

## REVIEW ARTICLE

# CLINICAL MANAGEMENT OF POLYPHARMACY IN THE ELDERLY POPULATION

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## KEYWORDS

polypharmacy

elderly

prescribing

medication

geriatric

## ABSTRACT

Polypharmacy is defined as use of multiple medications (>5) and is common in the elderly adult population. Polypharmacy typically results from the accumulation of treatments for chronic medical conditions such as hypertension, diabetes, coronary artery disease, and psychiatric illnesses. It is associated with problems such as increased risk of falls and adverse medication events. Elderly patients take an average of two to nine medicines per day, and prevalence of polypharmacy in the elderly is 11.5%–62.5%. Elderly patients are at higher risk of adverse drug reactions due to metabolic changes and reduced drug clearance. Evaluation of polypharmacy is an important part of clinical assessment of the elderly population. This process involves performing an adequate medication reconciliation, including supplements, followed by systematic evaluation of medications looking for benefits and harms. It then involves discussing goals of care with the patient and, if necessary, creating a deprescribing plan. When prescribing new medications, prescribers should consider starting at the lower end of the dosing range and increasing only after monitoring for benefits and harms.

## INTRODUCTION

There is an epidemiologic shift in the leading cause of death from infectious disease and acute illness to chronic degenerative diseases. These improvements in medical therapies have led to an elderly population with ever-increasing comorbidities. As patients age, alterations in physiologic processes lead to increased risk of medication adverse effects. It is estimated that elderly patients take an average of two to nine medicines per day, and prevalence of polypharmacy in the elderly is 11.5%–62.5%. With aging there is reduced body water and lean body mass with associated increase in fat mass leading to pharmacokinetic changes of reduced first pass metabolism, reduced renal clearance, and increased volume of distribution. Evaluation of polypharmacy defined as use of >5 medications, is an important part of clinical assessment of this population. The purpose of this review article is to address polypharmacy methods of individualization of care and deprescribing to improve care and reduce risk of medication-induced adverse events in the elderly population in the most common clinical scenarios in an outpatient setting.<sup>1,2</sup>

In addition to prescription medications, elderly patients often use over-the-counter (OTC) medications such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors (PPIs), antihistamines, and supplements. These patients are often not aware of the potential drug interactions with OTC and herbal medications and may not discuss their use. Thorough review and documentation of OTC and other herbal agents in medical record is important to optimize medication management in the elderly population.<sup>1</sup>

## CLINICAL APPROACH

Appropriate prescribing in the elderly ensures that, on balance, the medication regimen is of benefit to the patient. When new medications are expected to aid the patient, their addition should be weighed against the risks of polypharmacy. When starting new medications, the phrase “start low, go slow” is commonly applied to the geriatric population. This phrase prompts prescribers to start new medications at the lower end of an effective range, then monitor closely for benefit or harm prior to making any dose adjustments.<sup>2</sup>

While many medications are started to improve symptoms or control the progression of the disease, not all medications should be used lifelong. When patients accumulate medications that are no longer beneficial or possibly even harmful, they should be deprescribed. Deprescribing is “the planned and supervised process of dose reduction or stopping of medication that may be causing harm, or no longer be of benefit.”<sup>3</sup> The following steps provide a clinical approach to deprescribing: (Figure 1)

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1. Perform an adequate medication reconciliation, including supplements. Periodically, all the patient’s medications should be reviewed in detail to create a complete and accurate list of all their prescription medications, supplements, and OTC medications. This process is known as medication reconciliation, and it forms the cornerstone of appropriate prescribing in the elderly. Optimal times to perform medication reconciliation include at annual visits, at preoperative visits, and any time there is a change in the level of care (eg, transitioning to a new primary care provider, being admitted to a hospital, or moving from home to an assisted living facility).<sup>4</sup>

A complete medication reconciliation provides information regarding the drug, dose, and frequency of use. This information needs to be reviewed by the provider, but it can be obtained by allied professionals such as medical assistants, nurses, or pharmacists.

2. Systematically evaluate the medications to look for benefits and harms. For each medication, consider how the medication may be helping or harming the patient. It is important to consider not only physical or psychological harms, but also financial or social harms. Many medications are expensive or require caregivers to administer them.<sup>5,6</sup>

Several methods have been developed to determine appropriateness of medications that are prescribed to the elderly population. Methods like the Medication Appropriateness Index and Prescribing Optimization Method involve questions to evaluate appropriateness of each medication. These methods are patient-tailored and allow for flexibility in assessment and individualization of the pharmacotherapy to optimize medical therapy and evaluate for appropriateness of dose, frequency, and treatment duration. These two methods can be patient-centered, though time-consuming.<sup>1</sup>

Other methods like BEERS Criteria and START/STOPP screening tool are more rigid and are derived from literature review and expert consensus. BEERS criteria lists potentially inappropriate medications by drug class and disease state.<sup>1,7</sup> STOPP and START tools are used together to recognize medications that may be inappropriate and identify alternatives that can safely treat the condition.<sup>1,8</sup> However, BEERS Criteria and STOPP/START tools do not consider individual preferences, or the degree to which the patient has benefited from the medication.<sup>1</sup>

3. Discuss goals of care with the patient

Ask patients about their treatment goals. The benefits and harms of medications can be compared with the patient’s goals of care. If a medication is being discontinued or its dose reduced, explain to the patient why this is required.

4. Create a deprescribing plan

Once a decision has been made regarding which medications to change, consider possible consequences of the change. Some medications may create adverse drug withdrawal events, especially cardiovascular or central nervous system

medications. If a medication is being used to control symptoms, a plan should be made to monitor the symptoms and ensure they continue to be adequately controlled. Discuss nonpharmacologic options with the patient.

At the end of the visit, review the changes with the patient. They should receive a written copy of the deprescribing plan, as well as an updated medication list. Pharmacies may continue to dispense medications if they are not informed when medications are discontinued, or the dosage is changed. This can be mitigated by ensuring that pharmacies are made aware when changes occur. Many electronic health records automatically send updated information to pharmacies, making this step simple. If needed, it can be helpful to have a staff member contact the pharmacy to inform them of any changes.<sup>1</sup>

## SPECIFIC CONSIDERATIONS IN COMMON DIAGNOSES

### Hypertension

Hypertension is the leading cause of mortality worldwide contributing to up to 30% of all myocardial infarctions (Table 1).<sup>9,10</sup> Several recent trials have shown benefits of management of hypertension with regard to cardiac risk in the elderly population. Management of blood pressure with goal blood pressure of 130–150/70–90 mm Hg with a non-beta blocker medication such as calcium channel blockers, thiazide diuretics, or ACE/ARB [angiotensin-converting enzyme/angiotensin receptor blocker] inhibitors has been shown to reduce cardiovascular risk and improve cerebral blood flow and carotid distensibility in the elderly population without increasing the risk for orthostatic hypotension.<sup>11-13</sup>

TABLE 1:

Indications for treatment of hypertension and available nonpharmacologic treatments.<sup>10</sup>

INTERNATIONAL SOCIETY FOR HYPERTENSION CRITERIA FOR DIAGNOSIS OF HYPERTENSION
Consistent BP >140/90 mm Hg in health care setting
Consistent BP >135/85 mm Hg in home setting
Consistent BP >130/80 mm Hg on 24-hour ambulatory monitor
NONPHARMACOLOGIC MANAGEMENT OF HYPERTENSION
Reduction of salt intake
Smoking cessation
Increasing physical activity
Weight loss
Pharmacotherapy if BP >140/90 mm Hg or BP >130/80 mm Hg if individual cardiac risk is >10% with thiazide, ACE inhibitor/ARB, or calcium channel blocker to goal BP of 130-150/70-90 mm Hg. Beta blockers are second line due to risk of orthostatic hypotension.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure

### Hyperlipidemia and Vascular Disease

Statin medications are firstline therapy for management of hyperlipidemia and are frequently given to elderly patients.<sup>14</sup> Furthermore, statin therapy among elderly 75 years and older without atherosclerotic cardiovascular disease (ASCVD) has been associated with reduced risk of all-cause and cardiovascular disease (CVD)-related mortality.<sup>16</sup> Risks of statin-induced myopathy and decline in physical function remain low. Furthermore, a recent study suggests that statins may preserve function by reducing risk of vascular events and improving vascular health.<sup>16-18</sup> When managing cardiovascular risk in older adults it is important to incorporate concept of frailty to individualize their treatment plan as one size does not fit all. Statins should be deprescribed in setting of frailty, low functional capacity, and reduced life expectancy of less than 10 years (Table 2).<sup>15-18</sup> Frailty can be measured anywhere using gait speed with frailty cut off 4 m in less than 5 s.<sup>15</sup>

TABLE 2:

Guidelines on use of statins in the elderly population.<sup>18</sup>

AHA/ACC GUIDELINES ON USE OF STATINS IN THE ELDERLY POPULATION
Reasonable to initiate or continue current regimen of moderate-intensity or high-intensity statin therapy in patients 75 years and older after consideration and evaluation of:
<ul style="list-style-type: none"> <li>• ASCVD risk reduction</li> <li>• Adverse effect of medication</li> <li>• Medication interaction</li> <li>• Frailty</li> </ul>
In nonfrail elderly patients who are on high-intensity statin therapy or maximal tolerable statin therapy with high risk for ASCVD and LDL >70 mg/dL, it would be reasonable to add ezetimibe to lower ASCVD risk.
Stop statin therapy with functional decline, increased frailty, and reduced life expectancy, as benefits of statins in this setting are limited.

ACC, American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; LDL, low-density lipoprotein

### Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD) is common in elderly patients. However, its presentation may be different from the younger population. GERD symptoms in elderly include dysphagia, vomiting, and respiratory symptoms. Additionally, severity of GERD symptoms and esophageal inflammation increases with age.<sup>19</sup> Pharmacologic management of GERD includes PPIs. Prolonged use of PPIs can have some risks such as small intestine bacterial overgrowth, increased risk of Clostridium difficile infection, nutrient deficiencies (vitamin B12, calcium, magnesium, iron), increased risk of pneumonia, and development of chronic kidney disease. When PPIs are appropriately prescribed their benefits potentially outweigh their risks. PPIs should be prescribed at lowest possible dose. In the setting of uncomplicated GERD, they can be stopped after 2 months or switched to an H2 blocker.<sup>20</sup>

Nonpharmacologic options in management of osteoporosis include participation in a multicomponent exercise program involving balance and resistance training under supervision of a physical therapist.<sup>21</sup> Current pharmacologic treatments for osteoporosis include bisphosphonates, denosumab, parathyroid hormone, abaloparatide, and romosozumab.<sup>22</sup> National Osteoporosis Foundation guidelines recommend use of bisphosphonates as firstline therapy for management of osteoporosis with risk assessment of an individual patient after an initial period of 3-5 years of treatment. All medications reduce nonvertebral fractures except for ibandronate. Zoledronic acid, risedronate, and alendronate reduce risk of hip fractures and vertebral fractures.<sup>22,23</sup> Denosumab can be a safe and effective option for long-term use. Denosumab should not be stopped without continuing another antiosteoporotic medication due to increased risk in bone loss and fracture risk. Long-term use (>10 years) of bisphosphonates can increase risk of atypical femoral fractures and drug holiday should be considered after 3-5 years in most patients (Table 3).<sup>23,24,26,27</sup> Overall evidence on benefits of vitamin D screening and supplementation is controversial. United States Preventive Services Taskforce (USPSTF) recommends against use of vitamin D supplementation for fall risk and osteoporosis risk reduction in noninstitutionalized elderly patients.<sup>26</sup>

TABLE 3 :

Indications for treatment of osteoporosis and associated risk factors for atypical fractures with treatment.<sup>24,26</sup>

AHA/ACC GUIDELINES ON USE OF STATINS IN THE ELDERLY POPULATION
Long duration of treatment with bisphosphonate therapy of >5 years
Younger age
Asian race
Low vitamin D levels
Use of multiple antiresorptive drugs
Glucocorticoids
Diabetes
Rheumatoid arthritis
Indications for Pharmacologic Treatment of Osteoporosis
Low bone mass or osteopenia and history of fragility fracture at hip or spine
T score of less than -2.5
T score of -1 to -2.5 with FRAX score >20% for major osteoporotic fracture or >3% for hip fracture

FRAX, fracture risk assessment tool

FIGURE 1:

Clinical approach to deprescribing.

1. Perform an adequate medication reconciliation, including supplements
2. Systematically evaluate medications looking for benefits and harms
3. Discuss goals of care with the patient
4. Create a deprescribing plan

## Osteoporosis

Nonpharmacologic options in management of osteoporosis include participation in a multicomponent exercise program involving balance and resistance training under supervision of a physical therapist.<sup>21</sup> Current pharmacologic treatments for osteoporosis include bisphosphonates, denosumab, parathyroid hormone, abaloparatide, and romosozumab.<sup>22</sup> National Osteoporosis Foundation guidelines recommend use of bisphosphonates as firstline therapy for management of osteoporosis with risk assessment of an individual patient after an initial period of 3–5 years of treatment. All medications reduce nonvertebral fractures except for ibandronate. Zoledronic acid, risedronate, and alendronate reduce risk of hip fractures and vertebral fractures.<sup>22,23</sup> Denosumab can be a safe and effective option for long-term use. Denosumab should not be stopped without continuing another antiosteoporotic medication due to increased risk in bone loss and fracture risk. Long-term use (>10 years) of bisphosphonates can increase risk of atypical femoral fractures and drug holiday should be considered after 3–5 years in most patients (Table 3).<sup>23,24,26,27</sup> Overall evidence on benefits of vitamin D screening and supplementation is controversial. United States Preventive Services Taskforce (USPSTF) recommends against use of vitamin D supplementation for fall risk and osteoporosis risk reduction in noninstitutionalized elderly patients.<sup>26</sup>

## Thyroid disease

Hyperthyroidism can be treated with either I-131 iodine, thyroidectomy, or antithyroid medications, which are safe and equally efficacious. The antithyroid medications available are propylthiouracil (PTU) and methimazole. Methimazole is recommended over PTU as the antithyroid medication of choice for management of overt hyperthyroidism due to increased risk of fatal liver injury associated with PTU.<sup>27</sup> Subclinical hyperthyroidism generally is not treated as very few patients are symptomatic or develop hyperthyroidism and benefits of treatment remain controversial.<sup>27,28</sup>

Hypothyroidism can be managed by levothyroxine, which generally has a long half-life, is well tolerated, and is well absorbed. There is no evidence that treatment of subclinical hypothyroidism improves symptoms and reduces mortality and morbidity. Additionally, elevated thyroid-stimulating hormone (TSH) in the elderly is associated with increased longevity.

## Anxiety

Nonpharmacologic therapies for treatment of anxiety, such as cognitive behavioral therapy (CBT), should be optimized prior to consideration of pharmacologic management of anxiety. Appropriate medication management for anxiety in the elderly includes selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), or buspirone.<sup>32</sup> Venlafaxine is effective but can raise blood pressure and is often discontinued secondary to side effects.<sup>33</sup> SNRIs and benzodiazepines should be avoided, particularly those that are short or intermediate acting, due to increased risk of cognitive impairment, delirium, falls, fractures, and car accidents.<sup>34,38</sup> Escitalopram may be more effective than citalopram in cases of

panic disorder.<sup>35</sup> Evidence for use of mirtazapine for anxiety is limited.<sup>36</sup> Pregabalin has been shown to be safe and well tolerated for anxiety.<sup>37</sup>

## Depression

Behavioral intervention and/or psychotherapy, with CBT being the most studied, should be considered in place of or in addition to pharmacotherapy. SSRIs are firstline pharmacotherapy, particularly citalopram, escitalopram, and sertraline. Bupropion and trazodone are also reasonable options.<sup>38–41</sup> Mirtazapine can be helpful in adults with depression and comorbid appetite and sleep disturbance. Those at risk of hyponatremia may tolerate bupropion over SSRIs, SNRIs, or mirtazapine.<sup>38,42</sup> Newer antidepressants such as vilazodone, vortioxetine, and levomilnacipran have limited evidence for efficacy and safety in older adults. For refractory depression, other considerations include addition of low-dose atypical antipsychotics such as aripiprazole or quetiapine, or electric convulsive therapy (ECT).<sup>39</sup> Tricyclic antidepressants should be avoided due to anticholinergic properties. Monoamine oxidase inhibitors pose a risk of postural hypotension and sleep disturbance and also should be avoided. Those who are taken off antidepressants should slowly be tapered and monitored for signs of relapse.<sup>43</sup>

## Insomnia

CBT for insomnia and optimal sleep hygiene is firstline therapy for adults with chronic insomnia. There is insufficient evidence for effectiveness of melatonin, though many patients find this to be helpful and with a low side-effect profile. Ramelteon, a melatonin receptor agonist, reduces sleep onset latency with low-quality evidence but has relative lack of negative side effects.<sup>44</sup> Doxepin could be considered at low doses.<sup>45</sup> Benzodiazepines should not be used for insomnia as they only have modest short-term benefit and multiple risks including increased risk of hip fractures.<sup>46,7</sup> As of 2019, Beers criteria added that sedative-hypnotics should be avoided in the elderly population regardless of duration as they increase risk of delirium, falls, fractures, and motor-vehicle accidents.<sup>7,46,47</sup>

## Cognitive Decline

Treatment of mild cognitive impairment in older adults starts with early recognition, followed by implementation of aerobic activity, mental activity, and optimization of risk factors for CVD and stroke.<sup>48</sup> Additionally, polypharmacy should be considered in the differential for mild cognitive impairment. There is no effective medication for mild cognitive impairment and use of cholinesterase inhibitors and memantine is not recommended at this stage.<sup>49</sup> Pharmacologic recommendations for treatment of various types of dementia are beyond the scope of this article.

## Delirium

Nonpharmacologic strategies to prevent and treat delirium in the elderly population are first line. Pharmacologic management of delirium should only be considered when the safety of the patient or those around them is at risk or to perform necessary medical interventions. Antipsychotics, such as haloperidol, and atypical antipsychotics are effective but pose a risk of extrapyramidal side

effects, QTc prolongation, and increased mortality in those with dementia. Benzodiazepines worsen the duration and severity of delirium and should not be used.<sup>50</sup>

### Urinary Incontinence

To treat urinary incontinence, a careful review of offending medications or lifestyle factors should be done. Behavioral interventions such as timed voiding and pelvic-floor exercises should be maximized. Use of medications specifically for urinary incontinence should be used cautiously. Urinary antimuscarinics such as oxybutynin, tolterodine, and trospium pose a risk of anticholinergic side effects such as constipation, dry eye, and blurred vision.<sup>51</sup> Trospium may be a better-tolerated option due to less impact on the central nervous system. Long-acting formulas have better side-effect profiles than their immediate-release counterparts and are equally effective.<sup>52</sup> Beta-3 agonists such as mirabegron are associated with less adverse events but should not be used in those with uncontrolled or severe hypertension.<sup>53</sup> Procedural intervention may be considered but is beyond the scope of this article.

### Constipation

When possible, eliminate or replace medications that cause constipation (eg, anticholinergics, opioids, calcium channel blockers, NSAIDs). Address contributing lifestyle factors such as poor caloric or fluid intake, low-fiber diet, and physical inactivity. Toilet training to maximize the gastro-colic reflex and minimize straining may also be helpful. Osmotic laxatives, particularly polyethylene glycol, are effective.<sup>54</sup> Stimulant laxatives (other than bisacodyl and sodium picosulfate) and stool softeners have a lack of supportive evidence and should not be used for chronic constipation routinely.<sup>55,56</sup> Lubiprostone or linaclotide can be considered as next-line agents if less-expensive treatments are not helpful. Bulking agents can be used if the patient does not have slow-transit constipation. Fecal impaction is best treated with mineral-oil enema, warm-water enema, or glycerin suppository. Note that long-term use of magnesium-based laxatives and phosphate enemas should be avoided due to potential for electrolyte disturbance.<sup>57</sup>

### Antibiotics

Antibiotics should be selected choosing the narrowest spectrum and with the shortest treatment course possible. Fluoroquinolones should be avoided in the elderly when possible due to risk of tendon injury.<sup>58</sup> Nitrofurantoin is acceptable to use in those with creatinine clearance >30 for the short term, noting the uncommon but serious increased risk of pulmonary and hepatotoxicity.<sup>7,59</sup> Trimethoprim-sulfamethoxazole should be used with caution in combination with ACE/ARB in those with decreased renal function due to risk of hyperkalemia.<sup>7</sup> Long-term care facilities are common sites of development of multidrug resistant organisms such as methicillin-resistant staphylococcus aureus or vancomycin-resistant enterococci. Older patients are at particularly high risk of morbidity and mortality associated with antibiotic-induced diarrhea or Clostridium difficile colitis.<sup>60</sup>

## CONCLUSION

As the population continues to age, addressing polypharmacy in elderly patients will become even more important. A thorough medication review should be performed for each patient. Utilizing evidence-based, risk-vs-benefit assessments, and goals-of-care conversations provides a practical yet individualized approach to reducing polypharmacy in older adults for better clinical outcomes.

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