrow therapeutic index.

Supporting Evidence. Reduced drug clearance by the liver and kidneys is common in older patients, even those who are otherwise healthy, and is even more likely in vulnerable elderly with a multisystem disease. As a result, doses that are safe and effective in younger patients or in healthy older persons may be toxic in vulnerable elderly patients. This toxicity can develop suddenly if homeostasis is threatened by even a mild intercurrent illness, such as influenza or viral gastroenteritis. Drugs for which periodic monitoring should be considered in vulnerable elderly patients include warfarin, digoxin, anticonvulsants, and theophylline. Of these medications, warfarin was the drug chosen by the expert panel for this quality indicator.

For an elderly patient receiving warfarin therapy, many factors may cause a previously stable dose to become either excessive or inadequate. These factors may include the introduction of a medication that can increase or decrease the anticoagulant effect of warfarin (Table 3 in the article on quality indicators for stroke and atrial fibrillation, available at www.acponline.org/sci-policy/), reduction in the liver's capacity to synthesize coagulation factors, and dietary changes. When such changes occur, hemorrhagic effects are more likely to be fatal in elderly persons, particularly vulnerable elders. Consistent evidence from randomized trials suggests that patients receiving warfarin therapy should be maintained in the INR range of 2.0 to 3.0 for most indications; (19) a range of 2.5 to 3.5 is recommended for high-risk patients with mechanical prosthetic valves. Availability of an anticoagulation clinic has been shown to improve anticoagulation control and reduce bleeding and thromboembolic event rates (20). In patients with atrial fibrillation, the risk for ischemic stroke markedly increases at an INR less than 2.0 (21), the risk for intracranial hemorrhage increases linearly with an increase in INR, and the risk for a subdural hematoma increases markedly for INRs greater than 4.0 (22). Older patients are at greatest risk for these complications and need to be monitored carefully. One author recommends monitoring the INR every 6 weeks in patients with stable levels (23). No clinical trials have established the ideal monitoring interval.

Quality Indicator 7

Monitoring of Diuretic Therapy

IF a vulnerable elder is prescribed a thiazide or loop diuretic, THEN he or she should have electrolytes checked within 1 week after initiation and at least yearly BECAUSE of the risk for hypokalemia due to diuretic therapy.

Supporting Evidence. No published studies have assessed the effect of regular monitoring of electrolytes on patient outcomes, but it is clear that certain diuretics cause hypokalemia, which can lead to poor patient outcomes. A randomized, controlled trial found that thia-

zide therapy is associated with hypokalemia and possibly with ventricular arrhythmias (24). Serum potassium levels in study participants prescribed hydrochlorothiazide were 0.4 mmol/L lower than those in the placebo group ($P < 0.01$). The risk for developing severe hypokalemia (potassium level < 3.0 mmol/L) was also increased in patients receiving hydrochlorothiazide ($P < 0.01$). Among participants with a potassium level less than 3.0 mmol/L, the risk for ventricular arrhythmias increased twofold ($P = 0.02$). A case–control study of hypertensive patients (25), in which case-patients developed cardiac arrest, supports this recommendation. Higher doses of thiazide were associated with an increased risk for cardiac arrest, and the addition of a potassium-sparing medication reduced the risk.

It is unclear how frequently potassium levels should be checked in patients receiving thiazide diuretics to reduce such risk. However, monitoring potassium levels in patients after initiation of diuretics and regular monitoring thereafter probably will improve the probability of detecting and treating hypokalemia.

Quality Indicator 8

Avoid the Use of Chlorpropamide as a Hypoglycemic Agent

IF a vulnerable elder is prescribed an oral hypoglycemic drug, THEN chlorpropamide should not be used BECAUSE it has a prolonged half-life, particularly in elderly patients, which can result in serious hypoglycemia; this drug is also more likely to cause the syndrome of inappropriate secretion of antidiuretic hormone.

Supporting Evidence. Chlorpropamide is associated with increased risk for hypoglycemia compared with other oral hypoglycemic agents (26). Glipizide was associated with a significantly reduced risk for hypoglycemia compared with chlorpropamide (27). This risk appears to increase with age (28, 29).

Quality Indicator 9

Avoid Drugs with Strong Anticholinergic Properties Whenever Possible

ALL vulnerable elders should not be prescribed a medication with strong anticholinergic effects if alternatives are available BECAUSE of the potential for adverse effects such as confusion, urinary retention, constipation, visual disturbance, and hypotension.

Supporting Evidence. Older patients may be particularly vulnerable to the central nervous system effects of anticholinergic medication. A double-blind trial (30) of the effect of an anticholinergic medication on cognitive function in older patients without cognitive impairment found significant impairment in learning a list of words, recounting a short story, and performing a paired-associate learning task. Similarly, a study of hydroxyzine (31) found prolonged reaction times compared with the effects of terfenadine. More recently, a double-blind, placebo-controlled crossover trial (32) found impairment in recall in patients receiving diphenhydramine. Second-generation H_1 antagonists are less likely to have these effects when used in recommended doses (33).

Effective alternatives to highly anticholinergic medications are often available. Recent trials indicate that tolterodine (Detrol, Pharmacia & Upjohn, Inc., Kalamazoo, Michigan) is significantly better tolerated than oxybutnin (Ditropan, Hoechst Marion Roussel, Inc., Kansas City, Missouri) for the treatment of urge urinary incontinence and is equally effective; tolterodine also poses a lower risk for anticholinergic side effects (34, 35). Comparable examples exist in other therapeutic categories of older anticholinergic drugs (36). Amitriptyline (Elavil, Astra-Zeneca, Wilmington, Delaware) should generally be avoided in favor of less anticholinergic drugs (such as desipramine or serotonin reuptake inhibitors) for the management of depression. Likewise, diphenhydramine and other anticholinergic antihistamines (chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine, promethazine, tripelennamine, and dexchlorpheniramine) should be avoided as well. Clinical exceptions include use in patients with anaphylaxis, transfusion reactions, motion sickness, or severe pruritus.

Quality Indicator 10

Avoid Barbiturates

IF a vulnerable elder does not need control of seizures, THEN barbiturates should not be used BECAUSE these medications are potent central nervous system depressants, have a low therapeutic index, are highly addictive, cause multiple drug interactions, and increase the risk for falls and hip fracture in older women.

Supporting Evidence. The routine use of barbiturates has no indication in current practice, except to control seizures. Barbiturates have a low therapeutic index, are

highly addictive, and cause multiple drug interactions. Data from two large studies show an increased risk for hip fracture in patients taking barbiturates (37, 38). Given these potentially adverse effects, the drugs are not recommended for older patients unless they are being used specifically to control seizures. Even then, acceptable alternatives may be preferable. However, in patients with long-term use, withdrawal of these drugs must be attempted slowly and cautiously.

Quality Indicator 11

Avoid Meperidine (Demerol) as an Opioid Analgesic

IF a vulnerable elder requires analgesia, THEN meperidine should not be used BECAUSE it may be associated with an increased risk for delirium. A metabolite of meperidine, normeperidine, may also cause seizures.

Supporting Evidence. Case reports have long suggested that meperidine may cause delirium (39), perhaps secondary to its anticholinergic effects. This empirical observation was confirmed in a nested case–control study: Compared with other analgesics, meperidine increased the rate of delirium in patients who received the drug for postoperative pain (odds ratio, 2.7 [95% CI, 1.3 to 5.5]) (40). Data from a randomized, double-blind trial indicate that while meperidine was no more effective than nonsteroidal anti-inflammatory therapy for acute pain control, it may cause more sedation (41). Therefore, meperidine should not be used in older patients unless other alternatives are unavailable or clinically inappropriate.

Quality Indicator 12

Monitoring Renal Function and Potassium in Patients Prescribed Angiotensin-Converting Enzyme Inhibitors

IF a vulnerable elder begins receiving an angiotensin-converting enzyme (ACE) inhibitor, THEN serum potassium and creatinine levels should be checked within 1 week of initiation of therapy BECAUSE this may prevent the development of renal insufficiency and hyperkalemia.

Supporting Evidence. The use of ACE inhibitors can cause renal insufficiency and hyperkalemia, and these risks appear to be greatest in older patients. In 86 older patients (mean age, 78 years) with heart failure selected on the basis of intention to treat with ACE inhibitors, 34% had severe renovascular disease (42). A study that used data from the Studies of Left Ventricular Dysfunction (SOLVD) found that the decline in renal function (defined as a 44.2-μmol/L [0.5-mg/dL] increase in creatinine level) was more substantial in patients randomly assigned to enalapril than in controls (43); older patients had a significantly higher risk. A recent case–control study also demonstrated that risk for developing hyperkalemia with ACE inhibitor therapy was greater in patients who were older or had comorbid illness (44).

These studies point to the need to monitor renal function and potassium levels carefully in patients who begin receiving ACE inhibitors. In a study of general practitioners in Europe, renal function was monitored in only 29% of patients in general practice, and several admissions for uremia were attributed to use of ACE inhibitors (45). These authors concluded that guidelines are needed for monitoring renal function in patients receiving ACE inhibitor therapy. The greatest risk for developing acute renal insufficiency occurs immediately after starting therapy, but the risk for worsening renal function persists throughout the duration of therapy.

Discussion

Medication use provides an ideal opportunity for monitoring quality of care in the vulnerable elders. Because drugs are readily and unambiguously specified, and filled prescriptions and medication lists are increasingly computerized, automated screening is both practical and efficient. Furthermore, unlike many other health care interventions, the evidence base for medication use is often clearly defined, despite the continuing problem of under-representation of vulnerable elderly patients in clinical trials. Therefore, because medication use plays a central role in geriatric practice, taken together these characteristics of drug use make the systematic surveillance of the quality of drug use one of the most promising approaches to improving the care of this important population.

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