# Chapter 4
# Medication Management in Older Adults with Dementia


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**Main Points**

- Polypharmacy and the use of potentially inappropriate drugs are common in patients with dementia and associated with increased risk of hospitalization and mortality.
- Deprescribing, the planned and supervised dose reduction or discontinuation of a medication that may be causing harm or not helping can reduce adverse effects and pill burden.
- Medication nonadherence in patients with dementia can lead to poor health outcomes; many approaches to promoting medication adherence are available, though research on their effects on outcomes is limited.
- Transitions from one level of care to another present both challenges and opportunities for patients with dementia and require coordination between multiple prescribers, pharmacists, and others.

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**Case Vignette**
LE is a 77-year-old male who is being discharged from acute care after an 8-day stay for volume overload due to heart failure with preserved ejection fraction, for which he has been treated with furosemide and lisinopril. It is his third heart failure–related hospitalization in the last 6 months and, from his refill history, it is questionable how adherent he is with his furosemide regimen. He also has moderate dementia (Montreal Cognitive Assessment score of 13/20), well-controlled type 2 diabetes (A1C = 6.7%), and insomnia. In addition to the diuretic and angiotensin-converting enzyme inhibitor, his prescribed medications include donepezil, memantine, glyburide and simvastatin. He also takes ibuprofen and doxylamine over the counter. He typically lives at home with his son who works full-time. At this time, he is being discharged to a skilled nursing facility for physical therapy with an anticipated length of stay of 14 days.

## Introduction

Medication management in patients with dementia can be challenging and complicated. Because dementia is strongly age-related and concomitant diseases are nearly always present, polypharmacy is the norm. Furthermore, patients with dementia are frequently susceptible to medications that further worsen cognitive status. Memory loss and other cognitive deficits can make adherence to prescribed regimens challenging, and the often complex medication schedules and diminished mental capabilities seen in patients with dementia can make transitions from one level of care to another particularly difficult.

## Polypharmacy and Deprescribing

Polypharmacy is a growing phenomenon in older adults with and without dementia, likely due to the prevalence of complex comorbid conditions and advances in treatment options [12, 14]. Data from the National Health and Nutrition Examination Survey (NHANES) conducted in the United States revealed that the proportion of non-institutionalized adults aged 65 and older taking five or more medications tripled from 12.8% to 39% between 1988 and 2010 [14]. After accounting for differences in age, sex, and comorbidities, polypharmacy is higher in patients with dementia compared to their cognitively intact peers. [3, 15, 35]. Adverse consequences from polypharmacy include increased use of potentially inappropriate medications (PIMs), medication adverse effects, disability, healthcare utilization, and mortality [31, 38, 41, 43, 44]. Patients with dementia are particularly vulnerable

to these unfavorable outcomes due to impaired decision-making capacity, poorer adherence, and communication challenges [10].

Potentially inappropriate prescribing is common in the United States and Europe, ranging from 12% in community-dwelling older adults to 40% in nursing home residents [22]. In a cross-sectional study of over 5000 nursing home residents with advanced dementia, 54% received at least one medication with questionable benefit including cholinesterase inhibitors, memantine, and lipid-lowering agents [63]. Antipsychotics are also commonly prescribed off-label for the management of behavioral and psychological symptoms of dementia (BPSD), despite evidence-based recommendations and federal regulations discouraging routine use [21, 30, 56].

Several clinical tools using criteria that are implicit (judgment based), explicit (criterion based), or a combination of both are available to help identify PIMs for older adults in a variety of clinical settings [33]. The Beers criteria [2] and the Screening Tool of Older Person's Prescriptions (STOPP)/Screening Tool to Alert doctors to Right Treatment (START) [49] criteria are two well-known, validated tools.

The most recent update of the Beers criteria provides evidence-based recommendations by an interdisciplinary expert panel addressing the following categories: (1) PIMs in older adults, (2) PIMs to avoid with certain conditions, (3) medications to be used with considerable caution, (4) medication combinations that may lead to harmful adverse effects, and (5) medications that should be avoided or dosed cautiously in patients with poor renal function [2].

STOPP version two consists of 80 indicators including drug–drug and drug–disease interactions, therapeutic duplication, and drugs that increase the risks of cognitive decline and falls [49]. Conversely, START is a list of 22 considerations to minimize the possibility that older patients do not receive pharmacotherapy that may be indicated and beneficial.

It is important to note that these tools do not specifically address the complex needs of patients with dementia, particularly with end-of-life considerations in advanced disease. Future studies are needed to provide a framework for identifying PIMs throughout the spectrum of the illness [28, 37, 43].

Strategies to combat high-risk prescribing have been described in various settings including pharmacist medication review, involvement of a geriatrics specialist service, computerized alerts and clinical decision support tools, educational programs, and regulatory policies [1, 23, 34]. Diverse approaches were employed in these studies, making it difficult to assess the clinical effectiveness and sustainability of individual interventions. A systematic review conducted by Spinewine and colleagues revealed that studies incorporating geriatrics services, pharmacist involvement, and computerized clinical decision support resulted in considerable reduction in PIM use, while those focused on educational interventions had inconsistent results [61].

Because of the progressive nature of dementia, medication profiles must be reviewed and revised on a regular basis with careful consideration of the risks relative to potential benefits, life expectancy, and patient values and preferences [58].

Deprescribing methods applying patient-centered approaches have been shown to be safe and feasible and may improve patient outcomes [50, 55, 58]. In 2015, Scott and colleagues published a simplified five-step deprescribing protocol: (1) obtain a thorough medication history including indications, (2) ascertain individual patient risk to determine the appropriate intensity of a deprescribing intervention, (3) identify medications eligible for discontinuation if no valid indication, ineffective, or risk outweighs clinical benefit over patient's lifespan, (4) prioritize medications for discontinuation or taper that have the lowest benefit–harm ratio and likelihood of adverse withdrawal reactions, and (5) close monitoring, shared decision-making between patient and provider, caregiver support, and documentation of outcomes [58].

## *Deprescribing Antipsychotics*

As a specific example, antipsychotic use in patients with dementia has been linked to significant adverse effects including mortality, and little evidence of long-term clinical benefit exists [6, 17, 32, 57]. For the management of BPSD, international guidelines advocate for non-pharmacologic interventions as a first-line alternative when feasible. These interventions, which should be applied using a patient-centered approach to maximize overall benefit, include but are not limited to cognitive and sensory stimulation, music therapy, environmental modifications, and caregiver support and education [8, 39, 45, 56]. In some instances, behavioral changes may signal an underlying condition that needs medical attention such as uncontrolled pain. Routine assessment of pain and effective management may reduce BPSD and the need for antipsychotics [18, 29]. Furthermore, the dementia subtype will likely influence treatment choices. For example, patients with Lewy body or Parkinson's dementia may have more severe adverse effects with antipsychotics, including worsening cognitive and motor function compared to individuals with other dementia subtypes [62]. In cases where non-pharmacologic interventions are inadequate or patients demonstrate symptoms of severe agitation posing a considerable risk of harm to themselves or others, pharmacologic treatment may be considered at the lowest effective dose [8, 39, 45, 56]. Emerging evidence suggests that deprescribing antipsychotics can be accomplished safely in some patients with minimal withdrawal symptoms. The direct link of antipsychotic discontinuation to long term outcomes such as improved quality of life, mortality reduction, or cost savings needs to be further elucidated [11, 26, 65].

As a part of the Deprescribing Guidelines for the Elderly Project, a Canadian team of pharmacists, family physicians, specialists, and medical researchers developed an evidence-based algorithm for deprescribing antipsychotics in BPSD. For patients stabilized on at least 3 months of treatment, the recommendation is to taper slowly with a 25–50% dose reduction on a biweekly basis. Patients and caregivers should be engaged in the determination of taper regimens and monitoring plans. If BPSD relapses, it is recommended to incorporate non-pharmacologic interventions and re-attempt a trial of deprescribing in 3 months [8].

## *Deprescribing Cholinesterase Inhibitors and Memantine*

Four drugs are currently approved and marketed in the United States for management of symptoms of dementia: the cholinesterase inhibitors donepezil, rivastigmine, and galantamine, and the N-methyl-D-aspartate (NMDA) receptor antagonist memantine. These agents are widely prescribed despite their modest benefit [7, 42]. While they do not alter the underlying pathophysiology, they can provide clinically significant symptomatic improvement in some individuals.

As the underlying dementia progresses, family and prescribers often struggle with the decision to discontinue these agents. Similar to the previously mentioned algorithm for antipsychotics, the Deprescribing Guidelines for the Elderly Project has also published an algorithm to provide guidance for deprescribing cholinesterase inhibitors and memantine [54]. In the absence of adverse effects, a diagnosis significantly limiting expected lifespan, patient/family unwillingness or inability to continue the medication, or certain other criteria, a year or more of treatment with a cholinesterase inhibitor or memantine is reasonable. Beyond that point, an attempt at deprescribing is reasonable in patients who have experienced a significant loss of cognitive function in the previous 6 months, end-stage dementia (e.g., inability to interact with their environment or near complete reliance on others for activities of daily living), or if no perceived benefit is being seen. Tapering of the cholinesterase inhibitor or memantine is recommended, and the patient and caregivers should be assessed at least monthly.

## *Barriers to Deprescribing*

Optimizing medication therapy in patients with dementia can be challenging due to shifting goals of care along the spectrum of disease severity. Patients may be psychologically attached to chronic medications, and discontinuation may signal the perception of inadequate care, deteriorating medical condition, or coincidental terminal illness [5]. Behavioral and psychological symptoms of dementia are common, complex, and can be difficult to manage. The profound impact these symptoms have on patients, families, and caregivers have led to an overreliance on the use of psychotropic medications [26]. Resistance from patients or caregivers due to perceived benefit of medications may decrease the likelihood of deprescribing and, in some cases, damage the patient–provider relationship. Furthermore, the fear of destabilizing a patient or causing unfavorable sequela by discontinuing medications prescribed by a specialist or another clinician may be a deterrent to successfully withdrawing medications [24]. Lastly, there is a paucity of high-quality evidence-based guidelines supporting safe deprescribing practices [5, 58].

Deprescribing should be integrated into routine clinical practice to improve care and promote rational medication use in patients with dementia. Successful deprescribing requires open communication, shared decision-making, and continuous engagement of patients, families, and caregivers. Further research is warranted to develop evidenced-based systematic approaches for safe deprescribing.

## Improving Medication Adherence in Patients with Dementia

Adherence to prescribed medications is low in the general population, even lower in older patients, and especially poor in individuals with a diagnosis of mild cognitive impairment or dementia [66]. Nonadherence increases the risk of several clinically important outcomes including hospital admissions, nursing home placement, and mortality. Nonadherence also correlates with increased healthcare costs [36]. While a precise, standardized definition of adherence does not exist, it is generally accepted that taking <80% of prescribed doses is suboptimal and significantly increases the risk of poor outcomes.

Older patients with dementia face specific challenges to their ability to be adherent above and beyond those that are typical. Deficits in various areas of cognition can contribute to these challenges. For example, deficits in executive function may contribute to patients' inability to devise and follow through on plans to take medications as prescribed [40]. Declines in memory and attention can also negatively impact adherence. A decreased willingness to take medications and undergo other medical interventions as is sometimes seen in patients with dementia is also problematic. Finally, decreases in motor function, which are especially common in patients with more advanced cognitive impairment, can adversely impact patients' ability to take medications even if they are otherwise willing to do so. This is especially true for devices such as metered dose inhalers and dry powder inhalers that require a degree of dexterity to use properly [40].

### *"Low-Tech" Options*

Streamlining medication regimens is an important step in increasing adherence for the simple reason that the fewer medications and doses are prescribed, the more likely it is that the patient will be adherent [20, 36]. This streamlining includes stopping medications that are no longer needed, duplicative, or are more likely to cause harm than provide benefit, as mentioned in the deprescribing section of this chapter.

Only a limited number of studies have identified approaches to improve adherence specifically in patients with dementia. Regimens consisting of medications given no more than twice per day, simple pill boxes, increased caregiver involvement, and provision of blister packs of medications with the involvement of a pharmacist to deliver education and answer questions are among the interventions with documented effectiveness [66]. Furthermore, use of devices such as inhalers as opposed to a nebulizer to deliver inhaled drugs appears to adversely affect adherence [40]. Evidence also exists that patients are more adherent to transdermal rivastigmine than an oral cholinesterase inhibitor, though the significantly higher acquisition cost for the transdermal dosage forms as well as the modest effectiveness of all currently available treatments for dementia must also be considered [36].

### *"High-Tech Options"*

A number of more technologically elaborate approaches to increasing medication adherence in patients with dementia have also been evaluated. These include pill boxes, telehealth interventions, automated dispensing devices, and smartphone applications. Pill boxes with alarms that signal when a dose of medication is due may be useful in some individuals but, depending on the severity of cognitive impairment, these often require that a caregiver or healthcare professional fill and program them. [36] This is a relatively low-cost choice, with many options costing under $100.

Telehealth interventions consisting of either regular automated telephone calls or actual people (generally pharmacists) contacting patients to remind them when a dose is due and/or provide education and encouragement regarding their regimen have proven to be successful in some studies [13, 60].

Automated dispensing devices that release dose(s) at a specific time and signal the patient that a medication dose is due are available. Several different options exist; for some the equipment is purchased outright and others are a subscription service that is paid for monthly. In either case, as is true for most interventions designed to increase adherence, help from a caregiver or other individual is needed to stock the machine with appropriate medications and program it correctly is needed. Prices vary widely; upfront costs range from free to nearly $1700; monthly fees can be as low as $0 for certain products purchased outright to as much as $80 [59].

Smartphone applications that notify the patient/caregiver when a dose is due are also available. These also will generally require someone to program them as well as verify that doses are being taken as prescribed. Examples include Medisafe and Pill Reminder. Costs for these applications range from free to a few dollars.

Overall, nearly 200 studies evaluating interventions intended to increase medication adherence have been performed; only a small number have specifically enrolled patients with dementia [48]. Even in groups of patients who do not have the specific challenges and barriers to adherence that patients with dementia face, the evidence supporting specific interventions is weak. Still, strategies to improve medication adherence remain vitally important both for management of the underlying dementia as well as comorbid conditions.

## Transitions in Care in Patients with Dementia

Caring for patients with underlying dementia presents healthcare practitioners and caregivers with many challenges, especially when they are transitioning them from outpatient to inpatient settings and vice versa. In one study, greater than 40% of hospital admissions in older patients were due to drug-related issues [25]. This begs the question of how efficient the healthcare system is when conducting medication

reconciliation at every point where patients are seen. Caring for the elderly, regardless of care setting, can be challenging as these patients have many pathophysiologic and physiologic changes related to comorbidities and aging [64]. In addition to the normal changes that occur with aging, a patient with dementia may have difficulty comprehending instructions as well as remembering when to take medications without some type of additional help as discussed above [27].

In a study done in Australia, researchers found that patients with dementia are about twice as likely to be admitted to a hospital than a patient without dementia (25% vs. 12%). [4]. Studies have also shown that as dementia progresses, the rate of utilization of inpatient nursing facilities progressively increases; however, close to 50% of patients will return home at some point with or without formalized nursing services. Many patients will have at least one transition from a skilled nursing facility before reaching their long-term living situation. Every transition in care carries with it an opportunity for miscommunication between the patient or caregiver and health care providers regarding goals of care and medication changes [16].

Transitions in care pose a challenge to both caregivers and healthcare professionals because medication changes may be warranted due to the acute illness itself or as a result of abrupt cognitive status changes leading to an increase in the risk of medication errors. Acute declines in cognitive status can linger for some time after illness before returning to baseline. In some instances, the patient may establish a new cognitive baseline resulting in changes in medication needs as well as the appropriate level of care for them. Often, a baseline decrease in executive function before illness can negatively affect the recovery process as patients are less likely to fully participate in physical rehabilitation [52]. Because approximately 30% of adults over the age of 65 years are taking at least 5 medications, this creates more room for error and increases the importance of determining the need and appropriateness of each medication prescribed [53].

In a systematic review, between 0.4–51.2% of patients experienced medication-related harm after discharge from a hospital. Of these incidents, between 35–59% were found to be preventable [51]. Preventing medication-related issues while patients are transitioning between different levels of care has been a focus of National Patient Safety Goals for medical accrediting bodies, including the Joint Commission, for many years. Establishing best practices in transitions of care is something on which healthcare providers and institutions continue to spend significant time and resources [46, 47].

Patients with multiple co-morbidities are often prescribed medications from several providers. However, changes due to acute illness or in overall health status are not always communicated to all prescribers. A qualitative study conducted in Sweden showed that there were five important themes identified from multiple focus groups involving trained healthcare providers who cared for patients with dementia transitioning between levels of care.([9]) Because providers don't always have contact with the other providers caring for a patient with dementia, a good working relationship with the next of kin or caregiver that is routinely interacting with the patient living with dementia is vital. This is as important during the early stages of disease as it is in the more advanced stages. Next of kin and caregivers can provide important information and history regarding disease progression and

medication use. They are also able to share goals of care discussions that may have occurred within families and ensure that the patient's goals and wishes are being respected [9].

Medication reconciliation remains a large part of transitions in care and, because it is a highly involved and detail-oriented process, many issues can be overlooked and mistakes can be made. Thorough assessment in combination with detailed documentation can also aid health care practitioners in making educated decisions regarding medication changes. Communication between inpatient and outpatient providers can also help to ensure smoother transitions in care. Short hospital stays and rapid discharge planning often leave little time for a thorough process that ensures accurate reconciliation occurs. Inpatient practitioners often reach out to outpatient providers when a patient is hospitalized, but there may be lag time in response due to clinic responsibilities, leaving the inpatient provider to make decisions with only the information they have on hand. Likewise, providers who are on the receiving end of a patient, whether it be in an outpatient clinic or rehabilitation center, face similar challenges getting in contact with inpatient providers to find out more about what may have happened during an inpatient stay. Involving family members, caregivers, or the patient's regular pharmacist can be helpful in this area. Inpatient pharmacists can also play a role in ensuring accurate records are being utilized while decisions are being made [19].

## Discussion of Clinical Case

LE is experiencing medication management issues in all of the areas discussed in this chapter with polypharmacy/potentially inappropriate medication prescribing and poor adherence contributing to his frequent hospitalizations. He is also now transitioning to a different level of care, further increasing the risk for medication misadventures. Furthermore, opportunities for deprescribing are also present.

The causes or factors contributing to LE's non-adherence to his prescribed diuretic should be elucidated. If it is related to his underlying dementia, simple reminders such as a pill box or more complicated approaches such as setting an alarm as a reminder may be indicated. It may also be necessary for the prescriber to broach the subject of the patient receiving additional help from caregivers in order to improve adherence, either now or in the near future. However, it should not be assumed that the dementia is the only or even the main cause of the non-adherence. Reinforcing the purpose of the medication and the possibility that taking the regimen as prescribed may prevent hospitalizations could prove helpful, as often patients discontinue medications from which they do not perceive a benefit. The strong diuresis from loop diuretics can also be a challenge in patients with limited mobility who find it difficult to reach the restroom before voiding; if this is the case with LE, interventions such as a bedside urinal or commode could be warranted.

Discontinuing unnecessary or potentially inappropriate medications could decrease LE's pill burden and improve adherence to the rest of the regimen as well as decrease the risk for adverse effects. The use of the long-acting sulfonylurea

glyburide should be revisited, as it has a fairly high risk of causing hypoglycemia in elderly patients and is specifically mentioned in both the Beers criteria and STOPP. Metformin, if not contraindicated, may be appropriate as it does not cause hypoglycemia when used as monotherapy. Due to his age, comorbidities, and good glycemic control, non-pharmacologic approaches alone could also be reasonable. A discussion of the risks and benefits of simvastatin in this older patient with no history of cardiovascular events would be worthwhile. Finally, doxylamine and ibuprofen are potentially inappropriate due to their anticholinergic and gastrointestinal/renal toxicities, respectively, and should be replaced with safer alternatives including possibly non-pharmacologic options.

Transitioning from acute care to a skilled nursing facility and then back home is fraught with potential issues for LE. Medications started while in an acute care setting that are not needed in the long term, such as prophylaxis for deep venous thrombosis, sliding scale insulin, or proton pump inhibitors, should be discontinued. Furthermore, a thorough medication reconciliation should be performed at each transition of care. Patient and caregiver education covering both chronic and recently started medications, including the name, schedule, purpose, and potential adverse effects, should be provided, and barriers to the patient's ability to adhere to the prescribed regimen should be determined and dealt with to the extent possible.

## Conclusion

Medication management is always challenging and is even more so in individuals with dementia. Great caution is called for when initiating, modifying, or even discontinuing a drug in this population, but many patients can have their medication regimen streamlined or otherwise improved by reducing or replacing potentially inappropriate medications. Although little data on improving adherence in patients with dementia exists, some simple or technological approaches are available and may be of benefit. Finally, increasing awareness of the potential pitfalls and stumbling blocks in medication management in patients transitioning from one level of care to another can potentially decrease medication-related problems in this highly vulnerable population.

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