Geropharmacology

A Primer for Advanced Practice Acute Care and Critical Care Nurses, Part I

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ABSTRACT

Advanced practice nurses’ challenge in managing older adults’ medication regimens from an evidence base is particularly difficult because older adults are vulnerable to medication errors and adverse drug reactions related to a number of factors. Predicting patients’ responses to drugs is compounded during critical illness, adding to the heterogeneity and unpredictability of drug effects that are prevalent premorbidly. In the first part of this 2-part continuing education series, sources of medication errors and older adults’ vulnerability are discussed, including normal changes of aging affecting pharmacokinetics and pharmacodynamics, polypharmacy, self-medicating, patient-family noncompliance, and inappropriately prescribed medications.

Keywords: adverse drug reactions, geriatric pharmacology, pharmacodynamics, pharmacokinetics, potentially inappropriate medications

Older Adults’ Vulnerability to Medication Errors

Advanced practice nurses’ challenge in managing older adults’ medication regimens from an evidence base is particularly difficult because older adults are vulnerable to medication errors and adverse drug reactions (ADRs) related to a number of factors. Predicting patients’ responses to drugs is compounded during critical illness, adding to the heterogeneity and unpredictability of drug effects that are prevalent premorbidly, resulting in unanticipated drug reactions. In the first part of this continuing education series, sources of medication errors and ADRs are described, including potentially inappropriate medications (PIMs), normal changes of aging affecting pharmacokinetics and pharmacodynamics, polypharmacy, self-medicating, and patient-family noncompliance. The notion of PIMs and ADRs that are common to older adults is introduced as a segue to the second part of the series where major drug classifications and representative medications that pose particular problems for older adults are highlighted.

The first section of this 2-part series (part II appears in the next issue) identifies diverse factors that contribute to the challenges of managing older adults’ medications from an evidence base perspective. Specific topics to be covered include the role of PIMs, polypharmacy, effects of normal aging, and patient-specific factors in the contribution to ADRs and medication errors.

Challenges of Managing Older Adults’ Medications From Evidence Base

Scope of the Problem

The annual cost of medication-related problems is estimated at $85 billion. About 56% of
medication errors are prescribing errors, whereas 44% are errors of administration. Regrettably, prescribing guidelines are lacking, as are data about older adults’ adverse responses to drugs. Citing low study representation rates of 3.45% of 8945 randomized controlled trials, 1.2% of 706 meta-analyses, and 9% of women 65 years and older in breast cancer treatment trials—where prevalence rates approximate 50%, the synthesis of McLean and Le Couteur concludes that older adults are underrepresented in pharmacotherapy research and findings are skewed toward younger persons. From their synthesis of the geropharmacology research, McLean and Le Couteur conclude that the dearth of evidence-based guidelines is disproportionate to the large numbers of medications older adults are prescribed. Prescriptions for adults older than 65 account for 25% to 40% of all prescriptions written in the United States, with average yearly spending increasing by 130% between 1997 and 2004. While community-living older adults are prescribed between 4 and 6 medications for daily use, the numbers skyrocket with admission to hospitals, especially to critical care units (CCUs) where older adults “account for 42–52% of ICU admissions and for almost 60% of all ICU days.” With each additional drug prescribed, the likelihood increases that PIMs are being prescribed. The likelihood of polypharmacy, drug interactions, and ADRs—positively associated with PIMs—also increases. While age, severity of illness, comorbidities, premorbid genetic and immune status, and functional status have the greatest effects on surviving the CCU experience, iatrogenic injury and nosocomial events, such as medication errors, contribute to the morbidity and mortality of patients with critical illness. Because the older adult population is the fastest growing segment of the US population—with numbers “expected to double in the next three decades” and admissions to CCUs expected to escalate, advanced practice nurses are urged to remain current about older adults’ medication therapy management.

Older Adults’ Particular Vulnerabilities to Medication Errors

Medication prescribing errors commonly occur with older adults with a higher risk of adverse events because they are more vulnerable to medication errors than persons belonging to other age groups. Some reasons include:

- Medications are prescribed for which evidence suggests are potentially inappropriate for older adults.
- Even if prescribed medications are appropriate for older persons, dosages may be incorrect because dosing parameters were derived from studies of younger adults.
- Older adults may be experiencing ADRs even before admission to acute care settings—perhaps as a cause for admission; are prescribed additional medications to treat acute illnesses and extant ADRs; and are discharged with medications not required for recovery and health maintenance—increasing the likelihood and severity of ADRs after discharge as well as hospital readmissions.
- New prescriptions may be written without coordination among the patients’ diverse healthcare providers, leading to drug duplication, particularly when generic and brand names are used by different providers or there is no awareness by patient, family, or healthcare provider that the same drug has already been ordered.
- Prescribing practices may not account for heterogeneity and alterations due to normal changes of aging and declines in physiologic and psychologic reserves that affect pharmacokinetics (how drugs are metabolized, deposited in tissues and cells, and excreted) and pharmacodynamics (how the body and brain respond to drugs).
- Patients refill medications long after the indication for the medication has been resolved.
- Older adults self-diagnose and self-medicate with 40% to 50% of over-the-counter medications that are sold, thwarting compliance with prescribed regimens and increasing the likelihood of polypharmacy, drug interactions, and ADRs.

Common ADRs Experienced by Older Adults

Approximately 106,000 fatal ADRs occur annually in the United States, which are 7 times more prevalent among older adults than among younger persons. Systematically collected data about older adults’ responses to drugs are meager, but a comprehensive review of the research literature explicates certain trends. Common occurrences with
aging—falls, fractures, mental status and functional changes, increased instabilities in baroreceptor responses to changes in position, and incontinence of bowel and bladder—are known to be exacerbated by ADRs. Adverse reactions may occur long after maintenance or steady states have been achieved, because of increases in older adults’ vulnerability related to declines in (a) cognitive and physical health status, (b) compensatory or adaptive reserves, and (c) social and environmental resources, requiring continual follow-up. With the chances of ADRs increasing with age, comorbidity, concomitant polypharmacy, and the prescribing of PIMs, ADRs contribute to older adults’ hospitalization and mortality rates.5,10,17,21 One estimate suggests that ADRs explain almost 20% of hospital admissions and “50% of all medication-related deaths.”20(p90) Common ADRs affecting older and “50% of all medication-related deaths.”20(p90) Common ADRs affecting older adults’ health and functional status and increasing chances of injury and death are (a) anticholinergic symptoms, (b) mental status changes, (c) orthostatic hypotension, (d) mood and behavior changes, and (e) gastrointestinal tract disturbances.4,16,18,22,23 In the CCU, patients with heart disease may experience iatrogenic ADRs, such as arrhythmias, electrolyte imbalances, and excessive bleeding from drugs administered to treat their cardiac condition.24 Table I provides the list of the characteristics and possible risks of the most common ADRs, and part II of this series describes the most commonly prescribed classes of drugs that potentiate ADRs among older adults.

Generally, most prescribed medications for older adults have either anticholinergic effects or cognitive and mental status effects that increase risk of falls and other injuries,16,23,25,26 contributing to further declines in mental status and functional performance. For example, anticholinergic psychotropics and sedative-hypnotic drugs, such as benzodiazepines, have been associated with falls, hip fractures, and declines in cognitive and physical performance.1 Orthostatic changes from antihypertensives—medications that approximately half of the aging population take—affect cerebrovascular perfusion, mental status, and gait and balance. In addition to gastrointestinal tract disturbances, pain medication—whether narcotic analgesics or nonsteroidal anti-inflammatory drugs (NSAIDs)—exacerbates mental status changes and maximizes the likelihood of delirium from toxic-metabolic encephalopathy.22,23 Hypoglycemia from the medication management of diabetes and hemorrhage from anticoagulants, particularly warfarin, contribute to cognitive impairment and other complications challenging older adults’ medication management.

Common among these potentially problematic drug classifications are falls. Falls among older adults are on the increase related in part to the increase in numbers of medications taken by this group that are associated with anticholinergic effects, mental status changes, orthostatic hypotension, declines in physical and cognitive performance, and alterations in gait and balance. Any drug that depresses the central nervous system accounts for a 50% heightened risk of falling.4 In 2004, 40% of traumatic brain injury cases were explained by falls.27 The main sequelae of falls and brain injury of particular concern to patients, family, and healthcare providers is fractures, declines in physical and cognitive performance, and hazards of immobility—all of which contribute to loss of functional independence and quality of life.16,23,25,26

Delirium: ADR of Particular Relevance for Critical Care Settings

Although mental status changes and impairments in cognition may be an indication of stress and anxiety, late-life depression, or neurologic disease, acute confusion, or delirium is of particular concern in critical care settings.26 Because of diverse etiologies, delirium is often a medication-induced toxic-metabolic encephalopathy from ADRs.10,13,22,24,28 Unfamiliar and stressful CCU environments, severe illness, disruption of 1 or more organ systems, infections, surgery, metabolic disorders (eg, dehydration, electrolyte imbalances), declines in cardiac output, and use of central nervous system depressants can each contribute to neurological dysfunction, manifested as lethargy and confusion or delirium.10,13 Adding 4 or more drugs to what the patient was taking before hospitalization, although required for treatment, increases the likelihood of delirium.30 In one study of 312 hospitalized adults aged 70 and older, increasing numbers of medications and use of psychotropic medications, physical restraints, indwelling urinary catheters—in combination with an iatrogenic event, such as ADRs—precipitated delirium.30 Predisposing factors
Table 1: Common Adverse Drug Reactions Experienced by Older Adults

<table>
<thead>
<tr>
<th>Adverse Drug Reactions</th>
<th>Characteristics</th>
<th>Possible Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergic symptoms</td>
<td>Dry mouth, blurred near vision, hypotension, incident or exacerbated narrow-angle glaucoma, excessive sedation, cognitive impairment (confusion, disorientation, short-term memory loss, and hallucinations possible), dizziness, impaired gait and balance, impaired sweating, urinary hesitancy, urinary retention, or constipation</td>
<td>Delirium and declines in physical and cognitive functional performance, falls (resulting in traumatic brain injury, fractures), driving accidents, hyperthermia (resulting in heat exhaustion or heat stroke), urinary bladder infection, impaction, and paralytic ileus. Evoking the Valsalva maneuver for constipation may result in cardiac arrest, especially for those with heart disease.</td>
</tr>
<tr>
<td>Mental status changes</td>
<td>Alterations in levels of consciousness ranging from confusion (acute or chronic), excessive sedation (drowsiness to soporific states), delirium (acute onset of difficulty attending, thinking coherently, concentrating) to cognitive impairment (short- or long-term memory problems—sometimes referred to as pseudodementia). Symptoms may also include impaired gait and balance, difficulty learning or processing information, and deficits in judgment or orientation to time, place, or person.</td>
<td>Delirium is a medical emergency and may cause death, disturbances in gait and balance, falls, fractures, traumatic brain injury, muted response to treatment, medication errors if self-medicating. Depending on the cause, patient may experience psychotic symptoms, such as delusions and hallucinations, and be of danger to self and others.</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>Dizziness, sudden drop in blood pressure when changing positions</td>
<td>Falls that can result in fractures (especially hip and wrist) and traumatic brain injury</td>
</tr>
<tr>
<td>Mood and behavior changes</td>
<td>Depressed mood or chronic sadness, declines in energy, appetite, or motivation, agitation, and combativeness</td>
<td>Cognitive impairment or pseudodementia, aversion to influence, and harmful to self or others</td>
</tr>
<tr>
<td>Gastrointestinal tract disturbances</td>
<td>Acid reflux (heartburn), anorexia, gastritis (substernal pain), diarrhea, or constipation</td>
<td>Weight loss, gastrointestinal tract ulcerations, hemorrhage, anemia, hypovolemic shock, death, and impaction. Straining at stool while evoking the Valsalva maneuver increases risk of cardiac arrest among patients with heart disease</td>
</tr>
</tbody>
</table>
were severity of illness and impairments in vision, cognition, and fluid balance. CCU patients, especially those in surgical intensive care units postoperatively for cardiac procedures or hip fractures, are at particular risk of delirium due to severe disruptions in homeostatic mechanisms and the environmental stressors of CCUs, such as “high noise level, incessant monitor alarms, and bright lights.”

Typically, a reversible dementia, delirium (a) is experienced by up to 60% of hospitalized older adults; (b) is characterized by the acute onset of changes in mental status, including difficulty attending or focusing (or perseveratively focusing on minute details), disorganized thinking, easy distractibility, and altered levels of consciousness; and (c) is an independent risk factor for length of hospital and CCU stays, comorbidity, declines in physical and cognitive function, post–hospital placement in long-term care settings, and 6-month mortality.

Sleep deprivation can precipitate delirium, even in non-CCU environments. Using nonpharmacologic methods for sleep enhancement reduced incident delirium in one controlled intervention study of 852 older adults at Yale New Haven Hospital (P = .001). Nonpharmacologic nursing interventions can be effective in managing cognitive impairment and associated neurobehavioral disturbances of older adults.

Sources of Medication Errors and ADRs

Not Accounting for Normal Changes of Aging

Changes in aging confer variability in ADRs and in responses to medications—even among the healthiest of older adults. Moreover, sociodemographic differences compound this variability. Older adults are at higher risk for morbidity and mortality related to overdosing and ADRs than are younger persons. Dose for dose efficacy is not as great as in younger persons, yet the likelihood of ADRs in older persons is greater. Differences in aging between men and women in discrete age groups (65–74, 75–84, and ≥85) and among race and ethnic groups make prescribing medications for older adults an inexact science. In a large population study of older adults, differences in body mass index were identified between African Americans (n = 2260) and whites (n = 1876), conferring potential differences in the pharmacokinetics of medications. Additional research on subgroup differences is warranted to further advanced practice acute care and critical care nurses’ management of medications with older adults and their families.

Changes in older adults’ pharmacokinetics relate to age-related changes in organ functioning, which “may be affected to the greatest degree in the critically ill elderly.” Changes of aging, then, need to be taken into account when prescribing and managing medications for older adults.

Table 2 provides the list of the most common changes related to aging. Generally, with declines in organ system function, variability increases in the absorption, distribution, metabolism, and elimination of most medications. Drugs are dissolved more slowly and ionization of some drugs may be slightly changed. Hepatic blood flow decreases 12% to 40% with age, and renal blood flow declines 1% each year after the age of 50. Reduced blood flow through the liver and kidneys slows down drug clearance. Hepatic
perfusion and function are impaired further because of heart failure, sepsis, and shock in older adults with critical illness. With less efficient metabolism and excretion, drug concentrations remain elevated in the bloodstream longer than in younger persons. Less efficient elimination of drugs “commonly produces greater and more prolonged effects.” The most frequent cause of ADRs in older adults is the accumulation of drugs due to impaired kidney function.

Nonlinear progressive declines in physiologic and psychologic reserves also affect pharmacokinetics and pharmacodynamics. The decreases in organ function accompanying aging and disease reduce physiologic homeostatic and adaptive reserve capacities. Medications challenge reserves further, increasing the variability of physiological responses, resulting in a “divergence of drug effects.” With declines in physiologic reserves, such as cardiopulmonary and renal function, drug elimination is reduced, serum drug concentrations increase, and severe toxic effects may occur in doses considered normal (and even low) in younger persons. Declines in psychologic reserves, particularly cognitive functioning, may reflect disease states of normal declines in short-term memory and speed of information processing. Older adults’ compliance with

Table 2: The Effect of Normal Changes of Aging on Pharmacokinetics and Pharmacodynamics

<table>
<thead>
<tr>
<th>Effect of Normal Changes of Aging</th>
<th>Pharmacokinetics</th>
<th>Pharmacodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Declines in hearing, vision, and manual dexterity</td>
<td>May result in unintentional overdose and noncompliance with medication regimens.</td>
<td>May result in unintentional overdose and noncompliance with medication regimens.</td>
</tr>
<tr>
<td>Resting heart rate, stroke volume, and cardiac output</td>
<td>Decline that slows absorption, distribution, and excretion of drugs.</td>
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</tr>
<tr>
<td>The adaptive response of the baroreceptors (nerve endings in the arteries, concentrated in the internal carotid arteries and aortic arch) to pressure changes</td>
<td>Is impaired, resulting in blood pressure instability, especially during changes in position.</td>
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</tr>
<tr>
<td>Effects of drugs affecting the central nervous system</td>
<td>Are more heterogeneous in older adults related to reduced blood supply, changes in the blood-brain barrier (allowing fat-soluble drugs to permeate the brain), increases in monoamine oxidase, and decreases in acetylcholine, dopamine, and serotonin—potentiating ADRs.</td>
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</tr>
<tr>
<td>Number and sensitivity of receptor sites</td>
<td>Are altered, resulting in declines in neurotransmitter function and increased sensitivity of older adults to ADRs resulting from psychotropic medications.</td>
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</tr>
<tr>
<td>Respiratory capacity declines</td>
<td>Decreasing the elimination of volatile drugs, such as inhalation anesthetics.</td>
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</tr>
<tr>
<td>Acid secretion, blood flow, and gastrointestinal tract motility</td>
<td>Decrease and pH level increases, potentially reducing drug absorption.</td>
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</tr>
<tr>
<td>Hepatic blood flow, enzyme production, biotransformation, and phase I oxidation reactions</td>
<td>Are impaired, resulting in the accumulation of water-soluble drugs and the elimination half-life of fat-soluble drugs.</td>
<td>Are impaired, resulting in the accumulation of water-soluble drugs and the elimination half-life of fat-soluble drugs.</td>
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<tr>
<td>Total body water decreases</td>
<td>Increasing concentrations of water-soluble drugs and the elimination half-life of fat-soluble drugs.</td>
<td>Increasing concentrations of water-soluble drugs and the elimination half-life of fat-soluble drugs.</td>
</tr>
<tr>
<td>Lean muscle mass decreases and proportion of body fat increases</td>
<td>Affecting blood flow rates, solubility, and storage of fat-soluble drugs, resulting in accumulations of drugs in fat with potentially toxic metabolites released into the blood.</td>
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</tr>
<tr>
<td>Age-related declines in serum albumin concentrations</td>
<td>Can be exacerbated by disease and malnutrition, resulting in increased concentrations of pharmacologically active drugs, potentiating toxicities.</td>
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Abbreviation: ADRs, adverse drug reactions.
Data from references 5, 9, 19, 20, 22, 23, 36, 54, 55.
Drug and dosage requirements may be affected through memory lapses and difficulty in learning new information, potentiating errors and ADRs. Symptoms of cognitive impairment from delirium, depression, or dementia may reflect declines in both physiologic (neurologic) and psychologic (cognitive) reserves.1

Adding to the challenge of older adults’ medication management and the risk of errors are factors that compound the unpredictability of medications’ pharmacodynamics and pharmacokinetics—polypharmacy, noncompliance, and self-medicating.

**Prescribing More Medications Than the Aging System Can Manage Contributes to Medication Errors and ADRs**

Adding to the likelihood of medication errors and the challenges of managing older adults’ medication regimens is polypharmacy. As an independent predictor of drug interactions and ADRs, polypharmacy is defined as concomitantly using 9 or more medications—including both prescribed and self-selected medications.9 Drugs used in combination with certain foods, vitamin and mineral supplements, and herbal preparations—including teas—may also contribute to polypharmacy.6 According to estimates, taking 2 drugs confers a 5.6% chance of an interaction, but taking 8 drugs confers a 100% risk of an interaction.41 Most interactions occur because one drug (or nutrient) affects the metabolism of another drug or nutrient. With an increase in the number of drugs, these metabolic “enzyme-based interactions” increase in likelihood.8

Generally, polypharmacy (a) interferes with the actions of drugs, (b) increases risk of interactions and ADRs, (c) decreases patients’ confidence and reduces compliance with medication regimens, (d) impairs physical and cognitive performance, (e) produces life-threatening consequences, and (f) is costly to patients, families, and healthcare systems.4,20,41 Numbers of medications may not be as important as types of medications taken, however. In a study of 3075 community-living older adults aged 70 to 79, numbers of medications did not correlate with physical and cognitive functioning when anticholinergic and sedative-hypnotics were excluded from drug regimens—even when patients were receiving up to 20 medications.4

Polypharmacy occurs among all ages and in all healthcare settings, but most often occurs in the older adult population, adding to declines in compensatory reserves and increasing the variability of therapeutic action and ADRs. Most of the factors that contribute to polypharmacy, listed in Table 3, can be modified. Although lack of communication and coordination among healthcare systems may result in duplication of medications with possible toxicity, polypharmacy and concomitant interactions may result even with coordination. Older adults’ unique physiologic and cognitive responses to drugs, their noncompliance with prescribed regimens, and their self-medicating increase the likelihood of medication errors and ADRs.

**Noncompliance and Self-Medicating Add to Errors and ADRs**

Older adults have special problems complying with medication regimens, over and above medication compliance issues of younger adults.20 In addition to financial and transportation constraints of obtaining prescriptions, ADRs

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**Table 3: Factors Contributing to Polypharmacy**

| Related to lack of coordination and communication among healthcare systems, new medications are prescribed in isolation from current prescription drugs, potentiating duplication. |
| Time pressures, workload, and patient-family readiness to learn about drug interactions prevent comprehensive drug assessment and patient-family teaching. |
| Comorbid acute and chronic illnesses require multiple medications. |
| CCC treatment requires prescribing new medications, increasing the likelihood of drug interactions and ADRs. |
| ADRs—mimicking normal aging processes or diseases of aging—are treated with additional medications. |
| Preadmission to CCUs, patients self-diagnose with OTC and CAM remedies, unused medications, homemade remedies, medications from family and friends, and refills of no-longer-needed medications. |
| Medication history omits nonprescription OTC and CAM preparations, resulting in drug-drug or drug-nutrient interactions. |

Abbreviations: ADRs, adverse drug reactions; CAM, complementary and alternative medicine; CCC, critical care unit; OTC, over the counter.
and failure to experience expected benefits thwart confidence and impair compliance with prescribed medications. Of all age groups, older adults are most likely to self-diagnose, self-medicate, and be noncompliant with medication regimens. With the high prevalence of arthritis in the aging population, self-medication with anti-inflammatory analgesics is common. However, these are not without risk. NSAIDs, for example, are potentially nephrotoxic and ulcerogenic in older adults.

Consumer demand for OTC drugs and dietary supplements that promise youth and vitality will continue to escalate, particularly among older adults. With the popularity of complementary and alternative medicine (CAM) preparations, older adults may erroneously assume they are safe. Self-medicating for symptoms of depression with the herb St. John’s Wort, for example, can either interfere with or potentiate the effects of other drugs, and by itself, the herb has ADRs. Concomitant use of the herb with warfarin reduces the anticoagulant effectiveness of warfarin. Moreover, its use with digoxin decreases blood levels of digoxin. Additional information about the use of CAM supplements with prescribed medications can be found in the work of Swanson and colleagues. Table 4 provides the list of Web sites for assessing the safety of OTC and CAM preparations.

Prescribing PIMs to Older Adults
Use of inappropriate medications with the aging population “is a major safety issue” and source of medication prescribing errors. Differences between young and old and the heterogeneity of older adults’ responses to drugs make prescribing some drugs for older adults problematic or potentially inappropriate. PIMs are those medications for which the potential risks—ADRs, toxicities, and/or death—outweigh the potential benefits to the patient and “for which a good alternative drug is available.” The most frequently used guidelines for identifying PIMs are the Beers criteria, which delineate medications that should not be prescribed for older adults, exceed maximum recommended daily doses, and should not be prescribed with certain comorbidities. Laroche and colleagues report that PIMs are prescribed with relatively high frequency—between 12% and 40% in the United States—and “should not be prescribed to the elderly” except for treating conditions for which there is no alternative or on a very short-term and highly monitored basis. However, additional evidence is needed from diverse clinical populations to develop and validate general and settingspecific guidelines.

Using multiple measures of prescribing quality for older adults in their study of 196 randomly selected community-living veterans aged 65 and older, Steinman and colleagues found that (a) 37% of the participants were taking 1 or more of the drugs to avoid identified in the updated 2002 Beers criteria; (b) 82% were taking PIMs according to the Medication Appropriate Index; and (c) 37% were taking 9 or more drugs, the operational definition of polypharmacy in the study. In a 4-year (1997–2001) population-based study with number of older adult participants ranging from 18,030 to 29,605, approximately 20% were taking 1 or more PIMs, as measured by the updated 2002 Beers criteria. Using both the 1997 and the 2002 Beers criteria, van der Hooft and colleagues found that long-acting benzodiazepines, anticholinergic antidepressants, and anticholinergic and sedating antipsychotics were among the most frequently prescribed PIMs in the population. Cross-referencing medications that should not be prescribed with certain comorbidities, the investigators found that short-, intermediate-, and long-acting benzodiazepines were among the most frequently used PIMs with patients with syncope or falls (26.4%) and NSAIDs were most frequently prescribed PIMs to patients with gastrointestinal tract ulcers (26.6%) or patients who were on anticoagulant therapy (20.1%).

Studies of community-living older adults most likely underestimate the proportion of older persons with acute and critical illness who may be prescribed drugs to avoid. But studies of PIM prevalence in CCUs are rare. One study of 203 patients with chronic critical illness (median age = 72 years) found that opioids, sedative-hypnotics (especially benzodiazepines), and antipsychotics were the most frequently prescribed PIMs, which were administered either before (68.7%) or after (56.2%) episodes of delirium or coma in patients with normal cognitive functioning on
admission. Less than half regained normal cognitive functioning after hospitalization.26

A study of 350 older adults with acute illness used the Beers updated criteria and a measure designed for evaluating the prevalence of PIMs in acute care settings—the Improved Prescribing in the Elderly Tool47—and found that the proportion of PIMs was higher in the acute care setting than in the community.48 Prevalence of prescribing at least 1 PIM, according to Beers criteria that are independent of disease, was 34.6%. Using the Beers criteria that considers comorbidities, 86.7% of the inpatients were inappropriately prescribed medications, whereas with the Improved Prescribing in the Elderly Tool, 22% of the patients were receiving PIMs. The most consistently prescribed PIMs were benzodiazepines and NSAIDs. In a larger prospective study of 800 hospitalized older adults, disease-related PIMs ranged from 11.7% to 40.5% for older adults on medical units and 17.5% to 51.8% on dedicated geriatric units, with benzodiazepines and drugs with anticholinergic ADRs—antipsychotics in 39.5% of the cases—the most frequently prescribed PIMs.10 Noteworthy in the study’s findings were (a) an almost 3-fold increase in the prevalence of PIMs that were

Table 4: Websites for Assessing the Safety and Appropriateness of Medications for Older Adults and Additional Information on Evidence-Based Best Practices

<table>
<thead>
<tr>
<th>Drug-Related Resources</th>
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<tbody>
<tr>
<td>Potentially inappropriate medications for the elderly according to the revised Beers criteria. Available at: <a href="http://www.dcri.duke.edu/ccge/curtis/beers.html">http://www.dcri.duke.edu/ccge/curtis/beers.html</a></td>
</tr>
<tr>
<td>General information about drugs regulated by the US Federal Drug Administration, Center for Drug Evaluation and Research. Available at: <a href="http://www.fda.gov/cder/drug/default.htm">http://www.fda.gov/cder/drug/default.htm</a></td>
</tr>
<tr>
<td>Prescription drug information for professionals and consumer, including a drug interactions checker. Available at: <a href="http://www.medscape.com/druginfo/druginterchecker">http://www.medscape.com/druginfo/druginterchecker</a>; <a href="http://www.drugs.com">http://www.drugs.com</a></td>
</tr>
<tr>
<td>Drug information for professionals and consumer, specializing in senior advocacy. Available at: <a href="http://www.ascp.com/public">http://www.ascp.com/public</a></td>
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<tr>
<td>Evaluating the safety of complementary and alternative medicine preparations</td>
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<tr>
<td>National Medicines Comprehensive Database, includes natural product effectiveness checker and natural product drug interaction checker. Available at: <a href="http://www.naturaldatabase.com">http://www.naturaldatabase.com</a></td>
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<tr>
<td>Herb Research Foundation, includes specific health conditions and use of herbal remedies. Available at: <a href="http://www.herbs.org">http://www.herbs.org</a></td>
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<table>
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<th>Other Resources</th>
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<tbody>
<tr>
<td>General online search engines for information about older adults and health</td>
</tr>
<tr>
<td>National Institutes of Health PubMed—citations from medical, pharmaceutical, and nursing journals according to self-identified search criteria. Available at: <a href="http://www.ncbi.nlm.gov/entrez">http://www.ncbi.nlm.gov/entrez</a></td>
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<tr>
<td>Evidence-based best practices information</td>
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<tr>
<td>Agency for Healthcare Research and Quality includes clinical practice guidelines for selected disorders. Available at: <a href="http://www.ahrq.gov">http://www.ahrq.gov</a></td>
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<tr>
<td>Database of more than 500 evidence-based care summaries. Available at: <a href="http://www.cinahl.com">http://www.cinahl.com</a></td>
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<tr>
<td>Sigma Theta Tau’s database of research syntheses and evidence-based case studies. Available at: <a href="http://www.nursingsociety.org">http://www.nursingsociety.org</a></td>
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<td>Evidence-based best practices information and clinical recommendations on more than 50 topics. Available at: <a href="http://www.joannabriggs.edu.au/pubs/best_practice.php">http://www.joannabriggs.edu.au/pubs/best_practice.php</a></td>
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prescribed during hospitalization; (b) the high prevalence of benzodiazepines that were prescribed to patients with depression or a history of fainting or falls; (c) the use of NSAIDs with patients with a history of gastrointestinal tract ulceration; (d) the lack of awareness among healthcare providers that anticholinergics should be avoided; and (e) not finding differences in the frequency with which PIMs were prescribed by specialists in internal medicine and in geriatrics \( (P = .08) \).

Compared with general practitioners, geriatric specialists in another study of 2018 older adults with acute illness, however, reduced the use of inappropriate medications among older adults from 66% at admission to 43.6% at discharge \( (P < .001) \).\(^1\) Regrettably, neither group of healthcare providers was aware of Beers criteria, but used the occurrence of ADRs to discontinue causative agents. At both time-points, long-acting benzodiazepines, opioids, concomitant use of 2 or more psychotropics in the same drug category, and anticholinergic antidepressants were among the most frequently prescribed PIMs. The investigators concluded that collaborations among pharmacologists and healthcare providers and continued education in geropharmacology is requisite to reduce PIMs in the growing aging population.

The notion of multidisciplinary collaboration in acute care and CCU settings is supported by research demonstrating the reduction in polypharmacy, ADRs, PIMs, and other medication errors on units with clinical pharmacists who (a) collaborate with and provide continuing evidence-based education to patient care teams\(^49,50\) and (b) perform medication reviews at admission and discharge.\(^51\) In their systematic review of the multidimensional role and outcomes of on-site clinical pharmacists in CCUs, Kane and colleagues\(^52\) found that role components linked to outcomes included (a) checking and clarifying physician orders, (b) monitoring drug interactions and ADRs, (c) adjusting dosages for liver and kidney function test results, and (d) recommending alternative medications for PIMs. Outcomes included reduced rates of medication errors and ADRs with “significant economic advantage.”\(^52(p695)\)

One study where ADRs were reduced with on-site clinical pharmacists found that physicians welcomed their role and that nurses’ time and workload in managing patients’ medication regimens were reduced.\(^53\) Additional evidence about the collaborative efforts and outcomes of advanced practice acute care and CCU nurses with the patient care team is warranted, particularly in those settings where advanced practice nurses have prescribing privileges.

**Clinical Applications for Acute Care and Critical Care Nurses**

- Advanced practice acute care and critical care nurses need to engage in collaborative research to provide validating evidence for the Beers criteria for PIMs prescribing to older adults who are critically ill.
- Medication inventories and reductions in selected preadmission medications, such as psychotropic drugs, may be required to prevent ADRs, such as delirium. Sedative-hypnotics should be avoided, if possible. However, no medication should be abruptly withdrawn, but removed slowly, depending on the potential for interactions with CCU treatments.
- Because of reductions in distribution volumes and clearance, loading and maintenance doses of certain drugs should be reduced.
- Dehydration, resulting in reduced clearance of drugs by the kidneys, is reversible by rehydration, within limits imposed by cardiac, respiratory, and electrolyte status.
- Because most medications are cleared through the liver and kidneys, liver and kidney function tests are critical and need replicating at regular intervals and after new drugs are added.
- Given the vulnerability of older adults to the effects of polypharmacy, reductions in nonessential medications and close monitoring for toxic effects by healthcare professionals are needed until maintenance blood levels of newly prescribed medications are achieved. Further reductions in medications should follow resolutions of critical illness and improvement in organ function.
- Certain drug classes should be avoided or used judiciously, including psychoactive drugs such as anticholinergics, opioids, or narcotic analgesics, sedative-hypnotics—particularly benzodiazepines, and NSAIDs.
- Despite mental status ADRs to psychotropic medications—increasing the risk of delirium—treatment is needed for incapacitating anxiety, major depression, and agitation or combativeness.
nonpharmacologic methods and lowest dosages possible for efficacy may minimize emotional suffering without adding to risks associated with ADRs.

- Delirium from critical illness and medications that are potentially inappropriate for older persons requires prevention, monitoring, and immediate intervention.
- The diverse causes of delirium can be summarized with the initials ICM, adapted from Mick and Ackerman:

\[
\begin{align*}
I & = \text{Intoxication} \\
& \quad \text{Infection} \\
& \quad \text{Injury} \\
C & = \text{Cerebral anoxia} \\
& \quad \text{Congestive heart failure} \\
& \quad \text{Cerebrovascular accident} \\
M & = \text{Medications} \\
& \quad \text{Myocardial infarction} \\
& \quad \text{Metabolic disorders}
\end{align*}
\]

- To decrease prevalence of PIMs, polypharmacy, and posthospitalization ADRs, medication regimens need to be reviewed before discharge, ideally by teams of acute care or critical care nurses, clinical pharmacists, attending physicians, and prospective community-based providers. Involving family members in medication management discharge planning may alert them to ADRs and the ameliorative actions to take; help them discourage patients’ self-medicating, and promote compliance. Hospital readmissions for life-threatening ADRs may be curtailed.
- Decision-making tools that incorporate information about older adults’ vulnerability to ADRs from PIMs are needed to assist healthcare providers in their management of older adults’ medication regimens. In addition to the assignment of a clinical pharmacist to the CCU, other strategies include medication-prescribing algorithms, hospital formularies listing alternatives to PIMs for older adults, automated medication-dispensing systems, computerized physician order-entry systems—with demonstrable efficacy in reducing medication-prescribing errors—and computer systems with error-checking alerts and alternatives to PIMs, which in one study reduced PIM use by 58%

\footnote{Lists of PIMs relevant to older adults cared for in diverse settings are available online at http://www.dcri.duke.edu/ccge/curtis/beers.html and reported in the works of Fick and colleagues\textsuperscript{16} and van der Hooft and colleagues.\textsuperscript{19} Table 4 provides the list of additional Web sites for assessing the safety and appropriateness of medications—and interactions among them—and additional evidence-based best practices for caring for older adults. Part II of this series provides further discussion of problematic drug classifications and medications within these classes that may need to be avoided when caring for older adults.

- As summarized by Gutierrez:

Prescribing drugs for an older adult involves 6 basic principles: (1) start low and go slow; (2) start 1 (drug), stop 2; (3) do not use a drug if the adverse effects are worse than the disease; (4) use as few drugs as possible using nondrug therapies when able; (5) assess response frequently; and (6) consider drug holidays from time to time.\textsuperscript{41(p117)}

**Summary**

Understanding evidence-based strategies for managing older adults’ medication regimens will become increasingly important to advanced practice acute care and critical care practitioners for the following reasons:

- The population is aging and the healthcare needs of older adults are becoming increasingly complex, especially as baby boomers—the cohort born between 1946 and 1964—age. Older adults are the largest consumers of healthcare resources, currently representing 60% of critical care patient days.\textsuperscript{6} This trend is expected to increase over time.
- Critical illness and its treatment compound older adults’ heterogeneous responses to drugs.\textsuperscript{12}
- As life expectancies increase, the aging body’s responses to drugs will become progressively unpredictable due to normal changes of aging, as well as acute and chronic illnesses.\textsuperscript{23}
- Polypharmacy, patients’ self-medicating, and noncompliance exacerbate the heterogeneity and unpredictability in the metabolism, distribution, elimination, and efficacy of pharmacotherapy for older adults and contribute to ADRs.
- Prescribing PIMs for older adults, contributing to polypharmacy, and not assessing patients’ self-medicating and noncompliance complicate the already inexact science of
medication management and contribute to the incidence of medication errors and ADRs in the aging population.1-7

Given the associations among polypharmacy, drug interactions, ADRs, and PIMs described in the first part of this 2-part series, a balance between the benefits and risks in prescribing can be attained if certain drug classes are underused—or avoided when possible—such as anticholinergics, sedative-hypnotics, opioid analgesics, and certain psychotropics, described next in part II.

References


