



# Polypharmacy Management in Older Patients

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## Abstract

Medications to treat disease and extend life in our patients often amass in quantities, resulting in what has been termed “polypharmacy.” This imprecise label usually describes the accumulation of 5, and often more, medications. Polypharmacy in advancing age frequently results in drug therapy problems related to interactions, drug toxicity, falls with injury, delirium, and nonadherence. Polypharmacy is associated with resulting increased hospitalizations and higher costs of care for individuals and health care systems. To reduce polypharmacy, we delineate a systematic, consultative approach to identify highest-risk medications and drug-therapy problems. We address strategic reductions (deprescribing) of medications in palliative care, long-term care, and ambulatory older adults. Best practices for reducing opioids, benzodiazepines, and other high-risk medications include education about risk and agreement by patients and their families, advocates, and care teams. Addressing deprescribing should be within the framework of patients’ health status as their care and goals transition from longevity to a plan of maintaining alertness, comfort, and satisfaction of quality of life. A team approach to address polypharmacy and avoidance of high-risk therapy is optimal within long-term care. Patients with terminal illnesses or those moving toward a comfort-care emphasis benefit from medication adjustments that are recognized beneficially within each patient’s care goals. In caring for older adults, the acknowledgement that complicated regimens and high-risk medications requires a care plan to reduce or prevent medication-related problems and costs that are associated with polypharmacy.

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Medications are proven useful to manage the comorbidities of diseases and extend life. Improper overuse of medications often results in toxicity, morbidity, and a plethora of problems. Most care providers recognize the patients who are taking more medications than can be practically and safely consumed. We label this problem “polypharmacy,” which is a vague and imprecise word. Even though Centers for Medicare and Medicaid Services (CMS) does not list an *International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM)* code(s) for polypharmacy, it is often added to patients’ medical records. In a position paper, CMS defines polypharmacy as taking the taking of 3 to 5 or more medications by persons older than 18 years of age.<sup>1</sup> However, to define polypharmacy based upon the number of medications taken is lacking in utility

for our older adults being treated for multiple diseases.

We associate aging with an accumulation of comorbidities for which multiple medications predictably will be prescribed.<sup>2</sup> In a 2005-2006 study, a population-based survey of community-dwelling persons 57 to 85 years of age showed that 37.1% of men and 36% of women between 75 and 85 years of age took 5 or more prescription medications.<sup>3</sup> In the decade from 1999 to 2009, CMS reported that, for enrollees, the average number of prescribed medications rose from 6.4 to 6.9. The respective increase in annual costs per beneficiary rose from \$298 to \$572 (192 %).<sup>1</sup>

There are supporting data from pharmaceutical-care principals that, on average, patients taking 5 medications will average 1 significant drug problem.<sup>4,5</sup> What remains clear is that higher numbers of

medications increases the frequency of adverse drug events (ADEs), nonadherence, and costs.

A study of 5213 participants in England found the rate of falls was 21% higher in people taking 4 or more medications compared with those taking fewer (adjusted incidence rate ratio [IRR] 1.21, 95% confidence interval [CI], 1.11 to 1.31). Using a  $\geq 10$ -drugs threshold, there was an increase in rate of falls by 50% (adjusted IRR 1.50, 95% CI, 1.34 to 1.67).<sup>6</sup>

Meta-analysis, including 47 studies, further suggests that, by association, risk of mortality rises progressively as the number of medications rise from 1 to 4 (adjusted odds ratio [aOR] 1.24 [1.10 to 1.39]) up to aOR 1.96 [1.42 to 2.71] for those taking  $>9$  medications.<sup>7</sup>

Taking multiple medications is within guidelines for treatment of hypertension, diabetes, and heart failure for achievement of treatment goals. Additional patient comorbidities translate to concomitant medications, which may result in a “prescribing cascade.” This occurs with medications being added to treat or prevent side effects of other medications.<sup>8</sup> Polypharmacy is an expanding concern as younger patients acquire diseases, such as diabetes, necessitating medical management.

Beyond treatment guidelines, there are health care contributors to the problem of polypharmacy, including multiple prescribers; multiple pharmacies; and accessibility to drugs online, in stores, and in herbal shops. Often, health care is segmented, resulting in patient visits to multiple providers who do not have shared records and naively prescribe duplicative or interacting treatments. Except when pharmacies share integrated prescription records, pharmacists are often unaware of duplicates or interacting medications prescribed for their patients. The addition of medications without systematic professional screening for interactions and adverse drug therapy results in risk.

Treatments are prescribed to meet desired objectives, but there emerges the cultural paradigm that taking pills treats

#### ARTICLE HIGHLIGHTS

- Reducing polypharmacy starts with assessment and interview of the patient.
- Care team members can assist reconciling medications, assess adherence, and help systematically identify drug therapy problems. See [Figure](#).
- Choose pharmacotherapy that avoids drug therapy problems and risk of rehospitalizations. Tapering benzodiazepines, opioids, and others are noted.
- Simplify the regimen for ambulatory patients and in long-term care, whenever possible, to reduce hospitalizations or negative incidents.

problems. In a study of patients with diabetes, the majority of patients were ultimately treated on 1 to 4 medications and multiple daily self-glucose testing. Unfortunately, results disclosed that few people adopted recommended lifestyle changes and activities that could add achievement toward their treatment goals with possibly fewer medications.<sup>9</sup> Our patients add medications, purchased over the counter and from online sources, of which providers are often unaware. The conclusion that supplements are safe is naive, considering their many potential interactions and complications.

Prescribers treating older patients must consider aging physiology, functional status, cognitive issues, nutritional status, and social-support systems as well as mental, somatic, and psychological health. At some point, a regimen of multiple drugs to treat multiple diseases in an older person becomes overtly problematic. The heightened association between polypharmacy and negative clinical consequences in older patients is reportable.<sup>10</sup> Polypharmacy has strong associations with increasing risk of falls, emergency care, and hospitalizations in older adults, all resulting in high health care costs. In a study of 2735 patients with a mean age of 80 years, independent predictors of 30-day unplanned rehospitalization included the use of 7 or more drugs (hazard ratio [HR], 3.94; 95% CI, 1.62 to 9.54;

$P=.002$ ).<sup>11</sup> Aging interposes physiological changes including declining clearance and metabolism that contribute to drug accumulation. Adjusting doses of medications in patients with declining clearance—such as antibiotics, digoxin, anticoagulants, and hypoglycemics—is crucial. Laboratory-reported kidney clearance estimates should be systematically incorporated within prescribing systems to optimize medication safety, avoiding toxicity.<sup>12</sup>

Aging-related changes in individual pharmacodynamics results in heightened sensitivities to several asopioids, benzodiazepines, and drugs with anticholinergic properties, resulting in toxicity.<sup>13</sup>

We advocate a systematic team approach to address patients effectively with lengthy medication lists and assessing for adherence difficulties. The trained clinical pharmacist is equipped to assess the medications, indications, outcomes, and identify drug-therapy problems (DTPs) and propose a plan for optimizing therapy. In a Veterans Administration (VA) study of older adults, pharmacists performing medication consultations identified and reduced the number of potentially inappropriate medications by 36.4% and optimized medication adherence.<sup>14</sup>

### EVALUATION OF THE AGED PATIENT'S MULTIPLE MEDICATIONS

First, the patients' medication must be reconciled, which is a Joint Commission patient safety priority. Reconciling medications at care transitions from hospital and long-term care (LTC) has been shown to reduce errors in medication orders and addresses clarity of changes in therapy.<sup>14</sup> Next is an assessment of adherence, including methods patients use to manage medications, which often reveals difficulties taking their regimen. The application of tools such as the Morisky Medication Adherence Scale has validity in revealing breakdown in adherence and related barriers to taking medications and may be administered by a trained care team member.<sup>15</sup> Research repeatedly shows that adherence difficulties are rooted within higher numbers of

medications and escalating doses. Resolving adherence barriers in the older adult often involves decisions about supportive means for management of medication. Problematic adherence typically dictates simplification of the regimen to reduce complexity and barriers such as cost. A validated Medication Regimen Complexity (MRC) index was studied in patients being dismissed from hospitals. The MRC was predictive of patients' potential for ADEs and unplanned hospital readmission.<sup>16</sup>

The regimen in older persons is screened for high-risk drugs and those interacting with other drugs and affecting patient comorbidities. There is much information on high-risk drug therapy as defined by Beers Criteria, Screening Tool of Older Person's Prescriptions (STOPP) guidelines, and Drug Burden Index, and others.<sup>17-19</sup> These tools help to identify therapy that has a high probability of ADEs compared with benefits in the older adult. [Table 1](#)<sup>5</sup> is a step-wise process of discovering DTPs in patients taking 5 or more medications. The problems are delineated principles of drug therapy.<sup>5</sup> Recognition of DTPs within patients' medications is a crucial starting point for optimizing patients' medication regimens. Finally, the consultation should include an actionable therapeutic plan for optimizing medications within the patients' framework of their care goals ([Figure](#)). The plan is communicated with providers and is implemented and monitored with acceptance of the patient and caregivers. [Table 2](#) includes tools used to identify high-risk therapy and adherence issues.

### DEPRESCRIBING IN THE COMMUNITY-DWELLING SENIOR

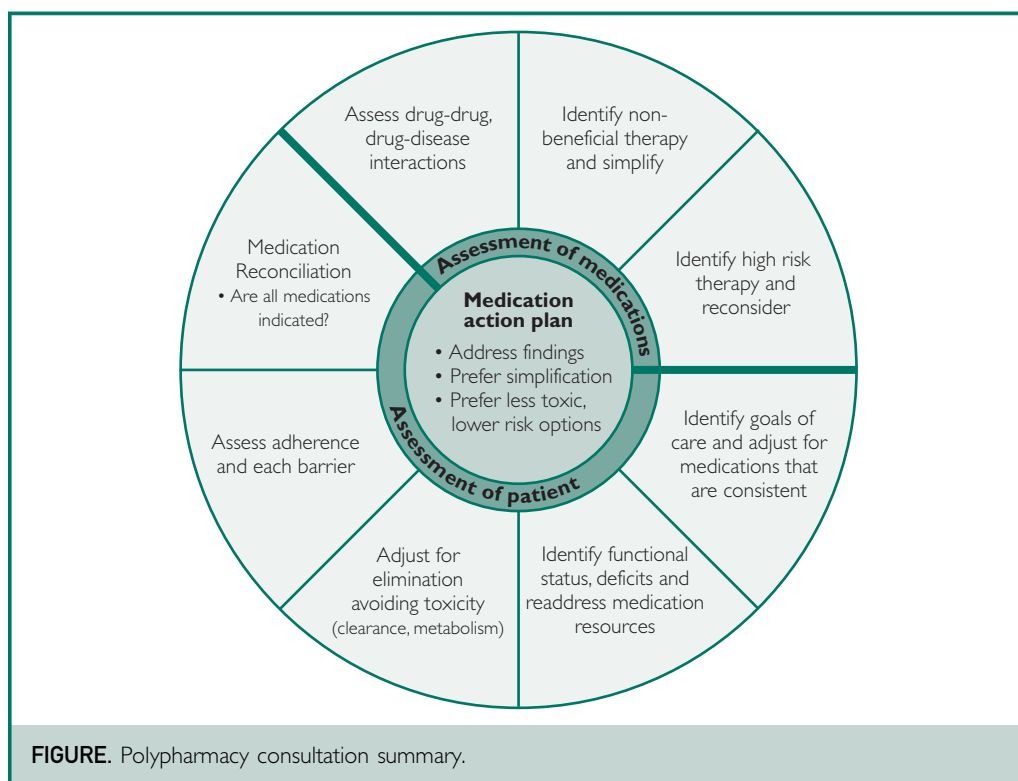
Deprescribing is the purposeful act of stopping or tapering 1 or more of a patient's medications. The objective is to target medications from which patients no longer derive reasonable benefit, prevent consequences of high-risk medication combinations, and reduce cost and complexity while patients remain on beneficial medications. Reducing polypharmacy by purposeful deprescribing has been shown to reduce

TABLE 1. Process to Identify Drug Therapy Problems in Cases of Polypharmacy: Seek Simplification Whenever Possible

Perform stepwise	Reasons/examples	Problems/risks to be found	Actions/simplify if possible
1. Medication reconciliation: an accurate medication list	-Know what patient actually takes -Discover unexpected or unfilled prescriptions	-Discontinued medications -Missing medications - Taking incorrectly	-Stop, modify or initiate appropriate therapy -Patient education
2. Adherence assessment: Identify missed doses using tools such as Morisky, review pill box and bottles, fill dates	Adherence barriers: complex therapy burden: 3-times-daily, 4-times-daily doses, missing inhalers (cost), missing bottles, duplicate bottles	Too many doses of medications daily Unfilled or perpetuated prescriptions Unaffordability of medications Presence of side effects	Simplify regimen burden, use cost effective alternatives; eliminate agent(s) with adverse side effects
3. Identify drug–drug interactions using interaction databases	Interactions risk: QT prolongation, anticoagulant and bleed risk medications: NSAIDs, anticoagulants; serotonin syndrome	Monitor the risk, eliminate when risk outweighs benefit	Select noninteracting agents; choose alternatives with lower risk
4. Drug–disease interaction screen	NSAIDs in CHF, CKD, hypertension; sulfonyleureas in CKD	High-risk therapy that exacerbates heart failure, hypoglycemia	Select alternate therapy; monitor for high-risk events
5. Overtreatment: accumulating therapy	Identify duplicate or concomitant therapy result in orthostasis, hypoglycemia	Duplicates, medications with additive side effects resulting in toxicity	Adjust doses, taper therapy; monitor results
6. Identify high risk drugs in older adults: Beers criteria, STOPP/START	Sedative/hypnotics, opioids, anticholinergics, benzodiazepines, anxiolytics, hypoglycemics	Monitoring of high-risk therapy is necessary; survey risk before it begins to outweigh benefit	Reduce or eliminate risk; educate patients about OTC anticholinergic avoidance
7. Undertreated indications or missed therapy. START criteria	Overlooked treatment: CAD without a statin, antiplatelet agent after coronary stenting.	In complex regimen, sometimes an indicated medication has fallen unnoticed	Initiate medications that decrease risk for the patient within goals of care
8. Medication monitoring for efficacy and safety	Insulin without glucose monitoring, TSH, warfarin: INR	Medication is fulfilling its purpose/ indication; safety monitoring for each medication	Routine labs (TSH), drug levels; assess kidney, liver function
9. Evaluate supplements, herbal supplements, multiple vitamins in most older American adults	Contribute to medication burden, cost, side effects, interactions: iron, multivitamin/trace elements	Except for recommended supplements such as vitamin D, many supplements are noncontributive	Discuss, simplify, educate patients

Terms of drug therapy problems include those from Strand et al.<sup>5</sup>

Afib = atrial fibrillation; CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; INR = international normalized ratio; NSAIDs = nonsteroidal anti-inflammatory drugs; OTC = over the counter; STOPP/START = screening tool of older persons' potentially inappropriate/screen tool to alert treatment prescription; TSH = thyroid-stimulating hormone.



medication-associated emergencies and hospitalizations, selectively.<sup>21</sup> Deprescribing is best achieved within an individualized therapeutic plan that is understood by the patient and caregiver. It specifically targets high-risk drugs (inappropriate by criteria), overdosing, drug interactions and side effects, regimen simplification, improving adherence, and decreasing cost.

Deprescribing in older adults includes consideration of patient functionality, support needs within living situations, and decisions regarding patients' ongoing care plans. Overarching objectives should go beyond eliminating targeted overuse of proton pump inhibitors or unnecessary supplements and be tailored to an individual patient's existing health and living status.

**TABLE 2.** Tools for Identifying Medication Risk and for Deprescribing in Older Adults

Beers Criteria, American Geriatric Society, Updated 6 times, recently 2019	Identifies potentially inappropriate medications that add risks; to be avoided in older adults
STOPP/START Criteria, <sup>18</sup> Version 2008, Version 2, 2015	Medications to avoid (STOPP) and potential prescribing omissions (START) in older persons
EMPOWER: tapering benzodiazepines <sup>19</sup>	Considerations for patients about successful benzodiazepine reductions
Medication Overload, Lown Institute	Overview and public education for decreasing medication overuse
Morisky Medication Adherence Scale (MMAS 4 or 8), Medication Regimen Complexity Index <sup>20</sup>	MMSA-8 Tool: short questionnaire (110 versions, 80 translations), validated assessment tool(s) to identify adherence problems, barriers, and regimen complexity; disease-specific validation, most common in HTN, asthma, etc

EMPOWER = Eliminating Medications Through Patient Ownership of End Results; HTN = hypertension.

## DEPRESCRIBE HIGH-RISK MEDICATIONS IN OLDER ADULTS

Studies have shown that upward of more than one-third of independent living adults, and half of those residing in LTC facilities, are taking medications that CMS has labeled “unnecessary.” These are referring to Beer’s Criteria of Potentially Inappropriate Medications, which are those drugs to be avoided in older adults because of the high incidence of ADEs. Both the Beers Criteria, and, similarly, STOPP/START criteria, have validating data that demonstrate the value of reduction of medications that add unnecessary risk to elders’ regimens.<sup>17</sup>

### Deprescribe Strongly Anticholinergic Medications

Older antihistamines such as diphenhydramine, muscle relaxants such as cyclobenzaprine, and overactive bladder agents such as oxybutynin have strong anticholinergic effects. These anticholinergic medications are usually poorly tolerated in aged patients. Their broad muscarinic receptor blockade results in negative effects on vision, urination, constipation, and cognition. A decline in acetylcholine physiology is associated with aging and is further blocked with anticholinergics. Patients taking multiple anticholinergic drugs, dubbed “anticholinergic burden,” often adversely affects cognition and functionality.<sup>22</sup> A Drug Burden Index shows drugs that are sedating or with strong anticholinergic properties are associated with a decline in cognition, functional status, and activities of daily living (ADL) scores in older patients.<sup>18</sup> Further research has defined the anticholinergic risk to elderly patients in a 2012 update to the anticholinergic cognitive burden scale.<sup>23</sup> The liabilities associated with anticholinergic and sedating medications—injurious falls, episodes of confusion or delirium, visits to the emergency department, and hospitalizations—all raise the cost of care.

### Deprescribe Nonsteroidal Anti-Inflammatory Drugs

Deprescribe nonsteroidal anti-inflammatory drugs (NSAIDs) to avoid furthering the

decline in kidney clearance and accumulations of medications. In the aging, the potential for NSAIDs to affect blood pressure (BP) and kidney function negatively and to cause heart failure and gastrointestinal bleeding often outweigh their benefits.

### Deprescribing Hypoglycemics

Episodic hypoglycemia remains a leading cause of admissions to emergency departments in older patients.<sup>24</sup> Deintensification of a diabetes regimen is paramount when patients are experiencing episodic hypoglycemia. Sulfonylureas and short-acting insulin are among the highest-risk medications. Guidelines suggest relaxing both glycemic and hemoglobin A1c goals. However, 1 study of 65 patients, mean age of 76, did not demonstrate less hypoglycemia when switched from multiple insulin injections to a basal once-daily insulin regimen with noninsulin agents.<sup>25</sup>

### Deprescribing Antihypertensives

Achievement of goal-directed blood pressure control has repeatedly proved to reduce neurovascular and cardiovascular complications of hypertension in large clinical trials, even in patients of advanced age. However, patients with limitations such as orthostasis, with related fall risk, necessitate careful monitoring. Scott et al<sup>26</sup> propose specifics in modifying antihypertensive treatment within a decision framework for older patients. It includes considerations for labile BP and determination of BP targets likely to confer benefit, considering frailty, comorbidities, and cognitive status. Patients exhibiting intermittent low pressures, syncope, or falls suggests BP regimen adjustments with monitoring.

### Deprescribing Statins

Lipid-lowering drugs—specifically, statins—are often considered for discontinuation in aging adults. These are typically not high-risk drugs, and, in patients older than 80 years of age, cardiovascular benefit continues to be conferred compared with those who do not take or continue on statin therapy. A recent trial in which statins were discontinued in 17,204 adults older than 75 years of age, who had no previous



cardiovascular disease, found an increased risk of 1.33 (95% CI, 1.18 to 1.50) for any cardiovascular event.<sup>27</sup>

We know from several studies that continual use of statins after a coronary event significantly reduces recurrences, and stopping results in risks of recurrence. One might rethink continuing statin therapy in primary prevention of coronary disease for a patient who is facing end-of-life issues.

### Deprescribing Herbal Supplements and Vitamins

Few herbal supplements have undergone controlled clinical trials; therefore, we have little evidence of efficacy to justify beneficial claims or safety. Herbal pharmaceuticals have potential deleterious side effects, interactions that are poorly understood, and are not Food and Drug Administration (FDA) regulated. Numerous community-dwelling adults take daily multiple vitamin and mineral supplements. Studies show, with few exceptions, that they add complexity and cost to a regimen without evidence of preventive benefits including mortality, cardiovascular disease, cancer, or cognitive function.<sup>28,29</sup>

Importantly, as aging occurs, independence and functional decline will circumstantially necessitate evolving independent goals. When patients' ADL requires extensive assistance, complex medication regimens demand external assistance to be maintained. Often, people employ the support offered by residing in long-term-care settings. Each patient's living situation, knowledge of his or her personal wishes and medication experiences, predicates adjustments to ongoing medications to the benefit of the patient. Whether living independently or in another care setting, a patient-centered approach is strongly recommended for successful optimizing the medication regimen.<sup>30</sup>

### DESPRESCRIBING IN PALLIATIVE-CARE SITUATIONS

The onset of life-changing illness and a potentially terminal disease brings about considerable change in each patient's health objectives. Clinician counsel given to patients and their caregivers must weigh potential

beneficial and undesired effects of treatments. Discussion engages a balanced appraisal of the relative benefits and risks when initiating acute and continuing long-term treatments.<sup>31</sup>

The patient's past medications often require adjustment, in consideration of the patient's revised clinical milieu. For example, our patients' established treatments within guidelines may add complications to patients with active malignancy. To those fitting the palliative care realm, or in an end-of-life setting, primary preventive therapy may no longer make sense. It is important to consider estimated disease trajectory and the anticipated life expectancy, both of which can be estimated using predictive tools that incorporate age, medical comorbidities, and degree of functional impairment (Holmes et al).<sup>32</sup> Once a prognosis is established for a potentially terminal illness, care goals may shift from healthy longevity toward maintaining comfort with alert mental status to sustain a shortened window of remaining opportunities. Inclusion of the caregiver and the patient regarding priorities is essential when discussions for deprescribing are weighed. Patients and supportive family members value communication, reassurance, education, and a gradual stepwise approach, along with follow-up.

Pain is a common occurrence in patients older than age 65.<sup>33</sup> In patients with terminal or ongoing pain, management objectives are an evolving challenge. Analgesic management in seniors is challenging in light of dynamic pharmacokinetics. The 1986 World Health Organization (WHO) analgesic ladder was devised for management of cancer-associated pain and offers a 3-pronged stepwise approach that is bidirectional, allowing for both titration as well as de-escalation of opioids. A revision of this algorithm offers a fourth paradigm: incorporating use of patient-controlled analgesia pumps for continuous intravenous, epidural, or subdural administration.<sup>34</sup> This valid approach has achieved adequate analgesia in 20% to 100% of patients.<sup>35</sup> One can extrapolate that this method be used to address other types of pain including nociceptive pain and neuropathic pain. For example, mild or

TABLE 3. Deprescribing in the Older Adult

Medications: pharmacologic examples	Risks in older adults	Tools: deprescribe methods
Anticholinergic medications	Broad muscarinic receptor blockade	Taper if using routinely and avoid
Old antihistamines: diphenhydramine, hydroxyzine	CNS impairment: delirium, slowed comprehension; impairs vision, urine retention, constipation, sedating, falling	Beers Criteria, STOPP Criteria, Anticholinergic Burden Scale; suggestion: avoid, use safer drugs
Muscle relaxants: cyclobenzaprine, metaxalone, and others		
Overactive bladder: oxybutynin		
NSAIDs: indomethacin, naproxen, ibuprofen, and others	Worsens clearance in kidney disease, hypertension, heart failure, GI ulceration/bleeding	Avoid
Sulfonylureas: glyburide, glipizide	Accumulation in CKD with higher risk of hypoglycemia	Taper, and substitute safer agents
Short-acting insulins, peak insulins	Accumulation and resulting hypoglycemic risk in AKI and as CKD progresses	Modify to avoid hypoglycemia
Antihypertensive drugs for hypotension or orthostatic blood pressure	Any/all classes can result in blood pressure drops with falls, injury, orthostasis	Monitor, adjust doses or deprescribe; titrate to control hypertension but avoiding hypotension
Multiple vitamin/mineral supplements, general use	Contributes to medication burden and occasionally anorexia without substantiated benefit	Exception: Vitamin D has evidence for bone health; Ca/Vitamin D studied with bisphosphonates
Herbal supplements: not regulated by FDA to provide evidence of claims: glucosamine, turmeric, ginkgo, and many antioxidants	Have actual drug interaction concerns, adds to medication burden and expense; poor to no evidence of pharmacological benefit	Stop and consider healthy dietary intake
Opioids: Short-acting, slow-release	Morphine, oxycodone, codeine, shared sedation, anticholinergic properties, addictive; withdrawal syndrome; cognitive impairment, falls	Avoid or taper gradually, as permitted
Benzodiazepines: avoid long-acting agents (diazepam) Moderate action: lorazepam, clonazepam Benzo- like GABA receptor hypnotics: zolpidem, zaleplon	Sedating, cognitive impairing, unsafe mobility with injurious falls, motor skill impairment; habituating, withdrawal syndromes including sleep disruption	Beers, STOPP criteria: avoidance. EMPOWER: taper technique; consider safer therapy; for anxiety and sleep: taper, consider cognitive behavioral therapy and adjuncts
Antipsychotics: for cognitive behavioral problems Typical agents: chlorpromazine, haloperidol long-term use Atypical agents: quetiapine, risperidone, olanzapine, and others	Avoid most sedating agents; they worsen cognitive function in dementia	Beers Criteria: taper/avoid if possible, especially as pharmacological behavioral control in cognitive disease; use redirection and other agents. FDA Box warning: risk of death when used for dementing disorders
Cholinesterase inhibitors: donepezil, galantamine: indicated for mild to moderate dementia (eg, Alzheimer disease).	Adverse effects: nausea, vomiting, diarrhea, nightmares, bradyarrhythmia Lacking long-term benefit, particularly in advanced dementia	Safe to taper to off, especially when there is perceived lack of benefit

AKI = acute kidney injury; CKD = chronic kidney disease; CNS = central nervous system; FDA = Food and Drug Administration; GI = gastrointestinal.



moderate musculoskeletal pain in elderly patients may be ameliorated by administering acetaminophen on a scheduled basis.<sup>33</sup>

### Opioid Deprescribing

Novel news cycles and legislation over the abuse of opioids have permeated clinical practice. Opioid use for chronic pain is indeed fraught with side effects, some of which may prove deleterious, including an increased risk for opioid-use disorder, overdose, myocardial infarction, and motor vehicle injury.<sup>36</sup> The decision to taper or discontinue opioid therapy begins with ensuring sound rationale for initiation of treatment in the first place. Opioids should be reserved for situations in which analgesia and functional independence cannot be achieved by other interventions, and the benefits outweigh the risk of therapy.<sup>37</sup> It is important to acknowledge that restoration of function can occur even in the presence of pain.<sup>37</sup> As such, firm and realistic expectations should be established before initiation of narcotics. It is imperative to identify associated adverse effects, prompting reduction of opioids.<sup>36</sup>

Plans to include nonopioid analgesics must be considered early as a viable treatment option for pain, regardless of acute analgesia. In older adults, acetaminophen has evidence in safely alleviating pain and augmenting analgesia. Chronic pain, such as arthritis, may be treated effectively with acetaminophen or NSAIDs; however, evidence is strong that routine use of NSAIDs in the elderly often exacerbates congestive heart failure, hypertension, and kidney disease and may cause gastrointestinal ulcers. Topical analgesics, such as diclofenac, have better safety profiles compared with systemic NSAIDs and are possibly as effective in reducing pain of acute injury.<sup>38</sup>

Use of other nonopioid adjuncts and non-pharmacological interventions must be considered as an integral component of opioid tapering. A multidisciplinary approach is needed to address the multifaceted etiology of pain syndromes. Various pharmacological agents, including anticonvulsants, tricyclic

antidepressants, and serotonin-norepinephrine reuptake inhibitors have been shown to provide adequate relief of pain in certain pain syndromes including diabetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, and fibromyalgia.<sup>36</sup> Cognitive behavioral therapy has shown efficacy in addressing the psychological aspects of pain, reducing disability, and thwarting catastrophizing.<sup>39</sup> Purposeful exercise composed of aerobic, aquatic, and resistance training demonstrated efficacy for patients with debilitating osteoarthritis involving weight-bearing joints.<sup>40</sup>

With implementation of alternative means of treating pain, reduction or discontinuation of opioids should be deliberate and gradual to minimize withdrawal symptoms.<sup>36</sup> Weekly dose reductions have been proposed, ranging between 10% and 50%.<sup>36</sup> Reduction in opioid dosing by 10% weekly has been suggested as a well-tolerated approach.<sup>36</sup> Experts acknowledge that a single tapering approach is not likely to succeed for every patient, and leeway must be permissible to achieve dosing reduction or discontinuation. Given the unpredictability of pain, it may be necessary to halt tapering temporarily or re-escalate treatment to accommodate the patient.<sup>36</sup> Once minimal dosing is achieved, it is reasonable to expand the interval between doses, ultimately discontinuing treatment once dosing frequency is reduced to less than once daily.<sup>36</sup>

### Benzodiazepine Deprescribing

Benzodiazepines are the most commonly prescribed anxiolytic medication in older patients (Grasso et al, 2007).<sup>41-43</sup> The benefits of these medications demonstrate allaying debilitating anxiety and can improve sleep.<sup>31</sup> Benzodiazepines and hypnotics that act on the benzodiazepine gamma aminobutyric acid (GABA) receptor complex (zolpidem, zaleplon) are associated with a multitude of onerous consequences including cognitive impairment, reduced mobility, unsafe driving skills, decline of functional independence, falls, fractures, and addiction.<sup>44-48</sup>

Current consensus guidelines advise use of benzodiazepines solely on a short-term

basis.<sup>31,49-51</sup> Mitigation of harm associated with benzodiazepines, especially in the aged, suggests using lowest doses to alleviate symptoms.<sup>31</sup> High potency, long-acting, or prolonged use of benzodiazepines and similar hypnotics are considered high risk by Beers and other criteria. Devising a practical approach to discontinuation of benzodiazepines begins with consideration of safer alternatives. Psychological or pharmacological treatments, ranging from use of antidepressants, cognitive-behavioral therapy, problem-solving, interpersonal and supportive psychotherapy, as well integrative strategies including prayer, massage, aromatherapy, music therapy, art therapy, and multisensory stimulation should be pursued.<sup>52,53</sup> A recent Cochrane review investigated the use of adjunctive pharmacological interventions to facilitate tapering long-term benzodiazepines. Included were carbamazepine, pregabalin, captodiame, paroxetine, alpidem, magnesium aspartate, tricyclic antidepressants, and flumazenil to mitigate benzodiazepine withdrawal symptoms. However, the studies were significantly underpowered and limited by heterogeneity. Antiseizure medications themselves necessitate tapering.

The Eliminating Medications Through Patient Ownership of End Results (EMPOWER) trial, which enrolled 261 older adults, demonstrated success by targeting education about benzodiazepine risks and benefits of tapering. Using this approach, 62% of independent seniors expressed interest in benzodiazepine changes, with 27% of patients stopping benzodiazepines compared with 5% in the control group.<sup>19</sup> To reduce the risk of rebound or withdrawal, the EMPOWER taper schedule involved a gradual reduction over many weeks to attain success. A similar feasibility study of 22 patients emphasized education and self-empowerment for some success in tapering benzodiazepines.<sup>54</sup> Mugunthan and colleagues<sup>55</sup> suggest withdrawing 25% of the daily benzodiazepine dose each week.<sup>55</sup> However, withdrawal should often be more gradual, considering the desirable end point.

### Antipsychotics in Older Adults

Antipsychotic medications are commonly prescribed in the geriatric population.<sup>56</sup> Older patients are 7 to 18 times more likely to be prescribed these medications when compared with a cohort of middle-aged adults.<sup>45</sup> They have been used when patients pose a serious risk of harm to themselves or others. However, use of these antipsychotics for management of neuropsychiatric symptoms and behaviors in the setting of dementia is off label, without supporting evidence and not FDA approved (US Department of Health and Human Services).<sup>57</sup> Moreover, these medications are associated with deleterious side effects including falls, stroke, and death.<sup>57,58</sup>

When considering deprescribing of antipsychotics, a gradual withdrawal strategy is recommended to minimize potential discontinuation effects.<sup>59</sup> Abrupt discontinuation has associated difficulties including dyskinesias, parkinsonian symptoms, dystonias, and neuroleptic malignant syndrome.<sup>59</sup> Withdrawal should be gradual, in most cases extending over a period of greater than 1 month.<sup>60</sup> One may need to re-escalate dosing in the event of persisting withdrawal symptoms that result in distress to the patient.<sup>61,62</sup> There is evidence to support the effectiveness of nonpharmacological psychosocial interventions for reducing antipsychotic medication to mitigate behavioral symptoms in nursing-home residents.<sup>63</sup> These include caregivers employing redirection and reorientation techniques, environmental interventions, simplifying tasks, participation in activities, optimizing sensorium, ensuring social engagement, and maintaining the sleep-wake cycle.<sup>64</sup>

### Deprescribing Cholinesterase Inhibitors

Donepezil, galantamine, and rivastigmine are cholinesterase inhibitors that are all FDA approved for treatment of mild to moderate symptoms of Alzheimer dementia. Memantine, an methyl-D-aspartate receptor antagonist, is indicated for moderate dementia. All these agents have been used off label for management of cognitive and functional symptoms of dementia; however, the

evidence of success is meager. Cholinesterase inhibitors have no proven benefit beyond 1 year, and discontinuation should be considered if the perceived benefit (eg, stabilizing cognition and function) are not achieved in the first 3 months of treatment or when a patient's dementia has progressed. After attaining agreement with family, it is reasonable to taper these medications over 2 to 4 weeks. Monitoring must be implemented following discontinuation to assess for worsening behaviors.<sup>65</sup> Table 3 summarizes deprescribing by medication group, examples of risk, and suggested means.

### LONG-TERM CARE AND SKILLED NURSING FACILITIES

A common care setting for polypharmacy involves the LTC environment. It is estimated that anywhere from 13% to 74% of patients in skilled nursing facilities and LTC (ie, senior assisted care; hereafter, referred to as skilled nursing facility/long-term care [SNF/LTC]) take 9 medications or more.<sup>66</sup> Further, approximately 59% of patients in SNF/LTC take a potentially inappropriate medication by STOPP/START criteria.<sup>67</sup> Patients in a licensed SNF either involves a short-stay medical care or rehabilitation, or they are in residential LTC as long-stay residents.<sup>68</sup> The risks of ADEs associated with polypharmacy are relevant in both groups of patients. However, there is a particular focus on LTC residents, as the need for medications and the goals of care obligate changes because of declining functionality. In a meta-analysis, deprescribing medications in LTC may reduce mortality and falls by approximately 25%.<sup>69</sup>

The nursing home-care team overseeing the medical treatment plan involves the nursing staff, the attending physician, the nursing-home consultant pharmacist, and—importantly—patients and family. Optimally, caregivers and providers contemplate medication reductions to avoid side effects and drug–drug interactions.<sup>70</sup> Advanced care planning expands the discussion toward individual health care objectives and treatments such as dyslipidemia, BP, and diabetes.<sup>71</sup>

Providers in the LTC environment face governmental oversight of medication use from the both state health and federal regulation of the nursing home. The survey process employs quality metrics, which are reported to the CMS.<sup>72</sup> In SNF/LTC, the survey and reporting mechanisms scrutinize psychotropic medication use, particularly antipsychotic medications, which are often employed off label. Guidelines from the American Psychiatric Association give specific guidelines on the use of any antipsychotic medications in treating episodic symptoms of psychosis in patients with dementia.<sup>73</sup> Specifically, the guideline recommends comprehensive assessment and development of a treatment plan that addresses clear assessment of the risks and objectives for use.<sup>73</sup> The efficacy of antipsychotic medications has a very small literature base. Treatment of behavioral issues in dementia with the LTC environment is limited to those exhibiting hazards to self or others.<sup>74</sup> With the acknowledged risks and limited benefits, there is pressure and recommendations by overseeing regulators to reduce and eliminate antipsychotic use. The Canadian group of family physicians recommends tapering antipsychotics after 3 months of use, employing input from the resident and family.<sup>75</sup> In the Cochrane review of the discontinuation of antipsychotic medications in patients with dementia, 10 studies found that discontinuation of antipsychotics after 3 months can be done successfully, with no change in behavioral symptoms.<sup>76</sup> The method of discontinuation of antipsychotic medication varied from abrupt discontinuation<sup>77</sup> to a tapering approach.<sup>78</sup> Although the meta-analysis indicated successful tapering, the overall quality of the studies was low.<sup>79</sup> Of the 2 primary studies with the largest numbers and the smallest bias,<sup>77,78</sup> the results differed from the meta-analysis. In a group of 110 patients with dementia randomized for discontinuation of risperidone, there was higher relapse of symptom in patients switched from risperidone to placebo (48%) compared with staying on risperidone continuously (15%).<sup>78</sup> In 165 patients with dementia,

there was no change in behavior after discontinuation of neuroleptics; however, the authors mentioned potential benefit for patients with highest degree of neuropsychiatric symptoms.<sup>77</sup> Practically, the tapering and discontinuation of antipsychotic medications remains a goal for LTC; however, there still may be relapses of symptoms and the need for continued use.

SNF oversight groups, guidelines, and medical providers recognize the high risks of benzodiazepines and similar hypnotics, and CMS regulations actually require consideration for deprescribing. Patients in LTC may be resistant to reductions of benzodiazepine.<sup>80</sup> The challenges of reducing of benzodiazepines, examined in a systematic review, showed variable rates of benzodiazepine discontinuation between 27% and 80%.<sup>81</sup> Practically, reduction of up to 25% of the dose every 1 or 2 weeks may be a reasonable starting point.<sup>82</sup>

Enlisting nursing staff, patients, and family support to monitor target symptoms during tapering of psychoactive medications enhances success. In a study of 125 patients with an average age of 79 years, using a multidisciplinary team including the patients, deprescribing benzodiazepines or hypnotic agents occurred in 10% of the patients.<sup>83</sup> The team switched patients to a better profile agent (such as a shorter-acting benzodiazepine) in 20% of the cases.<sup>83</sup> When residents and family are unwilling to discontinue benzodiazepines or hypnotics, the provider might change to a safer agent (such as melatonin or a benzodiazepine without active metabolites). If patients elect to maintain benzodiazepines or hypnotic agents, oversight groups expect explicit documentation, noting that the patient wishes to maintain benzodiazepine use despite recommendations. For many, the continuation of benzodiazepines or hypnotic agents involves a quality-of-life discussion.

Deprescribing in the SNF/LTC reduces resources expended in managing medications, especially high-risk medications. In 1 study using START/STOPP criteria, 79% of 100 patients in an Australian nursing home had inappropriate medications.<sup>84</sup> In a

systematic review, many providers target medications with little efficacy, such as supplements, in SNF/LTC.<sup>85</sup> Drugs for gastroesophageal reflux disease, such as proton pump inhibitors and histamine 2 blockers, are common targets for reduction because they lack long-term indications for use. Before reduction of guideline-suggested medications for heart disease such as aspirin, lipid medications, antihypertensives, and antidiabetic medications, a discussion regarding goals of care is imperative. Liberalizing target hemoglobin A1c or glucose ranges make perfect sense for aging patients in LTC.

Using a multidisciplinary team approach, a trial of 426 SNF/LTC residents in the Netherlands found that there was a 39% elimination of 1 inappropriate medication compared with 30% in control.<sup>86</sup> Successful deprescribing in SNF/LTC particularly requires inclusion of nursing team members who monitor and report patient responses to reductions of hypnotics, anxiolytics, and antipsychotic medications. Nurses and care assistants are instrumental in the engagement of nonpharmacological approaches, such as redirection, to reduce agitation. Most importantly, patients and their families are the crucial advocates to the success of deprescribing. Quality-of-life objectives for residents of SNF/LTC include management of symptoms and avoidance of risk, balanced with individualized care goals. It includes the potential that a medication reduction may be unsuccessful and resumed.

## CONCLUSION

Polypharmacy is common and repeatedly shows associations with complications such as falls, hospitalizations, and mortality, regardless of which drugs are involved. The application of guidelines such as Beers and STOPP/START criteria recognize high-risk medications in older adults and are shown to avert ADEs and overall health care costs. Although useful, these do not fully capture entire nuances of clinical decision making for deprescribing in individual patients. Obtaining a comprehensive assessment and deprescribing plan is helpful in complex

and transitional care situations. Careful vigilance for pharmacotherapy problems will always be important. The evidence concerning polypharmacy and high-risk medications suggests that our older patients benefit from a purposeful, dynamic move to fewer drugs. More often, prescribers are considering alternatives to prescribing medications that hold higher risks in aging patients.

**Abbreviations and Acronyms:** ADE = adverse drug event; CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; CMS = Centers for Medicare and Medicaid Services; CNS = central nervous system; DTP = drug therapy problem; EMPOWER = Eliminating Medications Through Patient Ownership of End Results; HTN = hypertension; NSAIDs = nonsteroidal anti-inflammatory drugs; PPI = proton pump inhibitors; QT = Q-wave T-wave; STOPP/START = screening tool of older persons' potentially inappropriate/screen tool to alert doctors to right treatment prescriptions; TSH = thyroid-stimulating hormone

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