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Polypharmacy and Deprescribing Implementation in Practice

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Adults 65 years and older — 55 million individuals — make up almost 17% of the U.S. population, per the 2020 Census.[1,2] Polypharmacy is defined as taking five or more medications, and more than 40% of geriatric adults do so. This article describes concerns associated with polypharmacy and strategies for deprescribing.

Deprescribing techniques and resources can help minimize the harms of high pill burden in the geriatric population. The following is an illustrative case.

CASE VIGNETTE

An 81-year-old male presents for a new patient visit to establish care. His past medical history includes chronic pain with opiate dependence, multiple joint replacements several years ago, recurrent deep vein thromboembolism (DVT), hypertension, post-surgical seizures following meningioma resection, depression, anxiety, and mild leg edema. The patient's medication list is presented in Table 1.

The patient notes that he has frustrations with how many pills he is taking and how often he takes them. He is not taking omeprazole, cyclobenzaprine, and diphenhydramine every day due to not having symptoms and not remembering to use them. Of note, the patient's phenytoin level has been subtherapeutic for several years, but he has not had any seizures. He reports experiencing sedation when his phenytoin was therapeutic in the past.

POLYPHARMACY AND DEPRESCRIBING

Polypharmacy is defined as the use of five or more medications. Over time, patients taking five medications will average one significant drug problem, including adverse events, undesired side effects, or drug interactions.[2] Older age also correlates with increased medical complexity, and a prescribing cascade to mitigate side effects from previous prescriptions can occur.[2,3]

Retention of these medications poses a higher risk of morbidity and mortality. A patient's changing physiology, social situation, and goals of care must be considered, as polypharmacy may put our geriatric patients at greater risk of adverse drug reactions (ADRs), serious complications, or death.[3]

The act of removing or reducing the dose of medications to avoid unnecessary adverse effects, reduce medication burden, and improve quality of life is called *deprescribing.* Patients also have a desire to reduce their medications; one study demonstrated 92% of older adults would be willing to stop one or more of their medications if their physician felt it was possible.[4] Oftentimes, patients may be more resistant to deprescribing with long-term use, continued effectiveness, or physical dependence.

Effective deprescribing in patients with polypharmacy starts with recognition that this population is at high risk for ADRs. Critical and holistic review of patient medications should occur during any hospitalization, as well as at least every six months in outpatient settings, especially in frail or elderly populations.[5] We should ask our patients to bring all medications, including over-the-counter (OTC) medications and supplements, to each appointment and perform a formal medication reconciliation.

During medication reconciliation, it is helpful to assess for adherence to medications and frequency of use, particularly with "as needed" medications. Medicines the patient is not frequently using or that no longer serve their intended purpose are often good medications to deprescribe if they are not providing the medical benefits needed.

Other priorities should include identification of drug-drug interactions, medications without indication(s), and evidence of class duplication that may have additive side effects.

Clinical decision support tools such as the Screening Tool of Older Persons' Prescriptions/Screening Tool to Alert to Right Treatment (STOPP/START), Anticholinergic Burden Scale, and other drug-drug interaction databases can be helpful in identifying drug-drug or drug-disease interactions.[5-7]

Determining the need for routine lab monitoring in the management of warfarin, lithium, amiod-

arone, and phenytoin is important, as is assessing if the treatment regimen can be simplified by choosing treatments that do not require monitoring. Supplements and OTC medications are often overlooked, but discontinuing these can also help reduce total pill burden.

BEERS CRITERIA

Since 1991, the Beers Criteria has served as a resource to guide prescribing practices to identify medications with potential harm that outweigh the expected benefit in nursing home residents. Formally known as the American Geriatrics Society (AGS) Beers Criteria® for Potentially Inappropriate Medications (PIM) in Older Adults, the Beers Criteria has now morphed into a multidisciplinary-reviewed document.

The 2023 update identifies PIMs for older adults in all care settings, except for hospice and end-of-life care. It is a tool for evaluation and consideration for health care practitioners and is not intended to serve as a binding guideline, recognizing that geriatric care means being thoughtful about a wide range of ages, health care statuses, and goals of care.[8]

The Beers Criteria is divided into five sections:

1. Medications considered to be potentially inappropriate.
2. Medications potentially inappropriate in patients with certain diseases or syndromes.
3. Medications to be used with caution.
4. Potentially inappropriate drug-drug interactions.
5. Medications whose dosages should be adjusted based on renal function.

Table 1. Example Patient's Medication List

Aspirin	81 mg daily
Clindamycin	600 mg prior to dental procedure(s)
Cyclobenzaprine	10 mg at night as needed
Warfarin	5 mg daily
Phenytoin	100 mg three times daily
Furosemide	40 mg daily
Diphenhydramine	25 mg daily
Metoprolol succinate ER	25 mg daily
Naloxone	4 mg/0.1 mL nasal liquid, one spray in a nostril as needed
Oxycodone	5 mg every 4 hours as needed
Potassium chloride ER	20 mEq daily
Duloxetine	30 mg three times daily
Escitalopram	10 mg at night
Omeprazole	40 mg daily

Section 1: Medications Considered to Be Potentially Inappropriate

This section covers common drugs to avoid in geriatric patients grouped by organ systems and therapeutic class. Commonly thought of medications within this first section are outlined in a-b. Recommendations c-f are notable updates. These recommendations include:

a. Avoid first-generation antihistamines due to anticholinergic properties and reduced clearance.
b. Avoid non-selective peripheral alpha-1 blockers as antihypertensives due to a risk of orthostatic hypotension and benzodiazepines, which can cause increased risk of sensitivity, cognitive impairment, delirium, falls, fractures, and motor vehicle crashes.
c. Aspirin can cause bleeding. There is lack of evidence of benefit and evidence of potential harm when used for primary prevention of cardiovascular disease.
d. Warfarin, when used for management of nonvalvular atrial fibrillation or venous thromboembolism (VTE), should be avoided as initial therapy unless alternative anticoagulants are contraindicated or there are other barriers to use. It would be appropriate to continue therapy if the international normalized ratio (INR) has been within range 70% of the time and there have not been adverse effects.
e. Rivaroxaban, when used for treatment of nonvalvular atrial fibrillation or VTE, can cause major, including gastrointestinal (GI), bleeding. This treatment option may be reasonable for treatment if daily dosing is needed.
f. All sulfonylureas are now discouraged due to the risk of cardiovascular (CV) events, all-cause mortality, and hypoglycemia compared to other available medications for type 2 diabetes management. In previous editions of the Beers Criteria, glipizide was not included.

Additional language and clarification of certain drug classes were revised in the 2023 update, including:

- Regarding proton pump inhibitors and the risks associated with C. *difficile* infection, bone density loss, and fractures, it is strongly recommended they be used for no more than eight weeks.
- Non-COX-2 selective oral NSAIDs may be reasonable for short-term use when other agents are inappropriate or ineffective.
- Skeletal muscle relaxants can cause anticholinergic effects, sedation, and fractures. The criteria differentiate between those used for musculoskeletal complaints, which are considered PIMs, and

those used for treatment of spasticity, which may be appropriate.

Section 2: Medications Potentially Inappropriate in Patients with Certain Diseases or Syndromes

The 2023 update added that dextromethorphan and quinidine should be avoided in the setting of heart failure, anticholinergics should be avoided in patients with cognitive impairment or a high risk of falls and fractures, and opioids may exacerbate delirium.

Section 3: Medications to Be Used with Caution

Sodium-glucose cotransporter-2 (SGLT-2) inhibitors are now widely used. While they can provide cardiovascular and renal benefits, SGLT-2 inhibitors were added to the list due to the risk of urogenital infections and euglycemic diabetic ketoacidosis. Prasugrel and ticagrelor were also included because of emerging evidence that these antiplatelet agents increase the risk of major bleeding in comparison to clopidogrel.

Regarding anticoagulation, while warfarin and rivaroxaban were identified as PIMs, dabigatran is regarded as one to use with caution due to the risk for GI bleeding when compared to warfarin and apixaban.

Other notable medications to use with caution include those medications that increase the risk for hyponatremia or syndrome of inappropriate antidiuretic hormone secretion (SIADH), including antidepressants such as mirtazapine, tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), as well as antiepileptics such as carbamazepine and oxcarbazepine, antipsychotics, diuretics, and tramadol. These have historically been listed in prior Beers Criteria, while SGLT-2 inhibitors and ticagrelor were new additions.

Section 4: Potentially Inappropriate Drug-Drug Interactions

Among updates are the recommendations to avoid the concomitant use of:

- Skeletal muscle relaxants added to any combination of three or more central nervous system (CNS) active drugs.
- Lithium with angiotensin receptor blockers and angiotensin receptor-neprilysin inhibitors.
- Warfarin with SSRIs.

Previous notable interactions identified in the Beers Criteria that remain in the most recent update include:

- Opioids and benzodiazepines, gabapentin, or pregabalin.

Table 2. Risks Associated with Example Patient's Medication List

Medical Issue	Medication	Medication Class	Adverse Reactions/ Side Effects	Lab Monitoring
Chronic pain	Oxycodone*	Opiate	**Sedation,** physical dependence	
	Cyclobenzaprine*	Muscle relaxant	**Sedation, anticholinergic properties**	
	Naloxone	Opiate antagonist		
Joint replacement	Clindamycin	Antibiotic	**Stomach upset,** diarrhea, increased risk of *C. diff* infection	
Seizure	Phenytoin	Anti-epileptic	Sedation, increased fall risk, **strong inducer of CYP450**	
Recurrent DVT	Warfarin*	*Anticoagulant*	**Increased bleeding risk** or increased risk of VTE if subtherapeutic, metabolized by CYP450	INR
	Aspirin*	*Anti-platelet*	**Increased bleeding risk**	Platelets
Lower extremity edema	Furosemide	Diuretic	**Hypotension, electrolyte disturbance**	Electrolytes, renal function
Depression/anxiety	Duloxetine	*SNRI*	**Headache, stomach upset**	Electrolytes, renal function
	Escitalopram	*SNRI*	**Headache, stomach upset**	Electrolytes, renal function
Hypertension	Metoprolol succinate ER	Beta blocker	**Hypotension, bradycardia**	
No diagnosis to associate from given past medical history	Omeprazole*	Proton pump inhibitor	Increased risk of *H. pylori* infection, vitamin and mineral deficiency	Vitamin D, vitamin B12, magnesium
	Diphenhydramine*	Antihistamine	**Sedation,** headache, anticholinergic side effects	
	Potassium chloride ER	Electrolyte	**Cardiac arrhythmia, muscle cramping**	Electrolytes

Medications included in updated Beers Criteria; **bolded side effects denote duplicate side effect of multiple medications; italicized items under medication class denote duplicate therapeutics; CYP450 = cytochrome P450, DVT = deep vein thromboembolism, VTE = venous thromboembolism, INR = international normalized ratio.*

Table 3. Proposed Changes to Example Patient's Medication List

Original Medication List		Revised Medication List	
Aspirin	81 mg daily	DISCONTINUE	
Clindamycin	600 mg prior to dental procedure(s)	DISCONTINUE	
Cyclobenzaprine	10 mg HS prn	DISCONTINUE	
Warfarin	5 mg daily	Apixaban	5 mg BID
Phenytoin+	100 mg TID	Levetiracetam	500 mg BID
Furosemide	40 mg daily	DISCONTINUE	
Diphenhydramine+	25 mg daily	DISCONTINUE	
Metoprolol succinate ER	25 mg daily	Chlorthalidone	25 mg daily
Naloxone	One nasal spray prn	Naloxone	One nasal spray prn
Oxycodone+	5 mg q4h prn	Buprenorphine patch	One 10 mcg/hr patch weekly
Potassium chloride ER	20 mEq daily	DISCONTINUE	
Duloxetine+	30 mg TID	Duloxetine	90 mg daily
Escitalopram	10 mg daily HS	DISCONTINUE	
Omeprazole+	40 mg daily	DISCONTINUE	
Total Medications	**14**	**6**	

+Medication notes: when changing from phenytoin, cross taper to minimize chance of breakthrough seizure; regarding diphenhydramine, if a patient has allergic symptoms after discontinuation, a second-generation antihistamine is preferred; oxycodone, 30 MME/day equivalent dose; max daily dose of duloxetine = 120 mg; if GERD symptoms return after discontinuing the proton pump inhibitor, an H2 blocker would be preferred.

- Two or more anticholinergic agents.
- Three or more CNS active agents.
- Warfarin and several antibiotics, including ciprofloxacin, macrolides (excluding azithromycin), and trimethoprim sulfamethoxazole.
- Warfarin and any SSRI.

Section 5: Medications Whose Dosages Should Be Adjusted Based on Renal Function

Notable updates to this section include an item regarding the anticoagulant apixaban. Previously, this medication was to be avoided in patients with a creatinine clearance <25 mL/min; however, emerging data regarding its use in patients with low renal function suggest it can be reasonable, thus it is no longer listed in this section of the Beers Criteria.

Renal dosage adjustments based on kidney function (eGFR) are recommended in patients using baclofen as an antispasmodic skeletal muscle relaxant.

Other medications in which impaired renal function increases the risk for side effects include gabapentin, duloxetine, pregabalin, tramadol, famotidine, levetiracetam, and colchicine, among others.

CLINICAL INERTIA

With the use of the Beers Criteria and an awareness regarding polypharmacy concerns, judicious deprescribing may be appropriate.

Clinical inertia is defined as "the lack of treatment intensification in a patient not at evidence-based goals for care."[9] Several causes, including complexity of polypharmacy, lack of awareness or training, systemic barriers, and patient factors, may contribute.

Fortunately, using resources appropriately can combat clinical inertia and provide better outcomes for the patient. A clinical pharmacist is recommended to help deprescribe medications.[10,11]

CASE VIGNETTE: MEDICATION CHANGES

Returning to our 81-year-old male who presented as a new patient, we note he has symptoms related to his polypharmacy. He is frustrated with the timing of medications, as well as his pill burden.

Complex patients require a holistic approach to better assess for medication necessity, streamline evaluation of side effect profile, and determine clinical adherence feasibility. Table 2 demonstrates one approach to synthesizing this patient's information.

The goal of a revised medication list is to safely discontinue or reduce doses, or to transition medications to safer or more effective alternatives. Table 3 represents a proposed improved medication list, including drug removal, substitutions, and dosing changes.

The proposed improved medication list was determined using a 10-step methodology and approach to deprescribing (see Table 4 on page 40).

Table 4. Ten-Step Methodology and Approach to Deprescribing	
1	Match diagnosis with medications.
2	Identify high-risk medications.
3	Assess for any duplicate medications.
4	Assess for drug-drug interactions.
5	Assess for drug-disease interactions.
6	Review OTC and supplement necessity.
7	Assess for needed lab monitoring.
8	Assess for drug adherence.
9	Assess for necessity of medications.
10	Optimize medications and simplify regimen.

Step 1: Match Diagnosis with Medications

Omeprazole, diphenhydramine, and potassium chloride were not associated with a specific diagnosis in this example. Table 2 on page 38 demonstrates which medications do and do not have a current diagnosis association.

Step 2: Identify High-Risk Medications

Particularly high-risk medications in the vignette include oxycodone and cyclobenzaprine. Regarding this patient's history of chronic pain and opiate dependence, tapering narcotic medications is preferred due to sedating side effects, but doing this quickly is often not practical. Transitioning the patient to a morphine-equivalent buprenorphine patch is preferable for more consistent pain control and to simplify the regimen.

In addition, this patient would likely benefit from discontinuation of cyclobenzaprine as it is not being used regularly, has great potential for side effects, and can interact negatively with other medications on the list. Other high-risk medications that will be discussed in more detail below include phenytoin and warfarin.

Step 3: Assess for Any Duplicate Medications, and Step 4: Assess for Drug-Drug Interactions

Duloxetine and escitalopram represent similar medication classes; SSRI and SNRI medications should not be taken simultaneously, as this increases the risk of hyponatremia and additive side effects. Maximizing the patient's SNRI dosage will allow discontinuation of the SSRI since duloxetine alone could treat chronic pain and mood issues in this case.

Phenytoin is known to react with warfarin as it is a cytochrome (CYP) P450 inducer. In this patient, subtherapeutic levels are of concern. Levetiracetam was chosen as an alternative as it has an easier dosing schedule and does not require blood monitoring. It is also worth considering that in the setting of subtherapeutic anti-epileptic drug levels and no recent history of seizure, this patient may not need an anti-epileptic drug.

Low-dose aspirin is no longer recommended for primary prevention of atherosclerotic cardiovascular disease; however, in this case it could be considered secondary prevention.[12] While this patient has had a DVT, he could be anticoagulated with a direct oral anticoagulant (DOAC). The benefit of aspirin would be modest and in the setting of a DOAC would pose an increased risk of bleeding.

Low-dose aspirin has been studied as an alternative for the extended prevention of VTE, yet DOACs decrease rates of recurrence and are therefore preferred.[13]

Step 5: Assess for Drug-Disease Interactions

Utilizing the side effects of one medication as a treatment for a secondary medical problem can be one strategy to reduce medication burden. In this patient case, transitioning from metoprolol succinate to chlorthalidone would remove an agent that is not considered a first-line agent for hypertension.[14]

Thiazide diuretics, angiotensin-converting enzyme inhibitors, or angiotensin II receptor blockers may be more helpful with mild leg swelling. The Dietary Approaches to Stop Hypertension (DASH) diet is also a consideration for adjunctive nonpharmacological management of hypertension and leg edema. In this patient's case, we would avoid calcium channel blockers, which can exacerbate leg swelling. Given that the leg swelling has been mild, the patient likely can discontinue his furosemide and potassium chloride by changing the antihypertensive.

Step 6: Review OTC and Supplement Necessity

This patient does not take over-the-counter medications or supplements.

Step 7: Assess for Needed Lab Monitoring

Changing warfarin to apixaban will negate the need for regular INR checks. Similarly, changing phenytoin to levetiracetam for seizure prophylaxis eliminates the need for drug concentration monitoring.

Step 8: Assess for Drug Adherence, and Step 9: Assess for Necessity of Medications

The patient was not taking omeprazole, diphenhydramine, and cyclobenzaprine regularly and therefore they were discontinued.

In elderly patients, medications such as dental prophylaxis and aspirin commonly linger on the medication list. Antibiotic therapy is no longer recommended routinely with dental work in a patient with stable joint replacements.[15,16]

There are always exceptions to this rule, however in this case clindamycin can be safely discontinued. Collaboration with specialists is encouraged when determining medication necessity.

Step 10: Optimize Medications and Simplify Regimen

Several changes were made to simplify the regimen, including a once-weekly buprenorphine patch and daily dosing of duloxetine instead of three-times-daily dosing. Twice-daily dosing of levetiracetam is also an improvement over that needed for phenytoin.

CONCLUSION

Polypharmacy is quite common among patients and creates risks for ADEs, as well as drug-disease and drug-drug interactions, especially in the geriatric population.

Routine hands-on medication reconciliation during patient follow-up is crucial in identifying opportunities to deprescribe.

Various resources, such as STOPP/START, the Anticholinergic Burden Scale, and the Beers Criteria, are available to help identify high-risk medications in older adults. Active discussion with patients and caregivers is encouraged during the deprescribing process.

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