

## PROFESSION



Anticoagulation clinics can help primary care doctors minimize the bleeding risks of warfarin, says John Benages, MD, who oversees such a clinic in Elmhurst, Ill. [Photo by Ted Grudzinski / AMA]

## Managing 4 risky drug types sending seniors to the ED

Patient safety experts and geriatricians warn that some medications require more attention from doctors. Reframing treatment goals with Medicare patients could help.

By **KEVIN B. O'REILLY**, amednews staff. Posted Oct. 1, 2012.

More than a half-million preventable drug-related injuries occur among Medicare outpatients each year. And a quarter of medication errors are attributed to poor drug packaging and labeling.

To combat this, the Institute of Medicine recommends generally applicable safety strategies such as reducing polypharmacy and spreading adoption of electronic prescribing, medication reconciliation and clinical decision support. Yet new research suggests that interventions are needed to target the specific medicines that most commonly harm patients.

Adverse drug events send at least 265,000 seniors to U.S. emergency departments every year

and hospitalize nearly 100,000 patients 65 and older, according to a Nov. 24, 2011, study in *The New England Journal of Medicine*. What is striking, experts say, is the study's finding that four kinds of medications — warfarin, insulins, oral antiplatelet agents and oral hypoglycemic agents — together account for seven in 10 emergency hospitalizations among seniors.

Warfarin, the generic anticoagulant marketed under brand names such as Coumadin and Jantovan, is responsible for a third of seniors' emergency hospitalizations — more than twice as many as all insulin drugs put together. The blood thinner can cause serious bleeding.

The insulins and oral hypoglycemics send more than 24,000 seniors to hospitals annually — most of whom are very dizzy, have seizures or lose consciousness due to drug-related hypoglycemia. Oral antiplatelets, meanwhile, land more than 13,000 Medicare patients in hospital beds. These drugs also pose bleeding risks, especially when combined with warfarin.

Nearly two-thirds of all emergency hospitalizations among Medicare patients are due to unintentional overdoses. For primary care physicians faced with helping their senior patients avoid the ED, the call to action goes beyond properly counseling patients on the absolute necessity of taking their medications exactly as directed and avoiding drug-drug and drug-food interactions, experts say. These data, they argue, reflect the challenge that a few medications pose to primary care physicians in using their individual judgment to prescribe prudently to the especially vulnerable geriatric patient population.

### Targeting safety efforts

"In the last decade or so, we've not made tremendous measurable progress by focusing on broad approaches to medication safety," says Daniel S. Budnitz, MD, MPH, lead author of the study. "Now it may be time to try an alternative approach that focuses on a few of the big players in terms of patient harm, and focusing on older folks who have even higher rates of harm."

A key tool is regular testing of patients' prothrombin time to adjust warfarin regimens as needed. Warfarin has an unpredictable dose response and numerous drug-drug and drug-food interactions.

[Photo by Ted Grudzinski / AMA]



The notion of placing extra scrutiny on the medications linked to the most harm resonates with Jerry H. Gurwitz, MD, chief of geriatric medicine at the University of Massachusetts Medical School in Worcester. Focusing on a handful of drug types is “a much more manageable situation for physicians and health care systems and hospitals and ERs to get their heads around.”

Michael R. Cohen, RPh, agrees.

“It just makes so much sense to be aware of the drugs that fall out at the top of these lists,” says Cohen, president of the Horsham, Pa.-based Institute for Safe Medication Practices. “To focus your attention on preventive measures, on the patients that you speak with and the education you give them and that your office gives them — it makes so much sense to focus on those drug categories.”

### **Risky medicines often essential**

The problem, experts acknowledge, is that managing these four medication types to reduce incidents of harm to seniors is no easy task. Each is widely prescribed and often critical in achieving key clinical goals. Warfarin is effective in treating deep venous thrombosis and pulmonary embolism. The drug also is used to treat atrial fibrillation, which increases the risk of stroke — the nation’s third-leading cause of death, killing nearly 130,000 annually.

Antiplatelets are another essential type of medication that can help prevent strokes and heart attacks, the latter of which kill nearly 600,000 Americans a year, according to the Centers for Disease Control and Prevention. Insulins and oral hypoglycemics are central tools in the battle to help diabetics control their glycated hemoglobin and stave off complications such as glaucoma, foot amputation and renal failure. Diabetes kills about 70,000 Americans annually.

“There is not an easy yes-or-no answer for these drugs, both on the physician side and the patient side,” says Dr. Budnitz, director of the Medication Safety Program in the CDC’s Division of Healthcare Quality Promotion. “If I’m a diabetic and I need insulin, then I want to take insulin.”

### **How seniors are different**

The key, experts say, is to take a comprehensive safety approach in treating the seniors who are usually prescribed these drugs. The first thing is to appreciate how older patients’ physiology differs from that of younger patients, says Sharon Brangman, MD, past president of the American Geriatrics Society.

“I give the analogy of the pediatrician. The approach to a 3-year-old is different from someone who’s 21 years old,” says Dr. Brangman, who often uses this example to explain geriatrics. “The same thing is true with aging. The normal aging and disease process means you need skills in managing the complex interactions with disease and aging and medications.”

The effect of aging increases the risks of anticoagulants, along with other drug types such as analgesics, antihypertensives and benzodiazepines, according to the American Medical Association’s 2011 handbook, *Geriatric Care by Design*. Seniors’ metabolism is often reduced, and they clear drugs from their system at a slower rate, which heightens the risk of unintentional overdose.

“Seniors’ resilience goes down, their ability to maintain equilibrium,” says Albert Wu, MD. Dr. Wu served on a medication errors panel for the Institute of Medicine, which published a 2006 report and made recommendations on drug safety. “None of their organs works as well as they used to. Their kidney function and liver function isn’t as good. If they fall down, they are more likely to break a bone.”

Next, experts say, physicians should reconsider their care plans in light of the patient’s age.

“What we have to do is look at the goals of care and how those may change as we get older,” says Dr. Brangman, chief of geriatrics at the State University of New York’s Upstate Medical University in Syracuse. “We do know that we don’t need really tight glycemic control in older diabetics. You can use a lower dose of insulin, monitor it carefully and not increase it.”

Dr. Brangman says very tight control of blood sugar is less important in seniors, because their risk of long-term complications such as renal failure is not as great as those of, say, a newly diagnosed 40-year-old diabetic. Properly counseling patients on use of insulin and oral hypoglycemics also is key. With both types of medication, it is essential for seniors to follow the diets prescribed by their doctors and keep their eating and exercise habits regular. Patients should be warned that serious adverse events are likely if they are careless.

“You get people who are older tea-and-toast ladies who don’t eat so much,” says Dr. Wu, professor of health policy and management at Johns Hopkins Bloomberg School of Public Health in Baltimore. “They don’t cook for themselves too much, or it’s too much hassle to prepare a meal. And, by the way, they’re on an oral hypoglycemic and they bottom out. It’s a common story.”

### **The warfarin puzzle**

The drug that sends the most seniors to the hospital — warfarin — also may be the most challenging to manage. The medication has an unpredictable dose response and numerous drug-drug and drug-food interactions and requires regular monitoring.

“One of the hardest things is educating patients,” says Albert L. Waldo, MD, professor of cardiology, medicine and biomedical engineering at Case Western Reserve University School of Medicine in Cleveland. “It can take over an hour to explain everything — all the interactions and all the other things. An hour would be great, but when you have an office full of people and a whole ton of problems to get to, it’s very hard to do that.”

Anticoagulation clinics, sometimes called Coumadin clinics, employ nurses and pharmacists to help devote the time to help

patients manage warfarin. The anticoagulation clinic that is part of Elmhurst Memorial Healthcare Network in suburban Chicago has about 450 patients enrolled.

“Our incidence of hemorrhagic complications is practically nil,” says John Benages, MD, chief medical officer of Elmhurst Clinic, of which the Coumadin clinic is a part.

He attributes that low rate to a nurse and a medical assistant, who often spend as long as 45 minutes in an initial overview visit with patients starting warfarin therapy. They discuss the importance of taking the medication at the same time daily, and avoiding alcohol and cranberries. They also advise patients on maintaining consistent intake of foods high in vitamin K such as pork, liver, spinach, kale and broccoli. Those foods can interfere with how warfarin, a vitamin K antagonist, functions in the body.

“This is a tremendous amount of information provided to patients about Coumadin, the benefits and the risks, and they monitor these patients very closely,” Dr. Benages says. “They are seen weekly until they are stabilized. The care that’s provided is very personal — it’s face to face.”

In the office, a measurement of patients’ coagulation is as easy as a finger prick and a result 30 seconds later. The result is entered, and an algorithm determines the appropriate warfarin regimen for patients to follow, which is printed out for them to take home. Getting the dose right is key to effective treatment, on one end, and preventing serious bleeding on the other.

Warfarin is not the only option for treating atrial fibrillation. Newer anticoagulants such as dabigatran (Pradaxa) and rivaroxaban (Xarelto) have fewer interactions with food or other medicines and do not require routine monitoring. However, these drugs lack validated tests to measure their anticoagulation effect, are much pricier than warfarin and make it harder to determine patient compliance, Dr. Waldo says.

“Nothing is perfect,” he adds.

Dr. Waldo cites research showing that 40% of patients with atrial fibrillation for whom the benefits of anticoagulation outweigh the risks do not get the medication.

Experts acknowledge that there is no quick-fix for the problem of serious adverse drug events among seniors, and ultimately it is up to individual physicians and patients to weigh the benefits and risks of a drug given the circumstances. A comprehensive strategy is needed to help reduce the toll these medications take on America’s seniors, says the CDC’s Dr. Budnitz.

“These are hard drugs to manage in our patients,” he says. “Doctors need support and help. We have to figure out, from a policy standpoint, what’s the best way to support physicians and patients in this way. Putting all the blame on physicians ... or saying patients just need to do a better job of taking their medications, neither of those approaches is likely to work. We have to look at systems and reimbursement.”

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#### ADDITIONAL INFORMATION:

#### How often 4 drug types land seniors in the hospital

Four kinds of medications are linked to a high rate of hospitalization for every 10,000 visits to the doctor’s office involving a prescription order. More seniors are prescribed warfarin than are prescribed insulins.

Medication type	Hospitalizations per 10,000 visits
Warfarin	20.02
Insulins	19.06
Oral hypoglycemic agents	4.08
Oral antiplatelet agents *	2.78

Note: The antiplatelets examined were aspirin, aspirin-dipyridamole (Aggrenox), cilostazol (Pletal), clopidogrel (Plavix), dipyridamole (Persantine, Antistenocardin), prasugrel (Effient) and ticlopidine (Ticlid).

Source: “Emergency hospitalizations for adverse drug events in older Americans,” *The New England Journal of Medicine*, Nov. 24, 2011 ([ncbi.nlm.nih.gov/pubmed/22111719/](http://ncbi.nlm.nih.gov/pubmed/22111719/))

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#### Risk of adverse drug events rises with age

The oldest seniors are more susceptible to having serious adverse drug events send them to the hospital than their younger counterparts.

Age	Emergency hospitalizations	Percent of total hospitalizations
85 and older	25,326	25.4%
80 to 84	22,619	22.7%
75 to 79	19,248	19.3%
70 to 74	18,257	18.3%

<b>65 to 69</b>	14,179	14.2%
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Note: Percentages do not total 100% due to rounding.

Source: "Emergency hospitalizations for adverse drug events in older Americans," *The New England Journal of Medicine*, Nov. 24, 2011 ([ncbi.nlm.nih.gov/pubmed/22111719/](http://ncbi.nlm.nih.gov/pubmed/22111719/))

### 10 risky medications for seniors

The American Geriatrics Society has identified 34 medications that are potentially inappropriate for use in patients 65 and older. The society also has spelled out 14 drugs that can worsen certain conditions in seniors and 14 types of medicines that should only be used with caution in these patients. The organization has drawn special attention to a smaller list of 10 medications whose side effects are pronounced among elderly patients. These drugs, by treatment use and potential adverse effects:

Drug type	Treatment use	Potential adverse effects
<b>Indomethacin (Indocin), piroxicam (Feldene)</b>	Pain and inflammation	Can increase the risk of indigestion, ulcers and gastrointestinal bleeding. Can also increase blood pressure, affect kidneys and worsen heart failure.
<b>Digoxin (Lanoxin)</b>	Heart failure/irregular heartbeat	Can be toxic in older adults and people with decreased kidney function.
<b>Glyburide (Diabeta, Micronase), chlorpropamide (Diabinese)</b>	Diabetes	Can cause severe hypoglycemia.
<b>Cyclobenzaprine (Flexeril), methocarbamol (Robaxin), carisoprodol (Soma)</b>	Muscle relaxants	Can leave patients feeling groggy or confused; can increase risk of falls; can cause constipation, dry mouth and urination problems. Little evidence of efficacy.
<b>Benzodiazepines such as diazepam (Valium), alprazolam (Xanax), chlorthalidone (Thalidon), zaleplon (Sonata), zolpidem (Ambien)</b>	Anxiety, insomnia	Can increase risk of cognitive impairment, delirium, falls, fractures and car crashes. Seniors have increased sensitivity to these anxiety or anti-insomnia drugs.
<b>Anticholinergics such as amitriptyline (Elavil), imipramine (Tofranil), trihexyphenidyl (Artane), dicyclomine (Bentyl), oxybutynin (Ditropan)</b>	Depression, Parkinson's disease, irritable bowel syndrome, overactive bladder	Can cause confusion, constipation, urination problems, blurry vision, hypotension. Especially problematic for men with an enlarged prostate.
<b>Meperidine (Demerol)</b>	Pain	Can increase risk of seizures and cause confusion.
<b>Diphenhydramine (Benadryl), chlorpheniramine (AllerChlor, Chlor-Trimeton)</b>	Allergic reactions, colds	Can cause confusion, blurred vision, constipation, urination problems and dry mouth. These drugs also are the active ingredients in some over-the-counter antihistamines and medications such as Tylenol PM.
<b>Haloperidol (Haldol), risperidone (Risperdal), quetiapine (Seroquel)</b>	Psychotic disorders	Can increase risk of stroke, death. Can cause tremors, increase fall risk. Avoid unless treating psychosis.
<b>Estrogen pills and patches</b>	Menopause	Can increase risk of breast cancer, blood clots and dementia. Evidence of carcinogenic potential; lack of cardioprotective effect and cognitive protection in older women.

Sources: "Ten Medications Older Adults Should Avoid or Use with Caution," American Geriatrics Society Foundation for Health in Aging, April; "American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults," *Journal of the American Geriatrics Society*, April ([ncbi.nlm.nih.gov/pubmed/22376048/](http://ncbi.nlm.nih.gov/pubmed/22376048/))

### 6 steps to preventing adverse drug events in seniors

Although special attention to managing blood thinners and diabetes drugs is warranted, physicians can use some broader strategies to cut the odds that prescription drugs will harm senior patients. Experts offer advice on dealing with the problem.

- Start low and go slow. Seniors process medicines differently from younger patients and often require lower doses than what is generally recommended as an adult dose. Titrate more slowly than with a younger patient.
- Counsel seniors on the name, dose, indication and potential side effects when prescribing new medications. Ask them to report any significant side effects immediately. Use the "teach-back" method, asking patients to repeat what they understand about what you have said.
- Ask patients to bring each of their medications to an appointment after a medication change. Seniors have greater trouble reading and understanding health information, such as prescription labels. Have them read each label and express in their own words what they believe it says about how and when to take the medication and what the drug's purpose is. Correct any misunderstandings about prescription labels and have patients or family write out, in the patient's own words, instructions for taking the medicines.

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- Keep an accurate medication list for each patient, and ask patients about medications prescribed by other physicians, as well as any over-the-counter drugs or herbal supplements. Watch for potential contraindications and superfluous medications. Update seniors' drug lists at least once or twice a year, reconcile medications after a hospital stay and routinely ask about side effects.
- Ask regularly if patients are taking their medicines, including as-needed drugs. If a prescribed medication is not being taken, it may signal that a patient had an adverse reaction to the drug. A patient's noncompliance could lead to higher doses and unintentional overdose if the senior then starts taking the drug.
- Submit adverse events to the Institute for Safe Medication Practices' National Medication Errors Reporting Program. Also, report serious problems to the Food and Drug Administration's MedWatch program.

Sources: American Geriatrics Society Foundation for Health in Aging; Sharon Brangman, MD; Institute of Medicine; Urmimala Sarkar, MD, MPH

## WEBLINK

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