POLYPHARMACY: OPTIMIZING MEDICATION USE IN ELDERLY PATIENTS

Debbie Kwan, BScPhm, MSc, FCSHP, *(Debbie.kwan@uhn.ca) is a pharmacist with the Toronto Western Family Health Team, University Health Network, and an assistant professor (status only) with the Leslie Dan Faculty of Pharmacy and Department of Family and Community Medicine, University of Toronto in Ontario.*

Barbara Farrell, BScPhm, PharmD, FCSHP, *(bfarrell@bruyere.org) is a pharmacist with the Bruyère Continuing Care Geriatric Day Hospital; clinical and research coordinator for the Pharmacy Department, Bruyère Continuing Care; scientist, Bruyère Research Institute; and assistant professor in the Department of Family Medicine, University of Ottawa in Ontario. She is also an adjunct assistant professor at the School of Pharmacy, University of Waterloo in Ontario.*

Originally published in *Pharmacy Practice* 2013;Apr/May:20–25. Available from www.CanadianHealthcareNetwork.ca. Reprinted with permission.

Mrs. Archibald, a 92-year-old woman, has been a customer at your pharmacy for many years. When her son, Ken, comes in to pick up her monthly blister packs, you tell him that she's been started on another medication and she now needs to use two blister packs daily to hold all of her 17 medications. Ken sighs heavily and says it's hard to get her to take the medications she already has. She's getting dizzy and confused, her nausea is worse, and she hardly eats. She's had several falls recently and is now afraid to go out.

The elderly represent one of the fastest growing segments of the population and their use of medication is increasing significantly. In Ontario, from 1997–2006, the population older than 65 years of age increased by 18% while their claims to the provincial drug benefit program increased by 214%.[1] The Canadian National Population Health Survey recently showed that 53% of seniors living in healthcare institutions, and 13% of those living in the community use five or more medications, with older seniors taking more medications than younger seniors.[2] This is consistent with Canadian Institute for Health Information data that show 23% of those older than 65 years of age and 30% of those older than 85 years of age had claims for 10 or more drug classes in 2009.[3] Mrs. Archibald's medication load is not that unusual.

The term polypharmacy refers to the use of multiple medications, typically five or more.[4] Recently, it has been used to describe the use of inappropriate medications, or more medications than clinically indicated. The prevalence of inappropriate medication use in the elderly ranges from 11.5%–62.5%.[5] Consequences of polypharmacy include adverse drug reactions and interactions, nonadherence, increased risk of cognitive impairment, impaired balance and falls, and increased risk of morbidity, hospitalization, and mortality.[6-11]

In a recent Canadian study, almost half of the 27% of seniors regularly taking five or more medications experienced an adverse effect requiring medical attention.[4] Of 661 community-dwelling seniors surveyed, 25% reported an adverse effect, with one-third of these considered ameliorable and 11% preventable; an increased number of medications was associated with an increased risk of adverse reactions.[12] Adverse drug reactions account for a significant portion of emergency room visits and hospitalizations—many preventable if they had been identified earlier.[13,14] Ultimately, the more medications taken, or the more potentially inappropriate medications prescribed, the higher the likelihood of serious adverse effects requiring medical attention.[15-17]

Why Are the Elderly at Risk for Polypharmacy and Adverse Drug Reactions?

As people age, they develop more chronic conditions, often resulting in more medications prescribed.[18] Prescribers are often reluctant to change drugs other prescribers (specialists or hospitalists) have started, and may have difficulty recognizing medication side effects, thus increasing the risk of prescribing cascades (ie, new medications added to manage side effects).[19] Pharmacokinetics and pharmacodynamics also change as people age, and very few clinical studies have been conducted in the elderly.

Age-Related Changes

With advancing age, progressive functional decline in organ systems (eg, kidney, liver) leads to changes in the way medications are handled and expressed.[20] Pharmacokinetic changes are outlined in Table 1.[20-22] As little pharmacokinetic data are available for the elderly, we must make assumptions about what drugs might be affected.

Pharmacodynamic changes (ie, physiologic and biochemical effects of drugs on the body) with aging include increased sensitivity to cardiovascular medications, anticoagulants, opioid analgesics, antipsychotics, and benzodiazepines.[20] Altered concentrations of neurotransmitters and receptors, as well as altered receptor binding properties and responsiveness, are thought to contribute to pharmacodynamic changes resulting in exaggerated drug effects. Functional reserves decline with age, affecting the cardiovascular, musculoskeletal, and central nervous systems; this

Table 1. Pharmacokinetic Changes with Age[20-22]

Parameter	Mechanism	Examples
Absorption	Decreased active transport decreases bioavailability for some drugs	Calcium with achlorhydria
	Reduced first-pass metabolism (reduced liver mass and blood flow) increases bioavailability of some drugs	Metoprolol Propranolol Nortriptyline Calcium channel blockers Tricyclic antidepressants
Distribution	Increased body fat prolongs half-life of fat-soluble drugs	Diazepam Amitriptyline
	Decreased body water increases serum concentration of water-soluble drugs	Digoxin Ethanol Levodopa Morphine
Metabolism	Hepatic disease or reduced hepatic volume and blood flow results in reduced oxidative metabolism (reduced metabolism through CYP450) and higher steady-state concentrations of some drugs	Diazepam Metoprolol Phenytoin Theophylline Alprazolam
Excretion	Decreased cardiac output (eg, in heart failure) results in less perfusion of kidneys and liver, which reduces elimination of high extraction ratio drugs	Imipramine Morphine Propranolol
	Reduced kidney function reduces elimination of renally excreted drugs or metabolites	Digoxin Cephalexin Morphine Meperidine Gabapentin Sotalol Lisinopril Ramipril Diuretics Metformin

can also predispose the elderly to exaggerated drug effects. Impaired homeostatic mechanisms can result in more pronounced side effects (eg, orthostatic hypotension with antihypertensives) or lack of compensatory responses (eg, impaired reflex tachycardia, impaired regulation of temperature and electrolytes).[20,23,24]

Patients previously stabilized on certain doses of medications may gradually begin to develop side effects over time because of these various changes. These side effects may be mistaken for new diseases, with new medications added for treatment.

Lack of Evidence for Medication Use in the Elderly

The elderly are underrepresented in drug trials, yet they are the greatest consumers of medications.[25-28] A study examining randomized controlled trials of four commonly used medications found that the proportion of older patients (> 65 y) enrolled was significantly lower than the proportion in the average population; of 155 trials, only three dealt exclusively with the elderly.[29] Despite the higher prevalence of many conditions (eg, hypertension, diabetes) in the elderly, exclusion criteria limit their enrollment in trials. The "healthy elderly" subjects included in clinical trials do not represent the population that would typically use these medications. Therefore, despite the wealth of guidelines available for chronic disease states (eg, hypertension, diabetes, cardiovascular disease), few specifically address how to approach the very old or frail elderly.[30,31] Adhering to guidelines often results in the addition of medications without considering remaining life expectancy, goals of care, and time to potential benefit of medications.[32]

Ken is clearly worried about his mom. You wonder whether her recent symptoms could be drug induced. You offer to take a closer look to see if any medications might be causing problems and whether her regimen can be simplified. You book an appointment to visit his mom at home and Ken happily pays the fee. He says having someone review all of her medications and work with the family doctor would be a great help.

Strategies for Reducing Polypharmacy

Pharmacists can take many practical and relatively easy steps to help reduce polypharmacy and promote medication adherence. Conducting a medication review for an older person taking many medications can be challenging but rewarding. Providing education and medication reduction suggestions to prescribers can reduce the overall number of medications and inappropriate medications.[33,34] Stopping medications is an effective and safe approach to reducing polypharmacy.[35,36] Interventions such as computerized decision-support systems and pharmacist involvement in multidisciplinary teams (eg, geriatric medicine services) can also positively affect prescribing.[37,38]

Step 1. Determine "Can This Be Caused by a Drug?"

One of the simplest ways to address polypharmacy is to use screening criteria to help identify potentially inappropriate medications (PIMs) in the elderly: medications with no clear evidence-based indications; medications that carry a substantially higher risk of adverse effects; or medications that are not cost- effective. Two commonly used screening tools are the Beers and STOPP criteria (Table 2[8,39,40]), which differ slightly in content and sensitivity for detecting drug-related problems. They can be applied manually by visually comparing a patient's medication list to each set of criteria or they can be incorporated into clinical decision support systems that flag PIMs at the time of prescribing. A strong association exists between medications listed in Beers and STOPP and poor patient outcomes (eg, adverse reactions, hospitalization, mortality).[39] Using these criteria does not replace the need for clinical judgment and understanding of a patient's values and needs; sometimes a PIM might be appropriate if the benefits outweigh the risks.

A quick check tells you that Mrs. Archibald is taking three medications that appear on both the Beers and STOPP lists: lorazepam, metoclopramide, and glyburide.

Considering whether a patient's abnormal signs or symptoms might be

Table 2. Beers and STOPP Criteria[8,39,40]

	Beers Criteria	STOPP Criteria
Origin	• Consensus list developed in 1991 by Dr. Mark Beers • Initially intended for elderly nursing home residents • Modified and adapted for different populations, including community-dwelling populations • Updated (2012) using an evidence-based approach	• Consensus list developed in 2004 • Designed to address some of the deficiencies of early versions of Beers
Format	• Fifty-three medications or classes; now divided into three tables in a database format that allows for continual upgrading: 1) medications to avoid regardless of diseases or conditions 2) medications considered inappropriate when used in patients with certain diseases or syndromes 3) medications to be used with caution	• Sixty-five clinically significant criteria for inappropriate prescribing, grouped by physiological system and including clinical context and stopping rules
Access	• Website: www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2012 • Hosts multiple user-friendly downloadable tools (eg, evidence charts)	• Website: www.biomedcentral. com/imedia/3973756062468072/ supp1.doc
Clinical utility	• Used to evaluate prevalence of PIMs, quality of care, associations with adverse reactions • Ongoing research to determine clinical impact of applying Beers criteria to patient populations	• Used to evaluate prevalence of PIMs, quality of care, medication appropriateness, associations with adverse reactions • Ongoing research to determine clinical impact of applying STOPP criteria to patient populations

PIMs—potentially inappropriate medications, STOPP—Screening Tool of Older Person's Prescriptions.

Table 3. Common Geriatric Presentations That Can Be Caused by Drugs

Signs or Symptoms	Common Drug-Related Causes
Falls	Sedatives, hypnotics, anticholinergics, antihypertensives, antidepressants, antidiabetics[10,42,43]
Cognitive impairment	Anticholinergics, benzodiazepines, antihistamines, tricyclic antidepressants[44,45]
Incontinence	Alpha-blockers, antidepressants, sedatives (eg, benzodiazepines), diuretics[46]
Constipation	Anticholinergics, opioids, tricyclic antidepressants, calcium channel blockers, calcium supplements[47]
Delirium	Antidepressants, antipsychotics, antiepileptics[48]
Diarrhea	Antibiotics, proton pump inhibitors, allopurinol, selective serotonin reuptake inhibitors, angiotensin II receptor blockers, psycholeptics (anxiolytics, antipsychotics)[49]
Gastrointestinal bleeding	Nonsteroidal anti-inflammatory drugs, oral anticoagulants[50]

the result of a medication, whether it is a PIM or not, is a key step in determining which drugs might be causing problems. Linking potential side effects with causative drugs requires knowledge of the pharmacology of each drug, its known side effects, and the time of onset in relation to starting the drug. This approach is consistent with the "therapeutic thought process" developed by Winslade and Bajcar.[41] Keep in mind that some side effects can manifest gradually as pharmacokinetic and dynamic parameters change in an individual, or quickly if parameters change rapidly during acute illness. Medications that may contribute to common geriatric presentations are outlined in Table 3.[10,42-50]

You think about Mrs. Archibald's recent symptoms—dizziness, falls, confusion, and nausea—and believe they might be related to her medications. Lorazepam could be causing dizziness, confusion, and falls. The many antihypertensive medications she is taking can all reduce blood pressure, which might result in dizziness, and hence falls. With a few questions, you determine that the nausea started soon after her metformin dose was increased. That's when the metoclopramide was started. Is this a prescribing cascade?

Prescribing cascades occur as a result of treating side effects of medications.[51] For example, furosemide prescribed for a patient might cause urinary frequency. Oxybutynin is prescribed to manage the urinary frequency. Oxybutynin leads to confusion and behavioural disturbances and an antipsychotic is prescribed. As the list of medications grows, it becomes more difficult to sort out which medications were prescribed to treat medical syndromes as opposed to drug-related adverse effects. Ultimately, the cumulative effects of multiple medications can lead to more serious complications (eg, falls, delirium). Identifying and dealing with prescribing cascades requires a thorough history, including the timing of new symptom onset in relation to medication starts or changes. Table 4 lists some common prescribing cascades the authors have seen in practice.

Step 2. Determine Which Drugs Are Still Providing Benefit

Determining which medications are still providing benefit can be more challenging than identifying PIMs. This is an important step in the pharmacotherapy workup described by Cipolle et al.[52] A good initial approach is to ask about the symptoms (eg, pain, sleep) for which each symptom-based drug is being used. Next, look at signs (eg,

Table 4. Examples of Prescribing Cascades

• Ibuprofen → hypertension → antihypertensive
• Metoclopramide → parkinsonism → levodopa/carbidopa
• Risperidone → parkinsonism → benztropine
• Amlodipine → edema → furosemide
• Gabapentin → edema → furosemide
• Ciprofloxacin → delirium → risperidone
• Lithium → tremor → propranolol
• Bupropion → insomnia → mirtazapine
• Donepezil → urinary incontinence → oxybutynin
• Amiodarone → tremor → lithium
• Venlafaxine → tremor → diazepam
• Meperidine → delirium → risperidone
• Beta-blocker → depression → antidepressant
• Amitriptyline → decreased cognition → donepezil
• Narcotic → constipation → sennosides
• Sennosides → diarrhea → loperamide
• Lorazepam → morning drowsiness → caffeine
• Enalapril → cough → dextromethorphan
• Furosemide → hypokalemia → potassium supplement
• Nonsteroidal anti-inflammatory drug → heartburn → H_2-antagonist or proton pump inhibitor
• Omeprazole → low B12 → B12 supplement

Table 5. Drugs Commonly Associated With Adverse Drug Withdrawal Events[58,59]

Drug	Suggested Monitoring for Withdrawal Effects
Amlodipine	↑ BP
Anticonvulsants	Anxiety, depression, seizures
Antidepressants (eg, citalopram, venlafaxine, mirtazapine, amitriptyline)	Early: chills, malaise, sweating, irritability, insomnia, headache Late: depression recurrence
Antipsychotics	Insomnia, restlessness, hallucinations, nausea
Baclofen	Agitation, confusion, nightmares, ↑ spasms or rigidity
Beta-blockers	↑ HR, ↑ BP, angina, anxiety
Corticosteroids	Anorexia, ↓ BP, nausea, weakness, ↓ blood glucose
Digoxin	Palpitations, ↑ HR
Diuretics (eg, furosemide, hydrochlorothiazide)	↑ Pedal edema, chest sounds, SOBOE, ↑ weight
Gabapentin (eg, for pain)	↑ Pain, ↑ PRN use, mobility changes
Hypnotics (eg, lorazepam, zopiclone)	Poor sleep, ↑ anxiety, agitation, tremor
Narcotics	↑ Pain, ↑ PRN use, mobility changes, insomnia, anxiety, diarrhea
NSAIDs	↑ Pain, ↑ PRN use, mobility changes
PPIs, domperidone	Rebound heartburn, indigestion
Transdermal nitroglycerin	Angina, ↑ BP

BP—blood pressure, HR—heart rate, NSAIDs—nonsteroidal anti-inflammatory drugs, PPIs—proton pump inhibitors, PRN—as needed, SOBOE—shortness of breath on exertion, ↑—increase, ↓—decrease.

blood pressure, blood glucose) to help determine whether medications used to treat hypertension and diabetes are needed. Keep in mind the need for more conservative blood pressure and diabetes targets in the frail elderly to reduce the risk of hypotension and hypoglycemia, respectively.[53-56]

In discussion with Mrs. Archibald, you find out that metoclopramide has not helped her nausea. You also discover that she started taking glyburide regularly again at the same time as her metformin dose was increased. She had been taking glyburide sporadically previously. When the doctor said her diabetes was out of control, and the pharmacist started making blister packs for her, she decided to start taking everything again. Her blood sugar log shows several recent readings between 3 and 4 when she gets up in the morning. You check her blood pressure to find that it's 105/60. She's taking four antihypertensives.

Assessing the continued benefit of preventive medications is likely the hardest step. As noted earlier, few clinical trials included frail elderly individuals, so we know little about benefit versus risk in this population. For example, in situations of no other compelling indication (eg, angina, atrial fibrillation), the proven benefit of a beta-blocker post-myocardial infarction, in terms of reducing cardiovascular mortality, has been shown for only two years, yet guidelines recommend indefinite therapy.[57] Appropriate duration of treatment for acute conditions is also often unclear. For example, four to eight weeks of proton pump inhibitor therapy is adequate for uncomplicated reflux or ulcers, yet many patients take them daily for years.

Step 3. Prioritize Drugs for Tapering and Stopping, Develop a Plan, Coordinate and Communicate with Prescriber and Patient

When deciding which medications to stop first, it is important to balance clinical impact (eg, reduction in side effects) with the risk of adverse drug withdrawal events (ADWEs, defined as clinically significant signs or symptoms caused by stopping a drug).[58] They can manifest as physiologic withdrawal reactions (eg, tachycardia with beta-blocker discontinuation), appearance of new symptoms (eg, sweating with antidepressant withdrawal), or exacerbation of an underlying condition (eg, worsening angina after stopping nitrates).[58] Table 5[58,59] lists drugs that often have ADWEs. Factors that make ADWEs more likely are long duration of use (eg, benzodiazepines), higher dose (eg, corticosteroids), and short half-life (eg, paroxetine). Patient risk factors include a history of drug dependence or abuse and lack of buy-in. Certain medications are often tapered to reduce the incidence and severity of ADWEs. To successfully discontinue unnecessary or inappropriate medications, it is important to know which drugs can be stopped abruptly and those that should be tapered.

It can be challenging to get patient and prescriber acceptance of the need to reduce medication dose, or discontinue or "deprescribe" unnecessary medications. Patient buy-in is important; in the absence of any acute adverse medication effects, collaboration with the patient can assist in deciding which medications to stop first. Asking a few simple questions can facilitate this process:

- What questions do you have about your medications?
- Which medications do you feel most strongly about keeping?

- Which medications do you wonder about with respect to how well they're working for you?

Talk about the goals of care with the patient, family, and physician. Typically, in the very elderly, goals are to maintain and improve physical function (eg, activities of daily living), psychological function (eg, cognition, depression), social function (eg, social activities, support systems), and overall health (eg, general health perception).

Mrs. Archibald repeats that the metoclopramide does not help her nausea. Her appetite is terrible and she does not want to go out with friends. She wants to keep acetaminophen—it effectively treats her knee pain and helps her get around the house. Her diabetes, diagnosed three years ago, is not a big bother; she doesn't think she needs all that medication. You start preparing a note to Mrs. Archibald's family physician. It's important to inform the physician that metoclopramide did not improve Mrs. Archibald's nausea. You suggest lowering the dose gradually and stopping metoclopramide over the next couple of weeks. Metoclopramide would be a good medication to prioritize tapering because of its potential to cause Parkinson-type symptoms (which you learned from the Beers and STOPP criteria). You include in your note that Mrs. Archibald's nausea started soon after the metformin dose was increased, which coincided with her starting to take all of her diabetes medications again; it is severely affecting her quality of life. You note her recent low blood sugars and suggest reducing metformin back to the previous dose and switching glyburide to an equivalent dose of once-daily gliclazide MR to reduce the risk of hypoglycemia. You note that you will ask Mrs. Archibald to continue to monitor her nausea and blood glucose, and you will update the physician with changes.

When preparing patients for medication discontinuation, make sure to offer safer alternatives, including nonpharmacologic approaches (eg, distraction techniques for pain management, sleep hygiene approaches instead of sedatives). Prepare patients by discussing anticipated withdrawal effects and involve them in monitoring for ADWEs. Let the patient know that several attempts at withdrawal may be needed. Regular follow-up will also provide support and reassurance. Use a variety of communication tools including verbal and written, and use tapering calendars for more complicated cases.

After successfully stopping metoclopramide and eliminating the nausea and low blood sugar readings by reducing the metformin dose and changing from glyburide to gliclazide, Mrs. Archibald calls to thank you. She is still dizzy, tired, and confused during the day and wonders if her medications might be the cause. Her low blood pressure, as well as lorazepam, might be contributing. When you mention the latter, she says no one has ever told her that sleeping pills might cause confusion. She tried to stop them once, but had trouble sleeping so she just kept taking them. You explain the natural history of rebound insomnia and that it improves within days of stopping. She's willing to try again and agrees to taper the dose. You call to update the family physician about this plan. You also discuss using a higher blood pressure target range, especially in light of her hypotension and dizziness. Her physician agrees to begin tapering doses of her antihypertensives. With the agreement of the patient and family physician, you email a lorazepam and antihypertensive tapering plan to her son, with a handout of withdrawal reactions to expect and information on an appropriate blood pressure target range.

Table 6. Key Resources for Individualizing Therapy and Reducing Polypharmacy in the Elderly

- Beers Criteria and STOPP (Screening Tool of Older Person's Prescriptions) Criteria (see Table 2)
- Rx Files: Drug treatment in the elderly and long-term care. Available from www.rxfiles.ca/rxfiles/Modules/ltc/ltc.aspx
- A practical guide to stopping medications in older people. Best Practice Journal 2012;27(April). Available from www.bpac.org.nz/magazine/2010/april/stopGuide.asp
- Medication Appropriateness Index: Hanlon JT, Schmader KE, Samsa GP, et al. A method for assessing drug therapy appropriateness. J Clin Epidemiol 1992;45:1045-51
- Palliative Geriatric Practice algorithm: Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy. Arch Intern Med 2010;170:1648-54
- Cruz-Jentoft A, Boland B, Rexach L. Drug therapy optimization at the end of life. Drugs Aging 2012;29:511-21
- Patterson S, Hughes C, Kerse N, et al. Interventions to improve the appropriate use of polypharmacy for older people. Cochrane Database Syst Rev 2012; Issue 5
- Gnjidic D, Le Couteur D, Kouladjian L, et al. Deprescribing trials: methods to reduce polypharmacy and the impact on prescribing and clinical outcomes. Clin Geriatr Med 2012;28:237-53
- Scott I, Gray L, Martin J, et al. Minimizing inappropriate medications in older populations: a 10-step conceptual framework. Am J Med 2012;125:529-37
- Alexander GC, Sayla MA, Holmes HM, et al. Prioritizing and stopping prescription medications. CMAJ 2006;174:1083-4
- Rudolph J, Salow M, Angelini M, et al. The anticholinergic risk scale and anticholinergic adverse effects in older persons. Arch Intern Med 2008;168:508-13
- Recommended journals:
  - *Drugs and Aging*
  - *Age and Aging*
  - *Clinics in Geriatric Medicine*

Step 4. Simplify to Reduce Pill Burden

Pill burden usually refers to the total number of pills or doses a patient must swallow during the day. Mrs. Archibald's original 17 medications carried a pill burden of 36 tablets or capsules daily. Complex regimens and poor timing or unnecessary separation of multiple medications can lead to errors in medication administration; they may also affect quality of life, as patients feel they cannot vary from their strict regimen and sometimes feel too full of medication to eat. Patients may complicate high pill burden regimens by creating more complex dosage schedules (eg, 7 times a day instead of qid), especially when medication instructions vary in wording (eg, twice daily vs every 12 hours).[60] Stopping or tapering unnecessary medications decreases the potential for adverse drug events and interactions; it also reduces pill burden, which may simplify medication scheduling.

Once unnecessary and side-effect causing medications have been stopped, steps to further reduce pill burden and enhance adherence include using combination products (eg, diuretic + another antihypertensive; cholesterol-lowering drug + antihypertensive; two hypoglycemics) or switching from multiple-times-daily to once-daily formulations.[61,62]

After checking with Mrs. Archibald every couple of weeks and working closely with her family doctor, your patient has been able to stop lorazepam and significantly reduce her antihypertensives. By combining several medications, you've reduced her number of medications to 9 and her pill burden to 16, now taken twice daily instead of four times daily—with only one blister pack! She is feeling much better, eating normally, and has started going out again to her various activities.

Conclusion

Polypharmacy is a growing problem in scope and impact. By 2036, one in four Canadians will be older than 65 years of age; this growing demographic is at risk for drug therapy problems.[63] With recent regulatory and reimbursement changes, pharmacists are even more well-placed to actively participate in optimizing therapy in the elderly. Helpful resources to assist pharmacists in individualizing therapy and reducing polypharmacy in the elderly are presented in Table 6. Pharmacists must share responsibility with prescribers and patients to ensure that potentially inappropriate medications are minimized, appropriate medications and doses are used, side effects are not treated with more medication without first investigating medication-related causes, and pill burden is minimized.

References

1. Bajcar JM, Wang L, Moineddin R, et al. From pharmaco-therapy to pharmaco-prevention: trends in prescribing to older adults in Ontario, Canada, 1997-2006. BMC Family Practice 2010;11:75-80.
2. Ramage-Morin P. Medication use among senior Canadians. Health Reports 2009;20(1):catalogue no. 82-003-XPE.
3. Canadian Institute for Health Information. Chapter 3: Primary health care and prescription drugs – key components to keeping seniors healthy. In: Health Care in Canada, 2011: a focus on seniors and aging. Ottawa, ON: Canadian Institute for Health Information; December 2011. https://secure.cihi.ca/free_products/HCIC_2011_seniors_report_en.pdf (accessed January 17, 2013).
4. Reason B, Terner M, McKeag AM, et al. The impact of polypharmacy on the health of Canadian seniors. Family Practice 2012;29:427-32.
5. Guaraldo L, Cano FG, Damasceno GS, et al. Inappropriate medication use among the elderly: a systematic review of administrative databases. BMC Geriatr 2011;11:79.
6. Salazar JA, Poon I, Nair M. Clinical consequences of polypharmacy in elderly: expect the unexpected, think the unthinkable. Expert Opin Drug Saf 2007;6:695-704.
7. Shah B, Hajjar E. Polypharmacy, adverse drug reactions and geriatric syndromes. Clin Geriatr Med 2012;28:173-86.
8. The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60:616-31.
9. Hayes BD, Klein-Schwartz W, Barrueto F. Polypharmacy and the geriatric patient. Clin Geriatr Med 2007;23:371-90.
10. Huang A, Mallet L, Rochefort C, et al. Medication-related falls in the elderly–causative factors and preventive strategies. Drugs Aging 2012;29:359-76.
11. Hajjar ER, Cariero AC, Hanlon JT. Polypharmacy in elderly patients. Am J Ger Pharmacol 2007;5:345-51.
12. Gandhi T, Weingart S, Borus J, et al. Adverse drug events in ambulatory care. NEJM 2003;348:1556.
13. Zed P, Abu-Laban R, Balen R, et al. Incidence, severity and preventability of medication-related visits to the emergency department: a prospective study. CMAJ 2008;178:1563-9.
14. Budnitz D, Lovegrove M, Shehab N, et al. Emergency hospitalizations for adverse drug events in older Americans. NEJM 2011;365:2002-12.
15. Wu C, Bell C, Wodchis W. Incidence and economic burden of adverse drug reactions among elderly patients in Ontario emergency departments, a retrospective study. Drug Safety 2012;35:769-81.
16. Stockl K, Le L, Zhang S, et al. Clinical and economic outcomes associated with potentially inappropriate prescribing in the elderly. Am J Manag Care 2010;16:e1-e10.
17. Hohl CM, Nosyk B, Kuramoto L, et al. Outcomes of emergency department patients presenting with adverse drug events. Ann Emerg Med 2011;58:270-9.
18. Canadian Institute for Health Information. Seniors and the health care system: what is the impact of multiple chronic conditions? Ottawa, ON: Canadian Institute for Health Information; January 2011. https://secure.cihi.ca/free_products/air-chronic_disease_aib_en.pdf (accessed January 17, 2013).
19. Anthierens S, Tansens A, Petrovic M, et al. Qualitative insights into general practitioners' views on polypharmacy. BMC Family Practice 2010;11:65.
20. Sera LC, McPherson ML. Pharmacokinetics and pharmacodynamic changes associated with aging and implications for drug therapy. Clin Geriatr Med 2012;28:273-86.
21. Zeeh J, Platt D. The aging liver: structural and functional changes and their consequences for drug treatment in old age. Gerontology 2002;48:121-7.
22. Catananti C, Liperoti R, Settanni S, et al. Heart failure and adverse drug reactions among hospitalized older adults. Clin Pharmacol Ther 2009;86:307-10.
23. Hajjar ER, Gray SL, Guay DR, et al. Chapter 11. Geriatrics. In: Talbert RL, DiPiro JT, Matzke GR, et al, eds. Pharmacotherapy: a pathophysiologic approach. 8th ed. New York: McGraw-Hill; 2011. http://accesspharmacy.com/content.aspx?aid=7967419 (accessed January 17, 2013).
24. Petrovic M, van der Cammen T, Onder G. Adverse drug reactions in older people: detection and prevention. Drugs Aging 2012;29:453-62.
25. Van Spall H, Toren A, Kiss A, et al. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. JAMA 297;1233-40.
26. Dodd K, Saczynski J, Zhao Y, et al. Exclusion of older adults and

women from recent trials of acute coronary syndromes. J Am Geriatr Soc 2011;59:506-11.
27. Zulman D, Sussman J, Chen X, et al. Examining the evidence : a systematic review of the inclusion and analysis of older adults in randomized controlled trails. J Gen Intern Med 2011;26:783-90.
28. Cherubini A, Oristrell J, Pia X, et al. The persistent exclusion of older patients from ongoing clinical trials regarding heart failure. Arch Intern Med 2011;171:550-6.
29. Konrat C, Boutron I, Trinquart L, et al. Underrepresentation of elderly people in randomized controlled trials. The example of trials of 4 widely prescribed drugs. PLoS One 2012;7(3):e33559.
30. Hilmer S, Gnjidic D, Abernethy D. Pharmacoepidemiology in the postmarketing assessment of the efficacy and safety of drugs in older people. J Gerontol A Biol Sci Med Sci 2012;67:181-8.
31. Wehling M. Guideline-driven polypharmacy in elderly multimorbid patients is basically flawed. JAGS 2011;58:376-7.
32. Holmes H, Hayley DC, Alexander GC, et al. Reconsidering medication appropriateness for patients late in life. Arch Intern Med 2006;166:605-9.
33. Zarowitz BJ, Stebelsky LA, Muma BK, et al. Reduction of high-risk polypharmacy drug combinations in patients in a managed care setting. Pharmacotherapy 2005;25:1636-45.
34. Spinewine A, Fialova D, Byrne S. The role of the pharmacist in optimizing pharmacotherapy in older people. Drugs Aging 2012;29:495-510.
35. Iyer S, Naganathan V, McLachlan AJ, et al. Medication withdrawal trials in people aged 65 years and older: a systematic review. Drugs Aging 2008;25:1021-31.
36. Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults. Arch Intern Med 2010;170:1648-54.
37. Kaur S, Mitchell G, Vitetta L, et al. Interventions that can reduce inappropriate prescribing in the elderly. Drugs Aging 2009;26:1013-28.
38. Topinkova E, Baeyens JP, Michel JP, et al. Evidence-based strategies for the optimization of pharmacotherapy in older people. Drugs Aging 2012;29:477-94.
39. O'Mahony D, Gallagher P, Ryan C, et al. STOPP and START criteria: a new approach to detecting potentially inappropriate prescribing in old age. Eur Geriatr Med 2010:1:45-51.
40. Gallagher P, Ryan C, Byrne S, et al. STOPP (Screening tool of older person's prescriptions) and START (Screening tool to alert doctors to right treatment). Consensus validation. Int J Clin Pharmacol Ther 2008;46(2):72-83.
41. Winslade N, Bajcar J. Therapeutic thought process algorithm. Ottawa, ON: National Association of Pharmacy Regulatory Authorities; c2009. www.napra.org/Content_Files/Files/algorithm.pdf (accessed January 17, 2013).
42. Ziere G, Dieleman J, Hofman A, et al. Polypharmacy and falls in the middle age and elderly population. Br J Clin Pharmacol 2006;61:218-23.
43. Allain H, Bentue-Ferrer D, Polard E, et al. Postural instability and consequent falls and hip fractures associated with use of hypnotics in the elderly: a comparative review. Drugs Aging 2005;22:749-65.
44. Tannenbaum C, Paquette A, Hilmer S, et al. A systematic review of amnestic and non-amnestic mild cognitive impairment induced by anticholinergic, antihistamine, GABAergic and opioid drugs. Drugs Aging 2012;29:639-58.
45. Wright R, Roumani Y, Boudreau R, et al. Effect of central nervous system medication use on decline in cognition in community-dwelling older adults: findings from the Health, Aging and Body Composition Study. J Am Geriatr Soc 2009;57:243-50.
46. Tsakiris P, Oelke M, Michel MC. Drug-induced urinary incontinence. Drugs Aging 2008;25:541-9.
47. Toney RC, Wallace D, Sekhon S, et al. Medication induced constipation and diarrhea. Practical Gastroenterology 2008 (May):12-28. www.practicalgastro.com/pdf/May08/PG_May08ToneyArticle.pdf (accessed January 17, 2013).
48. Wierenga P, Buurman B, Parlevliet J, et al. Association between acute geriatric syndromes and medication-related hospital admissions. Drugs Aging 2012;29:691-9.
49. Pilotto A, Franceschi M, Vitale D, et al. The prevalence of diarrhea and its association with drug use in elderly outpatients: a multicenter study. Am J Gastroenterol 2008;103:2816-23.
50. Lanza FL, Chan FKL, Quigley EMM. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol 2009;104:728-38.
51. Rochon AP, Gurwitz JH. Optimizing drug treatment for elderly people: the prescribing cascade. Br Med J 1997;315:1096.
52. Cipolle RD, Strand LM, Morley PC, eds. Pharmaceutical care practice: the clinician's guide. New York: McGraw-Hill; 2004.
53. Laubscher T, Regier L, Bareham J. Diabetes in the frail elderly – individualization of glycemic management. Can Fam Physician 2012;58:543-6.
54. Kirkman MS, Jones Briscoe V, Clark N, et al. Diabetes in older adults: a consensus report. JAGS 2012;60:2342-56.
55. Farrell B, Monahan A, Dore N, et al. Piloting a geriatric day hospital approach to targeting blood pressures in the very old. (article submitted to Canadian Family Physician)
56. Aronow WS. Treating hypertension in older adults. Drug Safety 2009;32:111-8.
57. Bangalore S, Steg G, Deedwania P, et al. Beta blocker use and clinical outcomes in stable outpatients with and without coronary artery disease. JAMA 2012;308:1340.
58. Graves T, Hanlon JT, Schmader KE, et al. Adverse events after discontinuing medications in elderly outpatients. Arch Intern Med 1997;157:2205-10.
59. Bain KT, Holmes HM, Beers MH, et al. Discontinuing medications: a novel approach for revising the prescribing stage of the medication-use process. JAGS 2008;56:1946-52.
60. Wolf MS, Curtis LM, Waite K, et al. Helping patients simplify and safely use complex prescription regimens. Arch Intern Med 2011;171:300-5.
61. Bangalore S, Kamalakkannan G, Parkar S, et al. Fixed-dose combinations improve medication compliance: a meta-analysis. Am J Med 2007;120:713-9.
62. Leichter SB, Thomas S. Combination medications in diabetes care: an opportunity that merits more attention. Clin Diabetes 2003;21:175-8.
63. Statistics Canada. A portrait of seniors in Canada. www.statcan.gc.ca/ads-annonces/89-519-x/index-eng.htm (accessed January 6, 2013).