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Managing medications in clinically complex elders: “There’s got to be a happy medium”

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Abstract

Multiple medication use is common in older adults and may ameliorate symptoms, improve and extend quality of life, and occasionally cure disease. Unfortunately, multiple medication use is also a major risk factor for prescribing and adherence problems, adverse drug events, and other adverse health outcomes. This article describes a typical case of an older patient taking multiple medications and summarizes the evidence-based literature about improving medication use and withdrawing specific drugs and drug classes. It also describes a systematic approach for how health professionals can assess and improve medication regimens. The application of these approaches should be of benefit to patients, caregivers and family, and to health professionals themselves.

THE PATIENT’S STORY

Mr L is an 84-year-old man with dementia first seen by Dr S in November 2008. His past medical history was significant for atrial fibrillation, diabetes mellitus, hypertension, hyperlipidemia, chronic kidney disease (estimated creatinine clearance of 42ml/min), and gastritis and gastroesophageal reflux disease. His past surgeries included a transurethral bladder resection for bladder cancer with subsequent urinary incontinence and a lumbar decompression for spinal stenosis in 2008.

Mr L lives with his wife, Mrs L, who cares for him. He is a retired writer and editor in the music business, and a lifelong tennis player. On first presentation, his initial complaints were forgetfulness, difficulty walking, and falling. His wife reported that he was “doing almost nothing,” maintaining a sedentary lifestyle at home and following her around. He needed considerable help with bathing and dressing and some assistance with toileting and transfers, and was dependent in most instrumental activities of daily living including shopping, housekeeping, and preparing meals. His wife hired a home health aide for several hours a day to help alleviate her substantial caregiving burden.

At his initial visit, blood pressure was approximately 135/60 mmHg, and heart rate was in the 50s. He scored 13 of 29 points on a Folstein Mini Mental Status Exam (MMSE)

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performed shortly before the visit, consistent with Dr S's clinical impression of moderately severe cognitive impairment. His medications were glyburide 2.5 mg orally daily, memantine 10 mg orally twice daily, metoprolol 25 mg orally twice daily, digoxin 0.125 mg orally daily, warfarin (varying dose) daily, multivitamin, iron, etodolac 200 mg 2 tablets orally in the AM, gabapentin 300 mg orally twice daily, docusate sodium 100 mg orally daily, essential fatty acids orally 3 times daily, acetaminophen 650 mg orally every 6 hours as needed, and lactulose as needed, for a total of 13 medications at 16 scheduled doses per day.

Mr L's hemoglobin A1c was 5.9% so Dr S stopped the glyburide. Dr S referred him to physical therapy and social services to discuss options regarding caregiving, social engagement, and long-term care plans. His warfarin dose was managed by nurse practitioners in a nearby hospital's Anticoagulation Clinic, and his INRs were maintained in the desired range between 2.0 to 3.0.

Mr L had been maintained on etodolac and gabapentin after his 2008 lumbar laminectomy, despite no longer having pain complaints. Dr S sequentially tapered off both medications, watching for increased complaints of pain. He did fine, his walking improved, and he had no further falls. Dr S also tapered off the digoxin. She first cut the dose in half for 1 week. His heart rate remained in the 50-70 range, so she stopped it entirely. He began going to yoga with his wife and then to the gym twice weekly.

His initial labs had shown a normal Hgb of 13 g/dL, and his physician decided to stop the iron; his Hgb subsequently remained stable. Seven months after his first visit, Dr S discussed with his wife whether the memantine was helping Mr L's memory (he previously had not tolerated donepezil). His wife was unsure, and together they decided to try tapering him off it. Thereafter, he had greater difficulty with nouns and names, so Dr S referred him to speech therapy for cognitive exercises and resumed the memantine at its full dose. He initially showed some improvement, but within 6 months cognitive decline was again apparent.

His wife continues to pay for his medication under a Medicare Part D plan. She reports that his activities of daily living have been stable. Socially, he is improved.

Mrs L and Dr S were interviewed by a *Care of the Aging Patient* editor in December 2009.

PERSPECTIVES

Ms L: Just looking at [some of his medications] you realized that you could keep taking it, but you don't really have to.... It's better to pull it out.

Use of multiple medications is a common source of concern for patients and clinicians. Nearly 20% of community-dwelling adults age 65 and older take 10 or more medications, a figure which can easily be reached by following practice guidelines for a handful of coexisting conditions.¹⁻² Multiple medication use is associated with greater use of inappropriate medications and non-adherence, and imposes substantial cost burdens on older patients even when they have prescription drug insurance.³⁻⁵ In addition, the frequency of adverse drug events rises in proportion to the number of medications used, including drug-specific phenomena as well as non-specific syndromes including weight loss, falls, and decline in functional and cognitive status.⁶⁻¹⁰ Such adverse drug events affect an estimated 5-35% of older patients living in the community per year, and are responsible for approximately 10% of hospital admissions in older adults.¹¹⁻¹⁵

Despite legitimate concerns over multiple medication use, believing that Mr L is on “too many” medicines does not help the clinician know which ones to stop. Moreover, such labels can distract from addressing underuse of potentially beneficial medications, which is as prevalent in older adults taking many drugs as in those taking relatively few.¹⁶⁻¹⁷ The task for Dr S is not to determine if her patient is on too many or too few medications, but if he is on the right medications tailored to his individual circumstances, including his constellation of comorbidities, goals of care, and preferences and ability to adhere to medications.

METHODS

We conducted several systematic literature reviews. Our main review evaluated the impact of interventions to improve suboptimal prescribing across the medication regimen (i.e., without focus on a single drug class or disease) for elders in ambulatory settings who were taking multiple medications. Searching PubMed and International Pharmaceutical Abstracts (IPA) from 1975 through March 2010, the search used a combination of the terms polypharmacy, multiple medications, polymedicine, suboptimal prescribing, medication misuse, inappropriate prescribing, elderly, geriatric, and aged, and was restricted to randomized clinical trials published in English that involved patients age 65 years and over and reported both process measures about improvement in prescribing and clinical outcomes measures. We also reviewed studies of the effects of discontinuing specific types of medications taken by Mr L. Details of search strategies are available in an e-appendix.

INFORMATION GATHERING: ASSESSING CURRENT MEDICATION USE

Before optimizing Mr L’s medication regimen, Dr S needs to assess what drugs Mr L thinks he should be taking, what he is actually taking, and the benefits and harms he is experiencing from his drugs.

Medication review

A good medication review is essential because discrepancies are common between what patients think they should be taking and what doctors record on their medication lists.¹⁸⁻¹⁹ There is little direct evidence to support 1 specific method of medication review over another in ambulatory settings.²⁰ However, a “brown bag” review in which patients are asked to bring in all of their medicines (including all prescription and over-the-counter medicines, vitamins, supplements, and herbal preparations) can provide a useful snapshot of the patient’s current medication use. The clinician can review each medication brought in the “brown bag” one at a time and inquire about how the patient takes it (e.g., by asking “tell me how you take this medication”).

Brown bag reviews often present an opportune time to review the effectiveness of medications (e.g., control of pain, constipation, or depressed mood) as well as their adverse effects. Patients often do not report drug-related symptoms to their physicians, in part due to limited physician efforts to solicit this information.²¹⁻²² In one major study, such communication gaps were responsible for 37% of remediable adverse drug events.²³ The question “In the past XX months, have you noticed any side effects, unwanted reactions, or other problems with medications you have taken?” has been validated as an effective way to inquire about adverse drug events.¹⁵ Directed questions about common or high-risk symptoms may also be necessary – for example, inquiring about postural symptoms in a patient taking antihypertensive medications.

Assessing adherence

Ms L: I opened his 7-day pill container on a Monday and it was wet. It turned out that he had been taking them out and moving them around and had spilled water in there somehow.

Mr L has several red flags for adherence problems, including his dementia, complex medication regimen, and previous drug adverse drug events.^{5, 24} Approximately half of older patients have problems with adherence to at least one medication, being evenly split between occasional, frequent, and near-universal omissions of drug doses, although patients non-adherent to one of their medications are commonly adherent to their others.²⁴⁻²⁵

Patients are often reluctant to admit to non-adherence, so a multifaceted approach to evaluating adherence is necessary.^{24, 26} During medication review, clues about adherence can be deduced from observing medication organization, pill counts, and refill history (using information on the refill date and quantity dispensed printed on the label). Asking patients and their caregivers about their understanding of why they take each medication can also be useful. Although older adults understand the purpose of up to 88% of their medications and age itself does not predict adherence, lack of understanding increases risk of non-adherence and provides a ready target for intervention.^{5, 27} More generally, non-adherence can be elicited by non-judgmental questions such as ““I know it must be difficult to take all your medications regularly. How often do you miss taking them?””²⁴ If non-adherence is identified, the patient should be asked why, with prompting as necessary for common reasons such as those listed in Table 2.^{5, 24} Interventions to improve medication use and adherence are most likely to succeed when they address the underlying reasons behind these problems.

For many physicians, ideal medication reviews and adherence assessments are a far-off reality given the time pressures of office-based practice.²⁸ In this setting, focusing on the highest-risk and highest-benefit drugs can yield good return on a limited time investment. Better yet is sharing these responsibilities with other health care providers. Contacting community pharmacists with concerns about patients can help engage their expertise in identifying and crafting solutions to problems with the medication regimen or adherence. Where health systems permit, nurses and clinic-based pharmacists should share medication management responsibilities as articulated in the patient-centered medical home model of care.²⁹ Finally, some medication management programs are available through pharmacy benefit management plans serving Medicare Part D patients (see Resources). Eligibility criteria and scope of these programs are often limited, although more widespread benefits are mandated for implementation by 2013.³⁰

GOALS OF MEDICATION USE

Ms L: The family is all guilt-ridden and they tell themselves that they have to keep dear old dad alive My stake is that he himself has a decent day-to-day life as much as he can.

Like many older patients in the final chapter of their lives, Mr L and his caregivers face choices about using medications that may increase his longevity but negatively affect his quality of life.³¹ When getting to know Mr L, one of Dr S's first tasks was to learn what he and his family are trying to achieve through medication use, including extension of longevity, reduction in symptoms, and minimization of pill burden, medication side effects, and costs.³² Many patients would like to achieve all these goals, but often they come into conflict. The physician's role is thus to clarify the relative prioritization of these values, which usually emerges from multiple conversations about specific medication decisions and general goals of care discussions.

Understanding the life expectancy of patients through application of prognostic tools and clinical judgment can help inform goal-driven decisions about prescribing (see Resources).³³ A short life expectancy affords patients limited opportunity to be helped by medications that take several years to start accruing benefits, such as drugs to improve glycemic control in diabetes.^{31-32, 34} In addition, for patients with advanced dementia and/or poor prognosis, consensus panels have failed to recommend (and in some cases advocated against) medications such as HMG-coA reductase inhibitors (statins), bisphosphonates, and cholinesterase inhibitors, although these positions are not universally endorsed.³⁵⁻³⁷

CAN STRUCTURED MEDICATION MANAGEMENT IMPROVE OUTCOMES?

Given Mr L's complex medication regimen and multiple comorbidities, he seems to be a good candidate for structured medication review and management. The evidence base to guide such approaches is limited. Among 6 studies of medication management that met inclusion criteria in our literature review (as described in the methods section), 3 tested the effect of a clinical pharmacist, 2 examined a comprehensive interdisciplinary medication review in a geriatric clinic, and 1 examined the impact of expert clinician recommendations through computer-based feedback (Table 1).³⁸⁻⁴⁴ Overall, these programs improved markers of pharmaceutical care quality such as reducing medication burden, correcting underuse of medications, and improving a multicomponent score of medication appropriateness. Less evidence is available about the impact of these interventions on clinical outcomes. In the largest study of its type, Schmader et al. reduced the rate of serious adverse drug events from 0.6 to 0.4 events per 1000 person-days ($P=.02$).⁴³ A similar degree of reduction in all adverse drug reactions was observed in a study of veterans age 65 and older by Hanlon et al, with adverse events in 30% of patients receiving medication management vs. 40% in patients receiving usual care, although the finding was not significant ($P=0.19$).³⁸ There is little conclusive evidence about the impact of comprehensive medication management on other clinical outcomes, including quality of life, health services utilization, and major clinical events, as in general these studies were underpowered for these outcomes.

Of note, most studies on improving medication prescribing for elders with multiple medication use evaluated an external intervention, such as pharmacist review or referral to a geriatric evaluation and management clinic. Few studies have evaluated clinicians' own attempts to integrate medication management principles into their practice.⁴⁵ However, limited data suggest that physicians provided structured assessment tools for medication review are able to identify and correct medication problems in a large percent of their patients, although time limitations impede widespread implementation of such reviews.⁴⁵⁻⁴⁷

CHANGING THE MEDICATION REGIMEN

Matching the medication regimen to the patient's conditions and goals of care

Although limited data is available about the impact of structured medication management on patient health and well-being, such approaches are endorsed by experts, in part due to clear evidence of beneficial effects on markers of prescribing quality.⁴⁸ A simple and effective approach to systematically identify prescribing problems is to match each of the patient's conditions with their medications (Table 3). Areas of mismatch can highlight drugs that are being overused (i.e., used with no indication), underused (i.e., conditions that may benefit from drug therapy that is not currently being offered), and misused (i.e., drugs given for an appropriate indication that could be improved by changing the dose, frequency, or substituting another drug with a better profile of benefits, harms, and costs).⁴⁹

Of note, the proper "match" between clinical conditions and medications is defined not only by guideline recommendations and best practices, but by how medication treatment for a

given condition will help the patient attain their goals of care. Thus, the optimized medication regimen for a patient desiring a palliative approach that minimizes medication burden may look quite different than the regimen for an identical patient whose overriding goal is maximizing longevity.

Should medications be discontinued or substituted? Which ones?

Dr S: A lot of the pain complaints that he used to have had disappeared after he had a lumbar surgery in 2008. [His wife] didn't know if he still needed the pain medication, but was too worried to stop them.

Without knowing anything else about Mr L, the fact that he was taking 13 medications when he first met Dr S suggests a high probability that 1 or more of his medications can or should be stopped.^{16, 50} Studies of community-based older patients have documented an average of 1 unnecessary drug per patient, including drugs with no identifiable indication or which provide little benefit for the indication for which they are prescribed.⁵¹⁻⁵² Perpetuation of unnecessary medications is particularly acute in older adults with multiple prescribers or transitions of care (e.g., recent hospital visits).⁵³⁻⁵⁶ In the hospital setting, a large study found that 44% of hospitalized frail older patients were discharged on at least 1 unnecessary medication; common culprits include proton-pump inhibitors, central nervous system medications, and vitamin and mineral supplements.^{54, 57-58}

In addition, drugs given for a useful clinical purpose are often mis-prescribed. For example, highly anticholinergic antihistamines, tricyclic antidepressants, and other high-risk drugs described in "drugs-to-avoid" lists for older patients are used by approximately 20-30% of adults over age 65, whereas in many cases drugs with better safety and/or efficacy would be a more appropriate choice for the target condition.⁵⁹⁻⁶³ Other common problems with mis-prescribing include use of inappropriately high or low doses, drug-drug and drug-disease interactions, incorrect directions, and choice of expensive drugs where less expensive alternatives would provide similar benefit at lower cost.⁴⁹

As shown in Table 3, matching Mr L's medications with his conditions shows several drugs without a clear current indication, including his etodolac, gabapentin, acetaminophen, multivitamins, and iron. These should be among the first drugs considered for discontinuation. Next are drugs which have a current indication but may provide limited or no benefit for the patient's condition, for example memantine for Mr L's dementia, glyburide for his diabetes, and digoxin for rate control of his atrial fibrillation. Finally, certain drugs may have benefits but an unfavorable risk profile and should be substituted for others with a more favorable ratio of benefits to harms.

Troublesome symptoms obviously caused by a drug provide a clear signal to consider discontinuation. However, the adverse effects of many drugs are non-specific and can mimic underlying disease processes, such as Mr L's generalized functional decline. Often, the only way to know whether or not a symptom is a drug side effect is to temporarily stop the drug(s) and see whether the symptoms improve.⁶⁴ While these are individualized clinical decisions, it can be useful to remember the adage that "any symptom in an older patient should be considered a drug side effect until proven otherwise."⁶⁵

With limited exceptions, there are very few studies about the benefits and harms of discontinuing specific types of medications.^{64, 66} In the case of Mr L, we could not identify any controlled studies that evaluated outcomes of withdrawing digoxin for rate control in atrial fibrillation, discontinuing hypoglycemic medications in diabetes, or withdrawing memantine in dementia (although we identified 1 randomized trial and 2 poorly-controlled

trials about withdrawal of cholinesterase inhibitors, which suggested worsening of cognition after stopping the drug).⁶⁷⁻⁶⁹

In the absence of high-quality trial data on discontinuing medications, discontinuation decisions should be guided by the epidemiology of prescribing problems and by common sense. In assessing harms, particular attention should be paid to drugs that carry a high risk of serious adverse effects, including warfarin, hypoglycemic medications, and digoxin (see Table 4). These three account for one-third of all emergency room visits in older patients due to adverse drug events.⁷⁰ In the case of Mr L, this provides extra reason to critically evaluate Mr L's diabetes regimen and digoxin. Mr L likely does not need medications for his diabetes, on the basis of guidelines and evidence that suggest that tight glycemic control in the setting of advanced age or multiple comorbidities can result in greater harms than benefits.^{34, 71} Even if Mr L did require medication for glycemic control, glyburide would be a poor choice, as this agent is relatively contraindicated for patients with creatinine clearance under 50ml/min and carries a higher risk of severe hypoglycemia than other sulfonylureas.⁷²⁻⁷⁴ Nonetheless, the presence of a high-risk drug should not automatically mandate a medication change without further exploration of context.⁵¹ For example, tricyclic antidepressants are often problematic in elders due to a high frequency of anticholinergic adverse effects. However, if an older patient is already taking a tricyclic antidepressant for a valid indication and reports excellent symptom control, has no anticholinergic symptoms, and is reluctant to switch medications, it may be reasonable to continue the medication while educating the patient to be vigilant for potential future adverse effects.

Underuse of potentially beneficial medications

While use of ineffective or harmful medications is common in older adults, the same patients often are not prescribed potentially beneficial medications, for example warfarin for atrial fibrillation, antidepressants for major depression, pain medications, and laxatives.^{16, 49, 75} Mr L has several conditions that may benefit from additional drug therapy above what he is currently receiving (see Table 3). In patients in their final years of life, preference usually should be given to ensuring that troublesome symptoms such as pain and depressed mood are adequately treated. However, some forms of primary prevention can be appropriate if consistent with goals of care. For example, Vitamin D deficiency is common in older patients and has been implicated in falls, and fracture risk (along with an emerging variety of other conditions), and repletion can reduce risk of these outcomes.⁷⁶⁻⁷⁷ Thus, Vitamin D supplementation (at a dose of at least 800 IU per day) should be considered for Mr L, particularly if his serum 25-hydroxy Vitamin D level is low.⁷⁷ For many conditions, the relative paucity of drug trials that include adults in the upper reaches of age or with extensive comorbid burden limits the evidence basis for treating patients such as Mr L. However, in many cases it appears likely that the relative risk reduction observed in middle-aged and "young-old" adults is not radically different in the old-old.⁷⁸

Stopping medications

Dr S: I very rarely stop things cold – especially something such as a pain medicine, which could very well be helping the patient; that might be the reason he's not complaining of pain.

When starting drugs in older adults, geriatricians often begin drugs one at a time and follow the dosing mantra of "start low and go slow." Limited evidence is available about the best ways to stop medications in this group, although in clinical practice many follow a similarly sequential, step-wise approach to discontinuing drugs.⁶⁴ In certain circumstances, an "all-at-once" approach may be warranted when dangerous signs or symptoms are thought likely to

be due to drugs but the exact culprit cannot be identified, or when tendencies toward clinical inertia in a patient or practice environment suggest that future opportunities for medication modification will be limited.

Medications can typically be effectively withdrawn once the decision has been made to do so, although unwanted reactions in the period after withdrawal are common.⁷⁹⁻⁸⁰ In 1 of the only broad-based studies of the topic in ambulatory older patients, 26% of drug discontinuations were accompanied by worsening of the underlying disease (eg, recurrence of angina or high blood pressure) and 4% were accompanied by physiologic withdrawal reactions (mostly to beta blockers and benzodiazepines).⁸¹ For many drugs, risk of adverse withdrawal events can be minimized by slow, careful tapering of drug dose. This is particularly true for drugs to which the body adapts over time, for example through up- or down-regulation of end-organ receptors, producing a physiologic withdrawal reaction if the drug is withdrawn abruptly.⁶⁴ While the scientific basis for how to withdraw specific drugs is scant, a rule of thumb is that drugs can usually be tapered down at the same rate at which they are titrated up at the initiation of drug therapy. Common drugs that require tapering include opioids, beta blockers, clonidine, gabapentin, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants.⁶⁴ Regardless of the speed of the taper, patients should be monitored for adverse withdrawal events, including educating and activating patients to recognize and report concerning symptoms.^{13, 29}

Sometimes drugs are stopped on a trial basis to determine if potential adverse drug effects resolve or symptoms of the underlying disease worsen. Such assessments can be complicated by fluctuations of symptoms and biomarkers in an individual patient; for example, it may be difficult to ascertain whether improvement in symptoms after withdrawing a drug was the result of stopping the drug or natural fluctuations in the disease course. In this case, a formal rechallenge with the drug (i.e., as part of an N-of-1 trial) may help to establish causality.⁸²

IMPROVING ADHERENCE TO THE NEW REGIMEN

Mrs S: We looked and saw how confused he was so I told him I was going to take over all of his medicines.

The benefits of changing the medication regimen are contingent on the patient adhering to the revised plan of care. Improving adherence requires diagnosing barriers to proper medication use and devising strategies to overcome those barriers (Table 2).

Randomized controlled trials of strategies to improve adherence to chronic medications have yielded mixed results, and often have studied multifaceted interventions in a manner that makes it difficult to unpack the contribution of each component to improving adherence.⁸³⁻⁸⁵ However, several lessons emerge from the data. First, education through oral counseling or written instructions is important, but often insufficient unto itself. Most randomized trials of intensive educational interventions have yielded minimal to moderate impacts on adherence and little effect on clinical outcomes.⁸³⁻⁸⁴ Nonetheless, common sense suggests it is useful to briefly discuss and write out instructions for how to take a medication that is being newly prescribed or modified. A “teach-back” approach, in which the patient or caregiver is asked to describe the purpose of the drug, instructions for its use, and adverse effects to be aware of can help to ensure comprehension.

In contrast to a focus on education, a potent intervention to improve adherence is simplifying medication dosing schedules. Observational studies have found that adherence drops steeply with increasing number of doses per day, with average adherence falling from

roughly 80% in patients taking once-daily regimens to 50% in those taking four-times-per-day regimens.⁸⁶ Randomized controlled trials have found large differences in adherence in patients randomized to medications requiring different numbers doses per day, although effects on downstream clinical outcomes were mixed.⁸³ Thus, where possible clinicians should minimize dosing frequency by prescribing longer-acting medications and dosing different drugs at the same time. In addition, pill burden can be reduced by using medications that can treat two or three conditions simultaneously (for example, beta blockers in a patient with hypertension, heart failure, and atrial fibrillation with rapid ventricular response). Attempts to reduce dosing frequency may be particularly potent for patients with cognitive difficulties, but are also helpful for cognitively intact patients or caregivers (such as Mr L's wife). Such persons can also frequently forget to take or administer medicines and may resist the pill burden and lifestyle impacts that come with multiple dosings.²⁴

Other approaches can help address common barriers to adherence, including behavioral interventions (e.g., cues, medication organizers, packaging), involvement of family and friends (e.g., support, monitoring, and administering medications, as was done for Mr L), and by having patients demonstrate ability to self-medicate in a controlled environment (e.g., in hospital or long term care facility) before discharged to home without support.⁸³⁻⁸⁵ In addition, addressing medication costs – for example, by prescribing lower-cost generic alternatives instead of brand-name drugs – can reduce cost-related non-adherence as well as negative impacts on other aspects of patient's financial well-being.⁸⁷ Many patients will need a combination of approaches and pharmacists can be helpful partners in devising and following strategies to improve adherence.

MONITORING AND FOLLOW-UP

Ongoing monitoring for the toxicity and effectiveness of drug therapy is critical to providing quality care and improving outcomes, but current practices often fall short.⁸⁸⁻⁸⁹

Approximately one-third to two-thirds of patients on ACE inhibitors, digoxin, carbamazepine, and other drugs that require laboratory-based safety monitoring fail to receive minimum standards for monitoring.^{48, 90-91} If suboptimal monitoring or frequent deviations from target levels have been present, barriers to monitoring and safe drug dosing should be assessed. If such barriers cannot readily be remediated, one should consider discontinuing the drug.

Finally, systematic review of a patient's medication list (for example, using the framework suggested in this article) is a form of monitoring that should be done periodically. While the frequency of such reviews should be tailored to patient circumstances, a good starting point is recommendations by the National Committee for Quality Assurance and the ACOVE program, which consider medication review at least once per year to be an important measure of care quality in older adults.⁹²⁻⁹³ Declines in function and the onset or worsening of geriatric syndromes such as cognitive decline or falls may represent adverse drug effects or signal a change in goals of care and should also precipitate medication review.

CONCLUSIONS

Prescribing for older patients is an extraordinarily complex endeavor. However, as illustrated by Dr S and Mr L, a thoughtful, systematic approach to addressing the medication regimen can bring order to complexity and make a meaningful difference in patient outcomes. The success of Dr S's care of Mr L was not in knowing the "right" answer for her patient from the beginning, but rather from employing a careful, step-wise process that merged key principles of pharmacologic care with the clinical reality, social situation, and goals of her patient.

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Appendix: Resources for clinicians

Table 5

ADHERENCE, MEDICATION MANAGEMENT, REDUCING DRUG COSTS

Tools to improve adherence

- Adherence tools from Dept. of Veterans Affairs: <http://www.hiv.va.gov/vahiv?page=ptli-04-01>
- National Council on Patient Information and Education (NCPIE) Medication Use Safety Training (MUST) Program: www.mustforseniors.org
- Center for Connected Health. <http://www.connected-health.org/programs/medication-adherence.aspx>
- Osterberg L et al. Adherence to medication. *N Engl J Med* 2005; 353: 487-497. <http://www.ncbi.nlm.nih.gov/pubmed/16079372>
- World Health Organization. Adherence to long-term therapies: evidence for action [report]. World Health Organization: Geneva, 2003. http://www.who.int/chp/knowledge/publications/adherence_report/en/

Medication management programs

- American Society of Consultant Pharmacists: www.ascp.com
- American Pharmacists Association: <http://www.pharmacist.com/MTM>

Assistance with payment for medications

- Medicare: <http://www.medicare.gov/medicarereform/> or 1-800-MEDICARE
- State pharmaceutical assistance programs: <http://www.medicare.gov/spap.asp>
- Industry and other assistance programs: <http://www.needymeds.com/>; www.rxassist.org/; <https://www.pparx.org/>

IDENTIFYING AND AVOIDING COMMON PRESCRIBING PROBLEMS

Identifying potentially inappropriate medications

- Fick DM et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med* 2003; 163: 2716-24. <http://archinte.ama-assn.org/cgi/reprint/163/22/2716>
- Gallagher P. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. *Int J Clin Pharmacol Ther* 2008; 46: 72-83. <http://www.ncbi.nlm.nih.gov/pubmed/18218287>
- Hanlon JT et al. A method for assessing drug therapy appropriateness. *J Clin Epidemiol* 1992;45:1045-51. <http://www.ncbi.nlm.nih.gov/pubmed/1474400v>

- Geriatrics at Your Fingertips: <http://www.geriatricsatyourfingertips.org/>

Identifying underuse

- Barry PJ et al. START (Screening Tool to Alert Doctors to the Right Treatment) – an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age Aging* 2007; 36: 632-638. <http://ageing.oxfordjournals.org/cgi/reprint/36/6/632>
- Shrank WH et al. Quality Indicators for Medication Use in Vulnerable Elders. *J Amer Geriatr Soc* 2007; 55: s373-382. <http://www.ncbi.nlm.nih.gov/pubmed/17910560>

Renal dosing for common drugs

- Creatinine clearance online calculator: http://www.globalrph.com/multiple_crcl.htm
- Hanlon JT et al. Consensus guidelines for oral dosing of primarily renally cleared medications in older adults. *J Amer Geriatr Soc* 2009; 57: 335-340. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2640432/>
- American College of Physicians Drug Prescribing in Renal Failure: http://www.acponline.org/running_practice/technology/mobile_computing/clinical_references/
- Olyaei AJ et al. Drug dosing in the elderly patients with chronic kidney disease. *Clin Geriatr Med* 2009;25:459-527. <http://www.ncbi.nlm.nih.gov/pubmed/19765493>

Identifying clinically significant drug-disease interactions

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Identifying clinically significant drug-drug interactions

- Online and PDA-based drug information and interaction checks:
 - o Free: www.epocrates.com;
 - o Subscription: www.lexi.com; www.factsandcomparisons.com; www.micromedex.com
- Common, clinically important drug-drug interactions in hepatic metabolism: www.drug-interactions.com
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Randomized controlled studies designed to improve pharmaceutical care quality in ambulatory older adults using multiple medications

Table 1

Study	Setting	Patients/Inclusion Criteria	Intervention (duration)	Process measures (Intervention vs. control)	Clinical outcome measures (Intervention vs. control)
<i>Pharmacist</i>	<i>Interventions</i>				
Hanlon and Cowper ³⁸⁻³⁹	1 VA general medicine clinic, USA	208 age ≥65 taking ≥5 medications	Pharmacist review, written drug recommendations to PCP and patient counseling at each clinic visit; 12 months	↓ Medication Appropriateness Index score (12.8 vs. 16.7, P<.001) (Lower is better)	NS differences in health-related quality of life (P=0.99); adverse drug events (30% vs. 40%, P=0.19); health care costs (\$7873 vs. \$5926; P>0.05)
Kraska ⁴⁰	6 general practices, Scotland	332 age ≥65 with ≥4 medications and ≥2 chronic disease states	Pharmacist review of medications and medication-related issues; pharmacist implemented recommendations agreed to by patient's GP; 3 months	↑ resolution of pharmaceutical care issues such as suspected ADRs, monitoring issues, ineffective therapy (83% vs. 41%, P<.001)	NS differences in medication costs, health-related quality of life, clinic visits, hospitalizations (all P>0.05).
Lenaghan ⁴¹	1 general practice, UK	136 age ≥80 taking ≥4 medications and 1 drug related risk factor	2 home visits by community pharmacist; 6 months	↓ in number of meds (↓ by 0.3 vs. ↑ by 0.6, P=0.03)	NS difference in hospital admissions (P=0.80)
<i>Multidisciplinary</i>	<i>Team</i>	<i>Intervention</i>			
Williams ⁴²	1 geriatric clinic, USA	133 age ≥65 taking ≥5 medications including ≥2 potentially problematic drugs	Single multidisciplinary review, contact with primary MD and changes implemented; 6 weeks	↓ in number of meds (↓ by 1.5 vs. ↓ by 0.1, P=0.001) and ↓ in monthly drug costs (savings of \$27 vs. \$1), (P=0.006)	NS differences in 9 measures of physical, cognitive, or affective functioning (all P>0.05)
Schmader ⁴³	Clinics at 11 VA medical centers, USA	834 frail persons age ≥65 after hospital discharge (mean ≥10 medications)	Multidisciplinary, protocol-driven geriatric evaluation and management clinic; 12 months	NS difference in # of unnecessary drugs, # of inappropriate drugs, or MAI score (P>.25 for each), ↓ number of conditions with omitted drugs (↓ 0.2 vs. ↑0.1, P<.001)	NS difference in all ADEs (RR 1.03; 95% CI 0.96 – 1.23); ↓ risk of serious ADEs (RR 0.65; 95% CI 0.45-0.93)
<i>Computer</i>	<i>Feedback</i>	<i>Intervention</i>			
Weber ⁴⁴	18 clinics, USA	620 age ≥70 taking ≥4 medications including ≥1 psychoactive	Pharmacist or geriatrician one-time medication review with message to primary care physician through EMR; 15 months	↓ use of psychoactive drug (effect size 0.2 drugs per patient, P=.04); trend toward ↓ number of medications (effect size 0.5 drugs per patient, P=0.09)	NS difference in risk of falls (OR=0.86; P>0.05)

Table 2

Selected barriers to medication adherence and targeted solutions

Barrier	Potential solutions
Forgetting, limited organizational skills	Pill organizers, medication calendars, blister packs, electronic dispensing devices, simplify regimen and reduce pill burden, encourage active family involvement, internet-linked adherence aids and reporting systems
Patient believes drug not needed, ineffective, or that he/she is taking too many drugs	Work collaboratively with patient to address concerns and establish shared goals of care, assess effectiveness, educate patient including with literacy-appropriate written materials, simplify regimen and reduce pill burden
Difficulty taking (e.g., opening pill bottles, swallowing)	Consider substituting with medication easier for patient to use (eg, liquid if trouble swallowing; ordering easy-off caps), simplify regimen and reduce pill burden, pill cutters, oral dosing syringes, insulin syringe magnification, spacer for inhalers
Cost	Substitute with lower-cost medications (eg, generic vs. brand-name drug), reduce unnecessary medications, assess prescription drug insurance and direct patient to application for low-income subsidy, prescription drug assistance programs.

Table 3

Matching Mr L's conditions and medications *

Condition	Drug given for condition	Potential problem *	Notes
Dementia	Memantine 10 mg bid	Potentially unnecessary	Withdrawal trial later attempted which suggested that memantine provided benefit, so restarted.
Atrial fibrillation	Digoxin 125 mcg daily	Probably unnecessary, potentially harmful	Likely not needed for rate control while also on a beta blocker and may be contributing to falls and cognitive and functional decline (drug-disease interaction).
	Metoprolol 25 mg bid		Will help manage hypertension
	Warfarin (varying dose)		PT-INR well-controlled with help of anticoagulation clinic. Given this, reduction in risk of stroke exceeds risk of serious bleeding complications
Diabetes mellitus	Glyburide 2.5 mg daily	Probably unnecessary, potentially harmful	Likely not needed due to good control of hemoglobin A1c (guidelines recommend goal A1c of 7-8% in older patients; overly aggressive control yields more harm than benefits). Any dosage of glyburide inappropriate given risk of hypoglycemia in patients with chronic kidney disease
Hypertension	Metoprolol 25 mg bid (2)		
Hyperlipidemia	Essential fatty acids tid	Potential underuse	Statin therapy reduces cardiovascular events in high-risk populations, may slow progression of vascular dementia; however is controversial in patients with limited life expectancy and may be inappropriate if goals of care focused on palliating current symptoms.
Chronic kidney disease			ACE-I may be considered but not strongly indicated in absence of proteinuria. Ensure that drugs are dosed for renal function.
Gastritis, gastroesophageal reflux disease (GERD)		Potential underuse	If symptomatic and refractory to lifestyle modification, consider proton pump inhibitor or H2 blocker
Incontinence following bladder cancer surgery			Likely not amenable to medication therapy; bladder antispasmodics (eg, oxybutynin) may worsen cognition
Falls and gait instability		Potential underuse	Consider adding Vitamin D, calcium, bisphosphonate for fracture prophylaxis. However, oral bisphosphonates may pose problem in patients with swallowing difficulty or difficulty staying upright after dosing and may be inconsistent with goals of care. Some of patient's drugs may worsen gait and increase fall risk; particularly digoxin, and maybe gabapentin (drug-disease interactions).
Functional/cognitive decline			Same drugs that may precipitate falls (above) may worsen cognition and functional status.
Constipation, hemorrhoids	Docusate 100 mg daily	Ineffective	Limited effectiveness for constipation.
	Lactulose as needed	Suboptimal choice	Long latency period before action and may not be best choice for as-needed medication. Dietary modification (increased fiber and water) may provide effective non-drug alternative.
Past history of pain from spinal stenosis that was surgically repaired	Etodolac 400 mg daily	? No current indication, potentially harmful,	No longer needs pain medications (pain resolved after spinal stenosis surgically corrected). Etodolac may worsen kidney function, hypertension and increase risk of gastrointestinal bleed (particularly in combination with warfarin). (Drug-drug and drug-disease interactions).
	Gabapentin 300 mg bid	? No current indication,	No longer needs pain medications. May worsen falls,

Condition	Drug given for condition	Potential problem *	Notes
		potentially harmful	cognition (drug-disease interaction).
	Acetaminophen 650 mg q6 hours prn	? No current indication, adherence	No longer needs pain medications. Difficult to use qid medication regularly.
Past history of anemia	Iron	? No current indication, potentially harmful	No current evidence of anemia. Can worsen constipation (drug-disease interaction)
Drugs being given for no readily identifiable reason	Multivitamin daily	No indication	Little evidence that multivitamins improve outcomes in unselected populations. Vitamin D can be useful for fall and fracture prevention, but standard multivitamins contain insufficient quantify.

* At the time the patient first met Dr S

Table 4

Selected high-risk drugs

Drug	Potential harm (selected)	Comment
Insulin and sulfonylureas	Hypoglycemia	May often be appropriate; however, aggressive glycemic control may often yield greater harms than benefits in older adults. ^{34, 71, 94}
Warfarin	Gastrointestinal, intracranial bleeding	Although a high-risk drug, benefits of warfarin therapy often outweigh harms. Maintenance of PT-INR in therapeutic range tightly linked to risk: benefit ratio ⁹⁵
Digoxin	Impairment of cognition, heart block	May have a third-line role in management of systolic heart failure; suboptimal choice for rate control in atrial fibrillation.
Benzodiazepines	Falls	Associated with up to a 60% increase in fall risk. ⁹⁶
Diphenhydramine, other first-generation antihistamines	Impaired cognition, urinary retention in men	Poor choice as sleep aid due to anticholinergic effects, next-day sedation, impact on performance including driving. Close medication reconciliation important as patients may obtain over-the-counter
Antipsychotics	Death, pneumonia	Elevated risk of death when used to treat behavioral complications of dementia, although in selected cases benefits may exceed risks if consistent with patient goals of care. ⁹⁷