

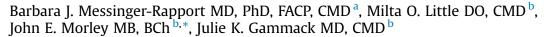
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ABSTRACT

Keywords:
Deprescription
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This is the tenth clinical update. It covers chronic kidney disease, dementia, hypotension, polypharmacy, rapid geriatric assessment, and transitional care.

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Deprescription

transfers

In response to concerns about polypharmacy in frail elders with multiple chronic conditions, there is growing interest in withdrawing, or deprescribing, medications (see Figure 1). Driving deprescription is the concern that guideline-directed prescription for each of multiple chronic conditions may have less benefit than predicted by each guideline. Guidelines derive their recommendations from clinical trials that, for the most part, do not incorporate patients who are very old, cognitively and/or functionally impaired, have multiple simultaneous conditions some of which are advanced, and/or who live in nursing homes. As a result, guidelines may not anticipate potential adverse outcomes to simultaneous prescription for multiple chronic conditions, including drug-drug or drug-disease interactions, higher cost, risk of noncompliance, and emergence of geriatric syndromes, such as anorexia, weakness, dizziness, gait abnormalities, bowel irregularities, and/or incontinence.

Additionally, aging may be accompanied by renal impairment. Chronic kidney disease (CKD) is common in older adults. In long-term care, approximately one-quarter of residents have mildly impaired glomerular filtration rate (GFR), and another quarter have moderate to severe impairment.² Drugs may need to be periodically reassessed for dose reduction or for discontinuation over time, particularly in those

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with vascular conditions at risk for progressively lower GFR. Continuation of medication without accounting for impaired renal function can potentiate geriatric syndromes, as well as accelerate loss of renal function. Another effect may be to potentiate cardiac problems, such as QTc prolongation, which until recently was not recognized as an adverse effect of many drugs prescribed to older adults. A good reference for assessing the burden of drugs in older adults, particularly with renal insufficiency, is the newly updated Beers publication from 2015, which incorporates several commonly prescribed drugs that require dosage reduction or elimination.³

There are several studies that suggest that deprescription can lead to improved outcomes for older adults. For example, analysis of the medication regimens of 150 patients discharged to home from an acute setting suggested that medications with a higher Medical Appropriateness Index were associated with a higher quality of life. In a small study, antipsychotic withdrawal from elders with dementia living in nursing homes in the United Kingdom did not lead to increased behavior problems, and the long-term outcome was a 40% improved survival compared with those who continued the antipsychotic. A nonrandomized withdrawal of chronic disease medications, such as nitrates, H2 blockers, potassium, iron, and antihypertensives, in a frail population resulted in a lower mortality rate and a lower referral to acute care.

On the other hand, the BELFRAIL observational study of community-dwelling patients 80 years and older with a median chronic medication use of 5 (range 0–16) incorporated validated criteria, START-2 and STOPP-2, to identity under- or overprescribed drugs. The study found that found that underprescription rather than overprescription was associated with hospitalization and mortality.⁷

The authors declare no conflicts of interest.

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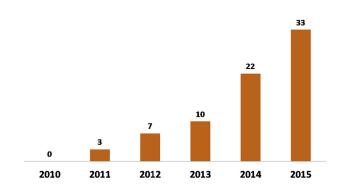


Fig. 1. Number of articles indexed in PubMed each year ("Deprescribe" OR "deprescription" OR "deprescribing").

A randomized antihypertensive withdrawal in 385 community-dwelling adults 75 years and older did not result in improved cognition or physical function in the 16-week-long Dante study. A substantial effort to withdraw proton pump inhibitors from 57 persons resulted in success in only 3 individuals. A randomized withdrawal of statins from patients with a life expectancy of less than 1 year and a recent functional decline did have a statistically higher quality of life (QOL) in the discontinuation arm, but the difference between 7.11 and 6.85 on the McGill QOL score may not reflect a clinically significant improvement. The number of cardiovascular events in both groups was small, and mortality was not statistically different in each arm of the study. 10

Anecdotal patterns of sequential medication prescription can be called the prescription cascade. Examples are treating the edema that results from amlodipine with furosemide; adding an antimuscarinic to treat the urinary incontinence resulting from a high-dose diuretic or cholinesterase inhibitor; adding off-label mirtazapine or an appetite stimulant to counter the anorexia from a cholinesterase inhibitor or metformin; or prescribing loperamide or diphenoxylate/atropine for the diarrhea caused by metformin and/or a cholinesterase inhibitor. Although the second medication addresses the adverse effect of the first in the short term, it increases the risk of more long-term problems, such as confusion, falls, dry mouth, or constipation, depending on the drug.

Rapid drug withdrawal can result in abrupt emergence of a symptom that the drug was thought to be treating (see Table 1). Symptoms are classified as recurrent, new, or physiological. Successful deprescription may require titrating a drug downward before

Table 1Potential Adverse Drug Effects From Deprescription

Drug	Type Reaction	Withdrawal Symptoms
Proton pump inhibitor	Recurrence	Gastroesophageal reflux disease
Baclofen	New symptom	Hallucination, paranoia
Benzodiazepine	New symptom	Seizure
Narcotic	New symptom	Abdominal pain, diaphoresis, diarrhea, insomnia, restlessness
Beta blocker	Recurrence and new symptom	Rebound tachycardia
Selective norepinephrine reuptake inhibitor	Recurrence and new symptom	Depression; anxiety, confusion, vertigo, pain
Anti-platelet inhibitors	Physiological	Thrombosis
Novel oral antithrombotics	Physiological	Thrombosis
Antiepileptic medication	Physiological	Seizure

Adapted from Bain et al.¹¹

discontinuation, then follow-up over weeks to months to monitor for symptom emergence.

Barriers to deprescription include ambivalent evidence-based benefit in the literature, as described previously. Lack of empowerment is a barrier. Even when the primary care practitioner is convinced that the burden outweighs the benefit of a drug, he or she may not feel comfortable deprescribing medications that appear indicated by clinical guidelines or were prescribed by another provider. In a facility, staff may express concern that adverse behavior will emerge when psychotropic medications are reduced. Additionally, communication barriers with the patient and/or family are likely underappreciated. Because medication use may be associated with needed care by families and facilities, withdrawing medications for chronic conditions may be considered withdrawal of care by the families. Practitioners need the same skills they use with the "serious illness conversation" to deprescribe.

An empiric approach to screening for polypharmacy is for a medical director or consultant pharmacist of an assisted living or nursing facility to screen for the prescription cascade described previously. One could screen for patients taking both mirtazapine and metformin, furosemide and amlodipine, oxybutynin and donepezil, or other combinations. The patient primary physician or nurse practitioner could then focus attention on the subset of patients in whom both these medications may be stopped. Another approach is to focus on chronic disease targets appropriate for life expectancy. A patient on 3 hypoglycemic agents with an Hgb A1c of 6% and a life expectancy of less than 5 years may be a good candidate for reducing the medication burden to 1 or 2 diabetes drugs.

There are international efforts under way to study deprescription and develop evidence-based guidelines, such as the Australian Deprescribing Network (ADeN)¹² and the Ontario deprescribing guidelines.¹³ We anticipate more directives to prescribers will be available over the next few years to address polypharmacy.

Behavioral and Psychological Symptoms of Dementia

Behavioral and psychological symptoms of dementia (BPSD) are the neuropsychological symptoms (or "noncognitive symptoms"), including aggression, apathy, depression, psychosis, and agitation. The prevalence of BPSD is 60% to 90%, depending on the underlying type of dementia, and leads to caregiver stress, institutionalization, increased cost, physical restraint use, and mortality. 14-16 There are 4 different subtypes of BPSD: (1) psychotic symptoms, such as delusions, hallucinations, and misidentification; (2) mood symptoms, including depression, anxiety, apathy, and euphoria; (3) restless/agitated behaviors, manifesting as aggression, wandering, vocally disruptive behaviors, and nocturnal disruption; and (4) disinhibited behaviors, like uncontrolled eating and socially and sexually inappropriate behaviors. 14 The subtype of manifested BPSD varies with the severity stage of cognitive impairment and can fluctuate in ways that make it difficult to distinguish from delirium. It is important to rule out delirium and distinguish the subtype of BPSD, as management depends on the type of behaviors being exhibited.

This review focuses on the pharmacologic management of BPSD. For nonpharmacologic management, please see the "noncognitive aspects of dementia" section in this article by John E. Morley.

A broad range of drugs are used to treat BPSD. Any discussion on pharmacologic management of BPSD needs to start with a disclaimer. NO medications have been approved by the US Federal Drug Administration (FDA) to treat BPSD! In addition, medications do not slow progression of disease, do not remove the cause or trigger of BPSD, and no single drug or drug group has consistently been shown to be more effective or superior to any other. ^{17,18}

The first medication class that is often used for management of BPSD is the antipsychotic class. In 2001, antipsychotic prescriptions

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