

Considerations for optimal prescribing in older adults

Julia Bareham BSP MSc Rae Petrucha MD CCFP Michael MacFadden MN NP-PHC CHPCN(C) Alex Crawley BSP

The care of older adults presents many challenges. This patient population is complex due to a combination of factors including, but not limited to, physiologic changes, comorbidities, polypharmacy, and increasing frailty. In addition to this, few randomized controlled trials (RCTs) have included individuals older than 80 years of age, especially those with multiple comorbidities. As comorbidities and polypharmacy increase, so does the potential for adverse drug-disease and drug-drug interactions. The number of medications prescribed to older adults is the number one factor responsible for adverse drug reactions resulting in hospitalizations.¹ As such, it is important to remain vigilant in assessing and regularly re-assessing medication use in adults older than 65 years of age, and to be alert for interventions that are no longer useful, no longer desired, or doing more harm than good.

To assist providers in navigating this complex population, this article will demonstrate an approach to assessing select medications commonly taken by older adults. While potential concerns for each medication are described below, individualization of approach, clinical judgment, and special consideration for principles of geriatric care remain foundational when prescribing and assessing medication regimens in older adults.

Case description

Ms L.F., a 78-year-old woman, is a long-standing patient of yours and is in the clinic today for a periodic health examination. Aside from hypertension, dyspepsia, and some mild osteoarthritis, she is quite well. She lives alone in her own home since the passing of her husband. One of Ms L.F.'s goals for her appointment today is to "get rid of some pills—there are so many!"

Her medication list indicates that she is currently prescribed 20 mg of enalapril daily, 2.5 mg of indapamide daily, and 20 mg of rabeprazole daily. Further discussion with Ms L.F. reveals that her son bought a dosette for her and fills it once a week when he comes to visit. Ms L.F. knows that there are several pills in the dosette that she takes every day but does not know what they are or what they are for.

The rest of Ms L.F.'s examination findings are unremarkable, aside from her blood pressure being a bit elevated in the clinic (150/92 mm Hg). Her bloodwork results are also unremarkable. Her dyspepsia appears well controlled and she reports no symptoms during the past year. Despite her osteoarthritis she does not report daily pain. She follows a healthy diet and eats a variety

of foods. You arrange for age-appropriate screening and ask that she follows up in the clinic to review the results, and that she brings her dosette and all her pill bottles from home with her next time so that you can go through her pills together. You also ask that she takes her blood pressure at home a couple of times a week between now and her follow-up appointment.

At her follow-up appointment Ms L.F. shows you her list of home blood pressure readings, which average about 146/92 mm Hg. She also hands you her dosette, which is chock full, along with a bag of prescription bottles and over-the-counter products. With her permission, you open her dosette and find that she is also taking the following daily: 81 mg of acetylsalicylic acid (ASA); 2, 220-mg naproxen tablets; 500 mg of calcium carbonate; a multivitamin; and 1000 µg of vitamin B12. When asked, Ms L.F. does not remember when or why any of these medications were added to her dosette, but has a vague memory of her son letting her know that he was adding some things "to help her feel better and keep her healthy."

Looking to the evidence to optimize medication use

Ms L.F. is relatively healthy, with only 3 diagnoses (hypertension, dyspepsia, and osteoarthritis) and 3 prescription medications (enalapril, indapamide, and rabeprazole), which highlights the need to query any medication use, both prescription and over the counter. Prescribed medications might be dispensed by the pharmacy but not taken as prescribed—or even taken at all. Over-the-counter medications, including vitamins, minerals, and other supplements, are readily available and, owing to effective marketing or misunderstood health information, might become part of your patient's daily regimen. To help ensure that you have all the information required to perform an optimal medication assessment, consider asking your patients to bring in everything that they take, prescription or otherwise.

Ms L.F. presents with a regimen that appears common and suitable for an older adult; however, consideration of the evidence for effectiveness and safety might allow you to address her polypharmacy concern and reduce her pill burden. **Table 1** contains information regarding possible indications for some of the medications and supplements that Ms L.F. is currently taking.²⁻⁸ In general, matching each medication to an indication, one medication at a time, is a valuable way to approach a medication review.

Table 1. Indications for the use of select medications and supplements in older adults

MEDICATION OR SUPPLEMENT	POSSIBLE INDICATIONS
Calcium	<ul style="list-style-type: none"> Dyspepsia: Calcium as an antacid might help to neutralize stomach acid and therefore reduce mild heartburn or GERD symptoms (eg, symptoms <3 times/wk of short duration and low intensity)² Duration of therapy: Use as needed, if it provides symptom relief Osteoporosis (for treatment and prevention): Calcium and vitamin D might increase bone mineral density and reduce the risk of hip fractures in postmenopausal women² Duration of therapy: Chronic therapy, but the optimal duration unknown. Individuals taking a bisphosphonate should take a calcium supplement if their dietary intake is insufficient The maximum amount of elemental calcium that can be absorbed at once is 500 mg.² Calcium carbonate is better absorbed when taken with food. Osteoporosis Canada has a useful dietary calcium calculator found at osteoporosis.ca/bone-health-osteoporosis/calcium-calculator Hyperphosphatemia in CKD: Calcium-based phosphate binders, such as calcium supplements, are first-line therapy in individuals with CKD when the serum calcium level is not elevated.^{3,4} Supplements can be used for treatment or maintenance Duration of therapy: Dependent on serum phosphate and calcium levels
Vitamin B12 or cobalamin ⁵	<ul style="list-style-type: none"> Vitamin B12 deficiency: Stomach acid is required to cleave vitamin B12 from dietary protein and only about 50% of the ingested amount is absorbed. As such, those with malabsorption conditions, poor nutrition, or taking certain medications (eg, alcohol, aminosalicic acid, colchicine, cotrimoxazole, histamine-2 blockers, isoniazid, metformin, neomycin, nitrofurantoin, oral contraceptives, proton pump inhibitors, sulfasalazine, tetracyclines, and triamterene) might be at risk of vitamin B12 deficiency Duration of therapy: Deficiency should resolve within 3-4 wk of therapy, but it might take more than 6 mo for neurologic improvements to occur Pernicious anemia: These individuals lack gastric intrinsic factor and are unable to cleave vitamin B12 from dietary proteins Duration of therapy: Chronic therapy
Multivitamin ⁶	<ul style="list-style-type: none"> AMD: Might slow the progression of intermediate to severe AMD Duration of therapy: Discontinue if or when benefit uncertain Cataract prevention: Might decrease the risk of developing cataracts; does not prevent surgery Duration of therapy: Consider discontinuing if cataracts develop Chronic alcohol use: Corrects folic acid, pyridoxine, and thiamine deficiencies, which are common with alcohol dependence Duration of therapy: Insufficient evidence to recommend a duration Compromised nutritional status: Meets nutritional requirements when there is insufficient dietary intake Duration of therapy: Until dietary intake can provide the required nutrients
Low-dose ASA (ie, 75-100 mg/d)	<ul style="list-style-type: none"> Secondary prevention of cardiovascular disease (ie, in people who have a history of cardiovascular or cerebrovascular disease) In older adults, low-dose ASA appears to produce more harms than benefits when used for primary prevention of cardiovascular disease, and is therefore no longer recommended⁷
NSAIDs (eg, naproxen, celecoxib, ibuprofen)	<ul style="list-style-type: none"> Treatment of acute or chronic pain Indomethacin might be more likely than other NSAIDs to have adverse CNS effects and should be avoided in older adults⁹ The 2019 Beers Criteria recommend that chronic use of NSAIDs be avoided in older adults unless alternatives are not effective and the patient can take a gastroprotective agent such as a proton pump inhibitor⁸

AMD—age-related macular degeneration, ASA—acetylsalicylic acid, CKD—chronic kidney disease, CNS—central nervous system, GERD—gastrointestinal reflux disease, NSAID—nonsteroidal anti-inflammatory drug.

Calcium. Calcium can be useful for dyspepsia (eg, the chewable antacid formulation), osteoporosis, and hyperphosphatemia in chronic kidney disease. Ms L.F. does not have osteoporosis or chronic kidney disease. She does have a diagnosis of dyspepsia but is already taking rabeprazole to treat this. Calcium is well tolerated in most patients; however, excess amounts (>2 g/day, possibly less) increases the risk of hypercalcemia in older adults, especially when they have renal impairment.² There is also the potential for constipation and the formation of kidney

stones.^{2,9} For individuals older than 70 years of age, the daily recommended intake of calcium is 1200 mg/day; however, dietary sources of calcium are preferred over supplementation.^{2,9} **Table 1** contains a link to the Osteoporosis Canada Calcium Calculator, which can be used to determine an individual's average daily calcium intake to help avoid excess or unnecessary supplementation.²⁻⁸ As Ms L.F. has a healthy diet and eats a variety of foods, determining her dietary sources of calcium would be valuable to assess the need for additional supplementation.

Vitamin B12. Vitamin B12 is indicated for vitamin B12 deficiency and pernicious anemia.⁵ Ms L.F. does not have either of these diagnoses. Adverse events with vitamin B12 are rare, but include diarrhea, pruritus, urticaria, and edema.

Multivitamin. Multivitamins might be useful in chronic alcohol use and compromised nutritional status; low-level evidence suggests that there are possible benefits for age-related macular degeneration and decreasing the risk of developing cataracts.⁶ Ms L.F. does not have any of these indications. In general, the best way to meet the nutritional needs of healthy older adults is through diet rather than a multivitamin (eg, increasing dairy intake to obtain calcium). Multivitamins and minerals are generally well tolerated when recommended daily amounts are not exceeded, but excessive amounts can lead to adverse events. For example, as stated above, excess calcium can lead to kidney stones, long-term use of high doses of iron can cause hemosiderosis,¹⁰ and hypervitaminosis A might cause various dermatologic symptoms (eg, dry, cracking, itchy skin) in addition to elevated liver enzyme levels and gastrointestinal symptoms (eg, diarrhea, nausea, anorexia).¹¹

Low-dose ASA. Low-dose ASA is indicated for the secondary prevention of cardiovascular disease⁷; Ms L.F.'s use would be considered primary prevention. The ASPREE (Aspirin in Reducing Events in the Elderly) trial examined ASA for primary prevention of cardiovascular disease in community-dwelling adults 70 years of age and older. It found no difference in the rates of cardiovascular disease (ie, fatal coronary artery disease, myocardial infarction, stroke, or heart failure hospitalization) but an increased risk of major bleeding (3.8% for ASA vs 2.8% for placebo, number needed to harm of 100 over 4.7 years).⁷

Naproxen. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as naproxen are useful for acute and chronic pain. Ms L.F. does have a diagnosis of osteoarthritis, which appears to be well controlled. However, it is worth exploring if there are other, safer ways of controlling her osteoarthritis. The risk of gastrointestinal ulcers and other complications is increased with NSAIDs; it is possible that naproxen is contributing to Ms L.F.'s dyspepsia. Nonsteroidal anti-inflammatory drugs can increase blood pressure and the risk of acute heart failure; naproxen might be worsening Ms L.F.'s hypertension (NSAIDs can increase blood pressure by 3/1 mm Hg).¹² Nonsteroidal anti-inflammatory drugs can also cause acute kidney injury; if Ms L.F. continues to take naproxen she should be cautioned not to take it during periods of acute illness when dehydration is likely (eg, from vomiting or diarrhea).

Enalapril and indapamide. Treating hypertension can be beneficial for many older adults but determining the

optimal blood pressure target can be challenging, as guidelines from various countries, RCTs, and observational studies provide a spectrum of blood pressure targets from a systolic blood pressure as low as less than 120 mm Hg to as high as 160 mm Hg. There is no definitive answer to the question: "What is the optimal blood pressure target for older adults?" A Cochrane review of 6 RCTs (AASK, ACCORD BP, HOT, PAST BP, SPRINT, and SPS3; **Box 1** provides the full study names) found no difference in total mortality, serious adverse events, or total cardiovascular events in people with hypertension and cardiovascular disease treated to a lower blood pressure ($\leq 135/85$ mm Hg) compared with a standard blood pressure target ($\leq 140-160/\leq 90-100$ mm Hg).¹³ However, some individual trials did show potential benefit with lower targets—and potential harms (eg, SPRINT showed a potential mortality benefit, but with an increased risk of harms such as acute kidney injury). The bottom line is that blood pressure targets in older adults should be individualized based on frailty (including mobility), risk of falls, comorbid conditions, time to benefit, and tolerability of the medications and adverse effects.

- Consider an intensive blood pressure target, if well tolerated, in an overall healthy older adult or an adult with a history of hemorrhagic stroke.
- Consider a less aggressive, more expansive blood pressure target in older adults at risk of adverse events, with limited life expectancy, or in whom aggressive pursuit of treatment targets does not align with their goals of care (perhaps owing to pill burden or a desire to reduce the risk of adverse events).

Applying evidence to practice

You explain to Ms L.F. that there are some changes that can be made to her pills.

- You advise stopping her multivitamin, as she is following a healthy diet.
- You advise stopping her vitamin B12, as she does not have an indication for this vitamin.
- You advise stopping her low-dose ASA, as she is considered to be taking it for primary prevention and

Box 1. Expanded Cochrane review study names

The following are the full names of the studies included in the Cochrane review by Saiz et al¹³:

- AASK—African American Study of Kidney Disease and Hypertension (2002)
- ACCORD BP—Action to Control Cardiovascular Risk in Diabetes—Blood Pressure trial (2010)
- HOT—Hypertension Optimal Treatment study (1998)
- PAST BP—Prevention After Stroke—Blood Pressure trial (2016)
- SPRINT—Systolic Blood Pressure Intervention Trial (2015)
- SPS3—Secondary Prevention of Small Subcortical Strokes study (2013)

recent evidence suggests that ASA increases her risk of bleeding without offering benefit. You remind Ms L.F. that exercise, healthy eating, and blood pressure control can help reduce cardiovascular risk and that she should consider focusing on those instead.

- You advise trying a discontinuation of Ms L.F.'s naproxen, as she is currently not experiencing regular pain, and as naproxen might be worsening (or even causing) her dyspepsia and worsening her hypertension. Instead, you recommend that she try acetaminophen for pain as needed and to keep the dose at less than 3.2 g/day if using it regularly. You also remind Ms L.F. that nonpharmacologic measures can be tried, including hot or cold packs, tai chi, or perhaps even hot baths.
- You calculate Ms L.F.'s average daily calcium intake using the Osteoporosis Canada tool (**Table 1**) and advise the discontinuation of calcium carbonate, as she is getting adequate calcium from her diet.²⁻⁸
- You advise that rabeprazole can be continued for now, but that an attempt could be made in the future to taper it if stopping naproxen is successful.
- You advise continuing treatment of Ms L.F.'s hypertension, as the benefits of blood pressure control are substantial. To reduce her pill burden, you decide to change her medication to a combination angiotensin-converting enzyme inhibitor–diuretic product (8 mg of perindopril and 2.5 mg of indapamide) so that she only has 1 antihypertensive pill to take each day.

Case resolution

Ms L.F. is happy with this plan and pleased to better understand why she is taking each of her pills. She likes the idea of reducing the number of medications she takes to prevent side effects and reduce costs. You ask her to follow up in clinic with you in 1 to 2 months to see what happens with her blood pressure after stopping the naproxen.

Two months later, you see Ms L.F. again and she notes that she has only needed to use the acetaminophen a couple of times a week for pain in her knees and that this only occurs on days when she goes out and is more active. You inform her that if she knows that she will have some knee pain based on the activities she has planned, then she can try scheduling the acetaminophen in conjunction with such activity, both before and after, to optimize her comfort. Ms L.F. then hands you her home blood pressure readings and is also happy that her average blood pressure is now 138/86 mm Hg without the naproxen. She reports being happy to no longer be “such a pill-popper.” Her current medications now are 20 mg of rabeprazole daily, a combination of 8 mg of perindopril and 2.5 mg of indapamide daily, and 325 mg of acetaminophen as needed. You decide to attempt to taper Ms L.F.'s rabeprazole, starting by reducing the dose to 10 mg daily.

Conclusion

Unnecessary medication use can put older adults at risk of adverse drug events and incur unnecessary costs for them. Periodic medication assessments, especially when there has been a hospitalization or involvement of another prescriber (eg, a non-family physician specialist), are integral to decreasing the risk that polypharmacy might pose.

When trying to decide where to begin when adjusting medication regimens in older adults, remember to discuss quality of life considerations and personal values and preferences, and engage in shared decision making. With limited evidence available to support drug therapy decision making in older adults with polypharmacy and comorbidities, health care providers must do the best they can with the information they have to help inform and educate their patients about their medication options. Providers can then support their patients by optimizing medications to ensure minimal risk and maximum possible benefit.

Ms Bareham is a pharmacist with RxFiles Academic Detailing at the University of Saskatchewan in Saskatoon. **Dr Petrucha** is Assistant Professor of Academic Family Medicine at the University of Saskatchewan. **Mr MacFadden** is Clinical Lead and Primary Health Nurse Practitioner at Samaritan Place Long Term Care Home in Saskatoon. **Mr Crawley** is a pharmacist and Associate Director of RxFiles Academic Detailing.

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Correspondence

Ms Julia Bareham, e-mail julia@rxfiles.ca

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