

Drugs in the Elderly: Preventing Adverse Events



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The Institute of Medicine report on the quality of care, entitled “To Err Is Human,” heightened the awareness of healthcare providers and patients to the opportunities of reducing the number of adverse events in hospitals. According to the report, medical errors are responsible for a large number of deaths, additional morbidity and increased costs in healthcare facilities.¹

A large proportion of medical errors are medication-related adverse drug events (ADEs). ADEs occur across the entire healthcare delivery system and are most common in older people, particularly those in hospitals and nursing homes. ADEs, defined as “noxious and unintended patient events (*i.e.*, symptoms, signs and laboratory abnormalities) caused by a drug,” are associated with 10% to 30% of acute care hospital admissions in the elderly.²⁻⁵

The most common cause of ADEs is inappropriate medication prescribing. Medications are considered to be inappropriate when they create more risk than benefit to the individual taking them. For the elderly, the consequences of ADEs and inappropriate medication prescribing include delirium, falls and fractures, urinary incontinence and other life-threatening events. At least one inappropriate medication is prescribed in 40% of nursing home residents and 21% of the community-dwelling elderly.⁶

Appropriate prescribing

The 1993 Canadian Medical Association Policy Summary on Medication Use and the Elderly (updated in 2002) noted that the elderly in Canada had a four to seven times risk of adverse drug

Meet Sandra

Sandra is a member of a busy community medicine practice and her colleagues acknowledge her as the regional expert in geriatrics and care of the elderly.

One of her responsibilities is to be the Medical Advisor and Director of the region’s 250 bed long-term care facility. The administrators of the long-term care facility have asked for her assistance in responding to a recent accreditation citing the facility for having a higher than acceptable medication per resident ratio. The average number of medications per resident is 10.

What would her approach be in assisting the administrator and her colleagues to ensure that her regional long-term care centre maintains its accreditation?

reactions and that these contributed to at least 20% of acute care hospital admissions in Canada.⁷ Their clearly outlined principles and basic steps to appropriate prescribing for elderly people included:

- Know the patient
- Consider non-pharmacologic therapy
- Know the drugs
- Keep the drug regimen simple
- Establish treatment goals
- Encourage the patient to be a responsible medication user

As noted in their guidelines, these prescribing principles represent common knowledge that all physicians possess, but apparently do not always use.

Hogan outlined a strategy for practicing physicians to reduce polypharmacy which included:

- regularly obtaining and updating a listing of all medications being used by the patient,



- being aware of the patient's current and relevant past medical problems,
- periodically reviewing the appropriateness of the patient's medication regimen and trying to perform a "therapeutic debridement,"
- considering an adverse drug reaction as a possible cause of any new medical problem,
- considering non-pharmacologic approaches first in treatment of medical problems and
- when a new drug is prescribed, ensuring that there is a clear indication for the medication and that the dose is correct (*i.e.*, start low and go slow).⁸

More recently, Lewis described the NO TEARS tool for medication review:⁹

- **Need/indication:** has the diagnosis changed? Was long-term treatment intended? Is the dose correct?
- **Open questions:** solicit the patient's opinion and concordance
- **Tests:** assess and monitor the disease. Are further tests or investigations needed?
- **Evidence:** is there a better approach to this illness now (*e.g.*, new guidelines)?
- **Adverse effects:** consider iatrogenic problems (*i.e.*, side-effects, interactions)
- **Risk reduction:** identify the individual patient's risks
- **Simplification/switches:** simplify the regime and implement cost-effective switches

Inappropriate prescribing to seniors continues to be widespread.

Despite a variety of public policies that have been implemented in Canada to maintain and control the public expenditures for prescription drugs, inappropriate prescribing to seniors continues to be widespread.¹⁰⁻¹⁷ Some of these strategies have included the establishment of the Patented Medicines Prices Review Board, drafting of pharmaco-economic

guidelines, adoption of restricted provincial formularies, rules for drug substitution, rules for price selection, changes in co-payment amounts or deductibles for publicly funded drug benefit plans and reference-based pricing.

Pharmacokinetic changes

The pharmacokinetic changes of drug metabolism associated with aging include the absorption, distribution, metabolism and elimination of the medication. With usual aging there is a relative decrease in lean muscle and increase in central fat. Thus, the volume of distribution of some medications is decreased and consequently, these medications will attain higher plasma concentrations if they distribute into muscle or total body water. This is particularly important for medications that require loading doses. The age-associated increased fat mass can serve as a depot for lipophilic drugs, such as benzodiazepines. In addition, the potency and duration of action of many drugs are prolonged and increased due to age-associated declines in renal and hepatic function.

It is possible to identify nursing home residents at high-risk of having an ADE. Particular attention should be directed at new residents, those with multiple medical conditions, those taking multiple medications and those taking psychoactive medications, opioids, or anti-infective drugs.¹⁸

Criteria for drug-disease interactions

A Canadian report by McLeod, *et al* was the first expert panel consensus criteria for drug-disease interactions in the elderly.¹⁹ Subsequently, Beers published a set of expert panel consensus criteria for drug classes that should not be used in the elderly with certain chronic diseases.²⁰⁻²¹

The Beers criteria were originally developed in 1991 for the nursing home setting. The criteria were updated in 1997 to include all geriatric patients regardless of setting and then again in 2003 to include new evidence on the pharmacologic changes associated with aging and its impact on safety and effectiveness. The list of criteria was



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developed by a national panel of experts in geriatric care and pharmacology to include 48 medications or classes of medications to avoid in individuals ≥ 65 years and 20 medications that should not be used in older persons known to have specific conditions. Drugs were deemed inappropriate for use among the elderly population due to:

- Lack of proven efficacy, high likelihood of adverse drug effects, potential for severe effects, or a high potential for an interaction with another medication or class of drug
- Specific medications or classes of medications that should not be used routinely in elderly patients with specific disease states
- Specific medications that pose a serious risk of causing an adverse event when safer alternatives are available
- High doses of certain medications
- Excessive dosing frequencies, which complicate compliance for elderly patients
- Extended duration of medications that were intended to be used for a limited time

Many of the medications classified as inappropriate for the elderly can produce anticholinergic effects and symptoms, such as dry mouth, constipation, blurred vision, hypotension, cardiac arrhythmias, urinary retention and delirium. In general, agents that cause anticholinergic properties should be avoided in this vulnerable population.

Tune, *et al* at the Johns Hopkins School of Medicine demonstrated that 14 of the 25 most frequently prescribed drugs in geriatric medical practice have anticholinergic effects.²² Many drugs that are not classically considered to be anticholinergic, such as digoxin, theophylline and amantadine, are highly anticholinergic in *in vitro* assays. Some of these drugs (*e.g.*, digoxin) may be difficult to avoid, but the synergistic effect from their use in combination puts the patient at risk.

In addition to anticholinergic agents, the Beers criteria identify several commonly used medications that place patients at increased risk for incurring adverse events (*e.g.*, long-acting benzodiazepines, amiodarone, doxazosin, diphenhydramine, meperidine, propoxyphene and long-term use of full dose NSAIDs).

Limitations to the Beers criteria include that they:

- do not identify all cases of potentially inappropriate prescribing,
- may sometimes identify appropriate prescribing as inappropriate and
- are designed for population-based screening and not intended to substitute for professional judgement regarding the individualized needs of particular older adults.

Possible strengths of the criteria include that in the community and long-term care settings, nurses may use the criteria to increase awareness of medications that may present increased risk for adverse drug reactions and nurses, primary care providers and pharmacists may collaborate to optimize individualized medication regimens and provide appropriate clinical monitoring and education.

The prescribing cascade

The “prescribing cascade” begins when an adverse drug reaction is misinterpreted as a new medical condition. Another drug is then prescribed and the patient is placed at risk of developing additional adverse effects relating to potentially unnecessary treatment. To prevent the prescribing cascade, physicians should always consider any new signs and symptoms as a possible consequence of current drug treatment. Before any new drug treatment is started, the need for the drug should be re-evaluated and a non-drug treatment should be considered. If the medication is deemed necessary, the lowest possible dose of the drug should be used, as well as consideration given to the use of alternative drugs that have fewer adverse side-effects.²³

Underused medications

Although most research has focused on the overuse of medications, there is evolving evidence that certain medications are under prescribed in older patients (*e.g.*, the significant underuse of treatments for osteoporosis, of warfarin in the treatment of elderly patients with atrial fibrillation and β -blockers in elderly survivors of acute MI).^{24,25}



Assessing Care of Vulnerable Elders (ACOVE) project

The ACOVE project developed a method of identifying a community-based sample of vulnerable elders, selecting clinical conditions for quality measurement and developing an evidence-based set of 236 ACOVE-1 quality-of-care process indicators to evaluate the care provided to vulnerable elders. These measures are useful in identifying specific processes of care for improvement and also permit evaluation of the overall quality of care provided to vulnerable elders.^{26,27}

Knight and Avorn²⁸ have published the following quality indicators for appropriate medication use in vulnerable elders. These quality indicators form a basis for what individual prescribers, as well as patients and caregivers can do to improve prescribing.

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.

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.

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. 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.

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 six months. 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.

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.

Monitoring warfarin therapy

If a vulnerable elder is prescribed warfarin, then an INR should be determined within four days after initiation of therapy and at least every six 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.

Monitoring of diuretic therapy

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

Avoid the use of chlorpropamide

If a vulnerable elder is prescribed an oral diabetic hypoglycemic drug, then chlorpropamide should not be used. 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.

Avoid anticholinergic drugs if 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.

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 fractures in older women.

Avoid meperidine

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.

Monitoring renal function and potassium in patients prescribed ACE inhibitors

If a vulnerable elder begins receiving an ACE inhibitor, then serum potassium and creatinine levels should be checked within one week of initiation of therapy. This may prevent the development of renal insufficiency and hyperkalemia.

Medication appropriateness

Hayley, *et al* have recently proposed a framework that may be helpful in the decisions involving the discontinuation or withholding of medications late in life for the frail elderly.²⁹ They suggest deliberations in the context of the individual's remaining life expectancy, time until benefit from the treatment, individual goals of care and treatment targets.

This model focuses on issues around medication use late in life that are not adequately considered with existing models of medication appropriateness and therefore might be used to develop guidelines aimed at reducing polypharmacy in patients who may have a limited life expectancy. The authors acknowledge

possible limitations in the model, which include:

- It is a time-consuming way of approaching pharmacotherapy
- Patients and family members may have difficulty making decisions about complex clinical situations and many doctors may have difficulty providing patients with the information needed to make decisions
- Provision of rational prescribing recommendations in the elderly are hindered by their lack of adequate representation in clinical trials and trial duration may be inadequate, making the concept of time until benefit difficult to apply for many medicines

Conclusions

In a recent systematic review of inappropriate prescribing in the elderly, Garcia noted that only a handful of randomized controlled trials have been conducted on the topic and that none of the trials involved people ≥ 85 -years-of-age.³⁰ In this review, the methods and practice recommendations to reduce inappropriate prescribing in the elderly that were supported by some evidence included:

- Obtain pharmacist recommendations to reduce inappropriate prescribing and ADEs
- In the inpatient setting, use computerized alerts to reduce serious medication errors and help prevent ADEs
- Review a patient's medications to reduce polypharmacy and inappropriate prescribing
- Educate patients to improve compliance with medications, reduce polypharmacy, reduce inappropriate prescribing and decrease ADEs
- Consider using the Beers criteria for avoiding inappropriate drugs in the elderly

Administrators, policy makers, physicians and other professionals now have access to the knowledge on which to build programs that can improve the effectiveness and efficiency of prescribing practice and result in a reduction of inappropriate prescribing and medication-related adverse patient events in the elderly.

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For references, please contact cme@sta.ca