

Strategies to reduce and prevent polypharmacy in older patients

Deprescribing can be accomplished by using tested tools, good judgment, and a team approach.

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PRACTICE RECOMMENDATIONS

› Use one of the available tested and recommended screening tools to identify polypharmacy. **C**

› Engage in collaborative medication review to reduce the incidence of polypharmacy. **C**

Strength of recommendation (SOR)

- A** Good-quality patient-oriented evidence
- B** Inconsistent or limited-quality patient-oriented evidence
- C** Consensus, usual practice, opinion, disease-oriented evidence, case series

CASE ►

Ronald W^a is a 74-year old man with an extensive medical history: diabetes, hypertension, heart failure, atrial fibrillation, pancreatitis, hyperlipidemia, gout, depression, generalized anxiety, obstructive sleep apnea, and benign prostatic hypertrophy. He arrives at the emergency department (ED) of the hospital by nonemergent ambulance from home for evaluation of lethargy and confusion over the past week.

In the ED, Mr. W is afebrile, normotensive, and oxygenating on room air. Mucous membranes are dry. On physical examination, he appears pale, fatigued, and modestly confused but is able to state his name and birthday, although not the location or date.

Laboratory testing reveals: blood glucose, 107 mg/dL; serum creatinine, 2.3 mg/dL; sodium, 127 mEq/L; and hemoglobin level and hematocrit, within normal limits. Urinalysis is negative. Renal ultrasonography is unremarkable, without evidence of urinary tract obstruction.

Mr. W is admitted to the general medical unit with hyponatremia. The pharmacy admission specialist begins reconciliation of the long list of the patient's home medications.

Overprescribing: Often, more is not better

Some experts consider prescribing medication to be the most common form of medical intervention; beyond that, polypharmacy—often defined as the use of more medications than are medically necessary (see the next section on terminology)—is recognized as an increasingly serious problem in many medical specialties.¹ Here are specifics about the extent of, and harm caused by, the problem^{2,3}:

- The US General Accounting Office reports that inappropriate polypharmacy is associated with significant morbidity and mortality.² Research has established a strong

^aA composite, hypothetical patient, based on the authors' clinical experience.

CONTINUED ON PAGE 435

CONTINUED FROM PAGE 429

relationship between polypharmacy and harmful clinical consequences,³ to which the older patient population is most susceptible.

- Polypharmacy is also recognized as an expensive practice; the US Center for Medicare and Medicaid Services estimates that polypharmacy cost US health insurers more than \$50 billion annually.²
- Worldwide, with more and more people older than 65 years, polypharmacy is becoming more prevalent, and a growing concern, in older adults; approximately 50% of them take ≥ 1 medications that are medically unnecessary.³

Despite many programs to help with deprescribing, drug–drug interactions and the so-called prescribing cascade (ie, when signs and symptoms of an adverse drug effect are misdiagnosed as a new medical condition) continue to affect patients, leading to comorbidities. It is important, therefore, for physicians to be aware of commonly used tools to prevent polypharmacy and its consequences.

What is “polypharmacy” understood to mean?

Despite the compelling association of polypharmacy with the presence of multiple morbidities in the older patient population, there is no consensus on its definition:

- Starting with the dictionary, “polypharmacy” derives from 2 words in Ancient Greek: poly, “more than one,” and “pharmakon, “drug.”³
- The definition can vary based on the number of drugs a patient has been prescribed, their safety, and the appropriateness of their use.¹
- Another definition is the use of more medications than are medically necessary; such a grouping includes agents that are not indicated, are ineffective, or constitute a therapeutic duplication. Although this definition is more clinically relevant than the others, it is premised on undertaking a clinical re-

view of a medication regimen.³

- A numerical definition is the most commonly reported category, a number that varies from study to study—from ≥ 2 to ≥ 11 medications. When applied to health care settings, accepted definitions are ≥ 5 medications at hospital discharge and ≥ 10 during a hospital stay.⁴ Numerical definitions of polypharmacy do not ascertain the clinical appropriateness of therapy nor the process of rationalizing those medications.¹

Appropriateness

Polypharmacy is classified as appropriate or inappropriate:

- *Appropriate polypharmacy* is the optimization of medications for patients with complex or multiple conditions, when the use of medicine is in agreement with best evidence.
- *Inappropriate polypharmacy* can increase the risk of adverse drug effects and drug–drug interactions and can be characterized by medication underuse and duplication.⁴

There are subdefinitions of “appropriateness,” but these are beyond the scope of this article.

What variables contribute to polypharmacy?

Multimorbidity is common in the older population. The presence of multiple chronic conditions increases the complexity of therapeutic management for health professionals and patients; such complexity can have a harmful impact on health outcomes. Combinations of medications to treat chronic diseases automatically push many patients into polypharmacy. Few treatment guidelines provide recommendations on when to stop medications.

Consequences of polypharmacy, some of which are masked as syndromes in the older patient, include delirium and dementia, urinary incontinence, dizziness, falls, adverse drug reactions, increased length of hospital stay, readmission soon after discharge, and death.³⁻⁵ Relatively high rates of drug con-



Polypharmacy is not only medically unnecessary; it also causes significant morbidity and mortality and is expensive.

➤ **Consequences of polypharmacy can be masked as syndromes in older patients—eg, delirium, urinary incontinence, dizziness.**

sumption and other variables (eg, decreased renal and hepatic function, decreased total body water and lean body mass, cognitive impairment, age-related decline in vision and hearing, frequency of chronic diseases and medical comorbidities, communication barriers, prescribing cascades, and health care delivery involving multiple prescribers) can contribute to an increased prevalence of medication-associated morbidity and mortality as the result of polypharmacy.

■ **In a descriptive study**⁶ that examined these variables, researchers explored whether general practitioners experience barriers to medication review in multimorbid patients with polypharmacy. They concluded that the primary barriers were (1) lack of communication and teamwork with specialists and (2) the challenge of handling polypharmacy in a culture that encourages adding medications and inhibits conversations about medication withdrawal.⁶

Reducing consequences of polypharmacy

Collaborative medication review

Interventions to help physicians reduce polypharmacy include reviewing medications with older patients at every office visit and during transitions of care into and out of the hospital or other care facility. A 2016 Cochrane review of 5 randomized trials of inpatient medication reviews led by pharmacists, physicians, and other health care professionals showed a 36% reduction in ED visits 30 days to 1 year after discharge.⁷

Patients can collaborate in this effort by bringing all medications to each appointment or upon hospital admission—not just a list but the actual supply, to ensure that a correct medication list is compiled and a thorough review conducted.⁸ Explicitly ask open-ended questions of the patient about over-the-counter medications, herbal products, and other home remedies that have not been prescribed; many patients may have trouble with recall or are uncertain what fits the definition of a nonprescription medication.^{8,9}

Compare the medication list with the patient's current problem list; consider removing medications that do not have a per-

tinuous indication. (Physicians can help in this regard when prescribing by making note in the medical record of the indication for each medication they prescribe.)

Evaluate the patient's signs and symptoms as a possible drug-related adverse effect, thus making an effort to minimize the chance of a prescribing cascade.⁹

Use Beers criteria,¹⁰ which list potentially inappropriate medications to be avoided in older adults. The criteria serve as a filter when considering starting a new medication and aiding in the review process.⁸

The NO TEARS tool¹¹ can be useful for simplifying the medication review process. Components of this tool are:

- **Need and indication:** Does the patient still require each of his medications? Was long-term treatment anticipated?
- **Open questions:** Ask the patient for his views about his medications; for example, "Do you think the drugs you take work?"
- **Tests and monitoring:** Are any of the patient's conditions undertreated, based on laboratory and clinical findings?
- **Evidence and guidelines:** Has the base of evidence been updated for each of the patient's medications since they were started?
- **Adverse events:** Is the patient experiencing adverse effects of medication? Have possible adverse drug interactions been noted?
- **Risk reduction or prevention:** Does the patient face risks of treatment (eg, loss of appetite, urinary incontinence) that can be reduced by optimizing the medication plan?
- **Simplification and switches:** Can treatment be simplified while maintaining effectiveness?

There are strategies to promote patient advocacy, as well. Encourage patients to use a holistic approach by asking you, their other physicians, and their pharmacist about how their condition is being treated:

- What other treatment options exist, including nonpharmacotherapeutic options?
- What are the possible benefits and harms of medical therapy?

- Under what circumstances would discontinuing a medication be appropriate?¹²

CASE ►

Medication reconciliation identifies > 20 medications that had been prescribed for the patient to take at home (TABLE 1). A clinical pharmacist then performs a home medication review as part of routine patient care upon transition of care into the hospital.

Identifying polypharmacy

Implementing polypharmacy identification tools is a necessary first step in the process of mitigating the risk of multiple concurrent medications (TABLE 2^{2,10,12-18}). In addition to tools that are used to identify polypharmacy, there are steps that physicians and pharmacists can take to decrease the risk of polypharmacy.

For example, in a longitudinal, time-series cohort study measuring polypharmacy events, a pharmacist intervention was used as the means to decrease polypharmacy.¹⁹ Pharmacists intervened twice (each intervention separated by 1 year) to identify and manage 5 categories of high-risk drugs in patients whose care was provided by a managed care plan.¹⁹ During that time, pharmacists provided drug therapy reviews, education to physicians and patients about drug safety, and information for physicians on ways to correct problems with polypharmacy.¹⁹

Over the course of the 2 interventions, the overall rate of polypharmacy events decreased 67% after the first intervention and 39% after the second. The practice of having pharmacists spearhead this task was shown to reduce the cost and number of prescriptions in patients at risk for polypharmacy. (In fact, some general practitioners report that they deem multidisciplinary decision-making with pharmacists a necessary component of managing polypharmacy effectively.⁶)

Screening for medications as a cause of signs and symptoms

As noted earlier, a prescribing cascade arises when a drug administered to a patient causes an adverse event that is then mistakenly identified as a new condition, resulting in a

TABLE 1

Mr. W's home medication list

- Allopurinol 100 mg qd
- Aripiprazole 15 mg qd
- Aspirin 81 mg qd
- Bupropion 200 mg bid
- Buspirone 15 mg bid
- Carvedilol 25 mg bid
- Fluoxetine 80 mg qd
- Fluticasone (Flonase) 50 mcg, 2 sprays each nostril qd
- Gabapentin 600 mg tid
- Ipratropium bromide–albuterol, 0.5-3 mg/3 mL qid
- Lisinopril 10 mg qd
- Lorazepam 0.5 mg qd, 1 mg at bedtime
- Metformin 500 mg bid
- Mirtazapine 7.5 mg at bedtime
- Hydrocodone bitartrate–acetaminophen (Norco), 5 mg/325 mg q6h
- Ondansetron 4 mg q6h prn
- Pantoprazole 40 mg/d
- Prazosin 1 mg at bedtime
- Quetiapine 75 mg at bedtime
- Ranitidine 150 mg bid
- Tamsulosin 0.4 mg qd
- Tizanidine 4 mg q8h
- Tramadol 50 mg q6h prn

new medication being prescribed.⁹ The pattern of a cascade then repeats itself, resulting in inappropriate polypharmacy.

Erroneous treatment of an adverse drug event as a medical condition is often the result of a lack of pharmacologic knowledge—which is why it is necessary to evaluate each new symptom with the mindset that a medication might, in fact, be causing the sign or symptom and with the aim of reducing the risk of a prescribing cascade.^{8,9} Routinely update a patient's medication list in the event that a medication no longer has an indication aligned with the patient's problem list; then, ideally, the initial therapy can be adjusted instead of starting additional medications.⁹

CONTINUED

►
Get patients to collaborate on deprescribing by having them bring all medications to appointments and hospital admissions—the actual supply, not just a list.

➤
Assess every new symptom as a potential adverse effect of a current therapy to reduce the risk of a prescribing cascade.

CASE ▶

A review of Mr. W's home medications reveals 1 therapeutic duplication and 2 drugs that lacked an indication. Application of the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP)¹⁵ and Beers criteria¹⁰ helped the pharmacist identify additional elements of inappropriate polypharmacy, including inappropriate medication use, drug-disease interactions, contraindications, and recommendations for dosage adjustment based on kidney function. Specifically:

- *Aripiprazole* and *quetiapine*: Present an increased risk of falls. (General recommendation: Avoid using ≥ 3 drugs that act on the central nervous system [CNS], due to an increased risk of falls.)
- *Fluoxetine*: Can cause the syndrome of inappropriate secretion of antidiuretic hormone. Use with caution.
- *Gabapentin*: Presents an increased risk of CNS adverse effects. Reduce the dosage when the estimated creatinine clearance is < 60 mL/min.
- *Hydrocodone-acetaminophen*: Presents an increased risk of falls. (Again, avoid or minimize the number of drugs that act on the CNS.)
- *Lorazepam*: Indication is missing. Avoid use of this drug due to an increased risk of cognitive impairment and decreased metabolism of medication.
- *Mirtazapine*: Can cause the syndrome of inappropriate secretion of antidiuretic hormone. Use with caution.
- *Pantoprazole*: Avoid scheduled use for > 8 weeks, except in high-risk patients, due to the risk of *Clostridium difficile* infection and bone loss and fractures.
- *Prazosin*: Indication is missing. Avoid use of this drug as an antihypertensive due to the high risk of orthostatic hypotension.
- *Ranitidine*: Duplicates concurrent treatment with pantoprazole. Reduce the dosage when the estimated creatinine clearance is < 50 mL/min.

The value of deprescribing

Direct evidence of the efficacy and safety of

deprescribing, and strategies for deprescribing, have been documented in the literature:

■ **Observational study.** Cessation of inappropriate antihypertensive agents was associated with fewer cardiovascular events and deaths over a 5-year follow-up period.²⁰

■ **Deprescribing protocol.** A method developed by Scott and co-workers²¹ is an additional resource to consider. Appropriate times to consider deprescribing are (1) when new symptoms suggest an adverse drug effect; (2) in the presence of end-stage disease, terminal illness, dementia, extreme frailty, or full dependence on others for all care; (3) upon receipt of high-risk medications or combinations; and (4) upon receipt of preventive medications for which risk outweighs benefit.²¹

This suggested method of deprescribing comprises several steps: (1) collecting all medications that the patient is taking and identifying the indication for each; (2) considering the overall risk of drug-induced harm to determine necessary intensity of deprescribing; (3) assessing each drug for its eligibility to be discontinued, such as no indication, part of a prescribing cascade, or lack of benefit; (4) prioritizing drugs for discontinuation; and (5) implementing and monitoring the drug discontinuation regimen.²¹

■ **Drug-by-drug elimination trial.** Reducing the dosage of, or stopping, only 1 medication at a time has been shown to be paramount to assessing development of medication-associated problems and then identifying a likely cause.¹⁴

■ **Good Palliative-Geriatric Practice algorithm.** This algorithm²² can be used to guide discontinuation of inappropriate medications and improve drug therapy in community-dwelling older adults. The algorithm has been shown to improve the overall well-being of patients studied; however, it has been tested only in patients in long-term care settings and community-dwelling palliative care patients, limiting its generalizability to a larger population. The algorithm is also difficult to apply to patients who have multiple comorbidities.

■ **Risk vs. benefit of discontinuing chronic medical therapy.** A systematic review of the effects of discontinuing chronic medi-

TABLE 2

Screening tools for identifying polypharmacy^{2,10,12-18}

Tool, URL (when available)	What is its purpose?	What are the positives?	What are the negatives?
Hyperpharmacotherapy Assessment Tool (HAT) ² www.ncbi.nlm.nih.gov/pmc/articles/PMC2546482/figure/fig1/	Outlines 6 goals to help physicians avoid polypharmacy prescribing for residents in long-term care	Well-organized tool Addresses patient adherence	Has not been studied (1) in primary care or (2) sufficiently to establish reliability and validity
Beers Criteria ¹⁰ www.sigot.org/allegato_docs/1057_Beers-Criteria.pdf	Developed to help improve the selection of prescription drugs, evaluate patterns of drug use within populations, educate on proper drug use, and evaluate health outcomes	Provides an evidence-based approach Evaluates inappropriate medications based on age and other diseases Lists medications to be used with caution in older adults	Does not address drug–drug interactions, dosing of drugs in renal impairment, and therapeutic duplications Does not provide alternative options
Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) ¹⁵ https://academic.oup.com/view-large/317587	Identifies potentially inappropriate medication use in the elderly, including drug–drug interactions and duplicate therapies	Identifies more potentially inappropriate medications than Beers Criteria ¹⁰ Medications identified are significantly associated with avoidable adverse drug events that caused or contributed to hospitalizations	Does not identify inappropriate nonprescription medications
Medication Appropriateness Index (MAI) ^{16,17} https://globalrph.com/medcalcs/medication-appropriateness-index-calculator/	Assists physicians and pharmacists in assessing appropriateness of medications in elderly patients	Helpful in identifying drug-related problems in the elderly Positive correlation between a high score and drug-related hospital admissions	Not drug-specific Does not account for underprescribing Studied in older inpatient adults; might therefore not be as specific to primary care
Anticholinergic Drug Scale ¹⁸	Rates 117 medications with known anticholinergic activity to identify and prevent adverse events related to cognition, functionality, hospitalization risk, and mortality	Useful in community, nursing home, outpatient, and hospital settings	One of several anticholinergic rating tools



Reduce the dosage of, or stop, only 1 medication at a time to best assess the development of medication-associated problems.

➤
Risks of discontinuing chronic medication might outweigh benefit. Consider those risks before removing or reducing a medication.

cation reveals that the risk of doing so might outweigh benefit¹⁴; this finding is thought to be due to potential relapse in the disease state being treated.¹¹ The risks of discontinuation should be contemplated before removing the medication or reducing the dosage. Medications that can be considered to present a risk when discontinued include, but are not limited to, benzodiazepines, oral corticosteroids, antidepressants, acid suppressants, bisphosphonates, statins, and transdermal opioids.¹

CASE ▶

After applying Beers criteria¹⁰ and STOPP¹⁵, the pharmacist makes several recommendations:

- Use aripiprazole and quetiapine with caution.
- Consider discontinuing fluoxetine, hydrocodone–acetaminophen, lorazepam, pantoprazole, and ranitidine.
- Reduce the dosage of gabapentin.
- Clarify the indication for prazosin. Consider discontinuing if being used as an antihypertensive.

In addition, the pharmacist recommends holding metformin because lactic acidosis can develop (however rarely) when a person taking metformin experiences acute kidney injury. **JFP**

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