Reconsidering Medication Appropriateness for Patients Late in Life

PROVIDING GUIDELINE-adherent care for many medical conditions increasingly means the addition of more medications to reach disease-specific targets.[1] When might it be best to withhold or discontinue medications that are otherwise appropriate on the basis of guidelines? Receiving facsimiles from the pharmacy serving a local nursing home encouraging us to prescribe statins for residents there symbolizes the issues. Most of these patients had a limited life expectancy, were older than 90 years, or had advanced dementia. Similar situations occur in patients with functional impairments, frailty, or diseases like emphysema, congestive heart failure, or coronary artery disease in their advanced stages, for whom starting or continuing many recommended drugs does not seem the best way to optimize care.

Investigators in a number of studies[2-4] have characterized inappropriate prescribing in the elderly, but there is little information to guide discontinuation of otherwise indicated medications in patients late in life. We propose a process for medication prescribing in patients late in life that builds on the principles of appropriate prescribing and includes a consideration of remaining life expectancy, goals of care, and potential benefits of medications. We use case scenarios to illustrate this model and discuss the implications of this approach.

APPROPRIATE PRESCRIBING IN THE ELDERLY

Motivated by the challenges of polypharmacy, adverse effects, and cost, investigators have made considerable efforts to examine medication appropriateness in the elderly. The Beers Criteria are an explicit list of medications, dosages, and durations of therapy that should be avoided in elderly persons that was developed for the nursing home setting and updated for patients 65 years and older.[2] The Medication Appropriateness Index is a list of implicit criteria consisting of 10 questions to identify potentially inappropriate elements of prescribing,[3] including indication, interactions, and others (**Figure 1**). Numerous other tools to evaluate medication appropriateness have been suggested, and the application of them has demonstrated widespread inappropriate prescribing in a variety of settings. Evaluation of large population databases shows that the prevalence of inappropriate medications in elderly outpatients is 21%.[5,6]

Despite the contribution that these guidelines have made, they have been limited to identifying inappropriate medications to be avoided and they do not approach more general considerations such as when to discontinue otherwise appropriate medications. Intuitively, one might think it best to withhold or discontinue the use of certain medications in patients late in life that are otherwise appropriate to use to prevent exposure to therapies that may result in undue suffering or adverse effects with little clinical benefit.

A MODEL FOR APPROPRIATE PRESCRIBING FOR PATIENTS LATE IN LIFE

To guide the discontinuation of such therapies, any process should include patients' remaining life expectancy and goals of care as major components. These components parallel those used when considering whether to conduct cancer screening in older persons.[7]

REMAINING LIFE EXPECTANCY

By using life tables, life expectancy can be stratified into the top 25th, middle 50th, and lowest 25th percentiles (**Figure 2**)[7] such that 75%, 50%, and 25% of people will live fewer than the upper, middle, and lower number of years, respectively. The healthiest 25% of people may live as long as the top 25th percentile, and those with multiple comorbidities, functional impairment, or disease-specific markers of poor prognosis may live a shorter time than the lowest 25th percentile.[8]

TIME UNTIL BENEFIT

To determine if a patient's life expectancy is long enough that he or she would benefit from a particular medication, the amount of time until benefit will be achieved should be considered. Medications for symptom relief, such as analgesics, may have a short time until benefits are seen and would continue to benefit all patients including (or especially) those close to death. Medications used for primary or secondary prevention may have a time until benefit of years before their outcome is achieved and therefore treatment with them might

1. Is there an indication for the drug?
2. Is the medication effective for the condition?
3. Is the dosage correct?
4. Are the directions correct?
5. Are the directions practical?
6. Are there clinically significant drug-drug interactions?
7. Are there clinically significant drug-disease/condition interactions?
8. Is there unnecessary duplication with other drugs?
9. Is the duration of therapy acceptable?
10. Is this drug the least expensive alternative compared with others of equal usefulness?

Figure 1. The Medication Appropriateness Index.[3] Reprinted with permission from Elsevier.

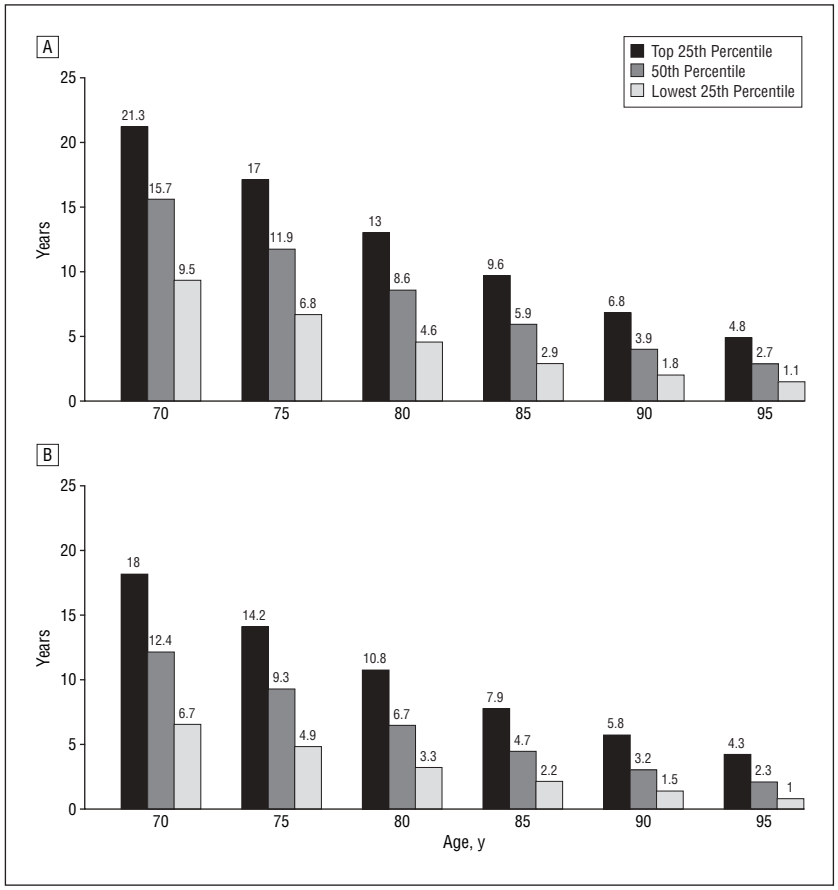

Figure 2. Upper, middle, and lower quartiles for life expectancies for women (A) and men (B) on the basis of the US life tables. The 3 numbers provided for each 5-year age cohort reflect remaining life expectancy for the top 25th, middle 50th, and lowest 25th percentile. For example, 75%, 50%, and 25% of 75-year-old women will live fewer than 17, 11.9, and 6.8 years, respectively. Although the median life expectancy for 75-year-old women is 11.9 years, women with advanced comorbidities and functional impairments may live fewer than 6.8 years. Reprinted with permission from *JAMA*.[7]

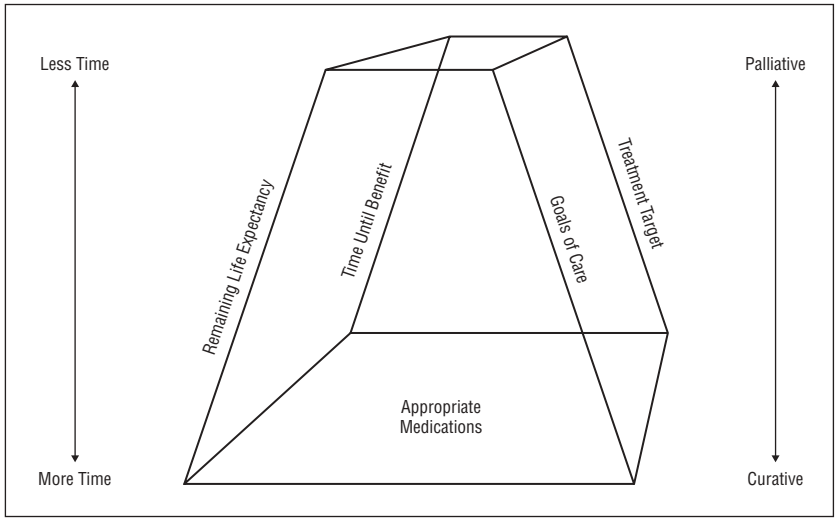

Figure 3. The model shows that the 4 steps in medication decision making form a pyramid, visually representing the appropriate medications at any level. At the top are represented patients for whom remaining life expectancy is limited, drugs should have the shortest time until benefit, goals of care are palliative, and treatment targets are focused on symptom management. Moving toward the bottom, the base of appropriate medications expands as the patient's life expectancy is longer, time until benefit may be longer, goals of care are more aggressive, and treatment targets are aimed more at preventive strategies. The bottom of the pyramid therefore contains all medications that are otherwise appropriate according to existing criteria for patients 65 years and older.

not be started or might even be discontinued in patients with a limited life expectancy. Unlike the *number needed to treat*, which adds information about the likelihood that a population will benefit from a medication, the notion of *time until benefit* may be more useful in individual patient discussions.

GOALS OF CARE

Goals of care can be challenging but may be the component of the prescribing process over which physicians have the most influence. Regardless of standards of care, practice guidelines, and other clinical pathways, shared decision making among physicians, patients, and families about goals of care is important when deciding whether to stop, start, or continue therapy with a medicine for a patient late in life. As disease progresses and it is clearer that cure is not realistic, an individualized approach to a patient's treatment may become increasingly palliative.

TREATMENT TARGETS

After goals of care have been established, they must be compared with the treatment targets that a medication may achieve to ensure agreement. For example, patients may establish goals based on a more palliative model in which the only medications prescribed would be those addressing particular symptoms. Examples of other treatment targets include life prolongation, prevention of morbidity and mortality, maintenance of current state or function, and treatment of acute illness.[9]

CASE STUDIES WITH THE MODEL

These concepts become 4 components in a model of appropriate prescribing late in life: remaining life expectancy, time until benefit, goals of care, and treatment target (**Figure 3**). Ideally, each of the 4 components is consistent with the others, yielding a general idea of appropriate medications and reasonable limitations. Efforts then should be made to discontinue use of medications identified according to these components as inappropriate for pa-

tients late in life. The following cases will help demonstrate how this approach may aid individualized decision making regarding medication discontinuation (**Figure 4**).

Case 1

A 75-year-old woman with hypertension and osteoarthritis diagnosed as having type 2 diabetes mellitus. She is functionally independent. Laboratory test results were as follows: low-density lipoprotein, 143 mg/dL (3.7037 mmol/L); creatinine, 1.0 mg/dL (88.4 µmol/L); glycated hemoglobin, 8.7% (0.087). Currently prescribed medications include chlorpropamide, atorvastatin calcium, lisinopril, and aspirin.

Remaining Life Expectancy. Remaining life expectancy on the basis of the life tables is at least 17 years.[7]

Time Until Benefit. Treatment of hyperglycemia and hypertension with a sulfonylurea and an angiotensin-converting enzyme inhibitor may show benefit on average after about 10 years, when about 25% of patients with type 2 diabetes mellitus develop proteinuria and/or significant renal damage.[10] Treatment with a statin could reduce her risk for vascular events after about 2 years of treatment and significantly reduce cardiovascular events at 5 years.[11] Use of aspirin for primary prevention could reduce her risk of myocardial infarction at 5 years.[12]

Goals of Care. The patient wishes to prevent progression of her disease while maintaining her excellent function as long as possible.

Treatment Targets. Consistent treatment targets include primary and secondary prevention strategies. A hypoglycemic agent such as glipizide should replace chlorpropamide because of its long half-life leading to prolonged hypoglycemia in the elderly.[2] Use of the other medications in question is justifiable according to our model.

Case 2

A 72-year-old man with stage D congestive heart failure and emphysema with a forced expiratory volume in 1 second of 0.5 L is hypoxic and dyspneic at rest and currently is receiving maximal medical therapy: furosemide and metolazone, lisinopril, isosorbide mononitrate, albuterol sulfate and ipratropium bromide, inhaled fluticasone propionate, and theophylline, among others.

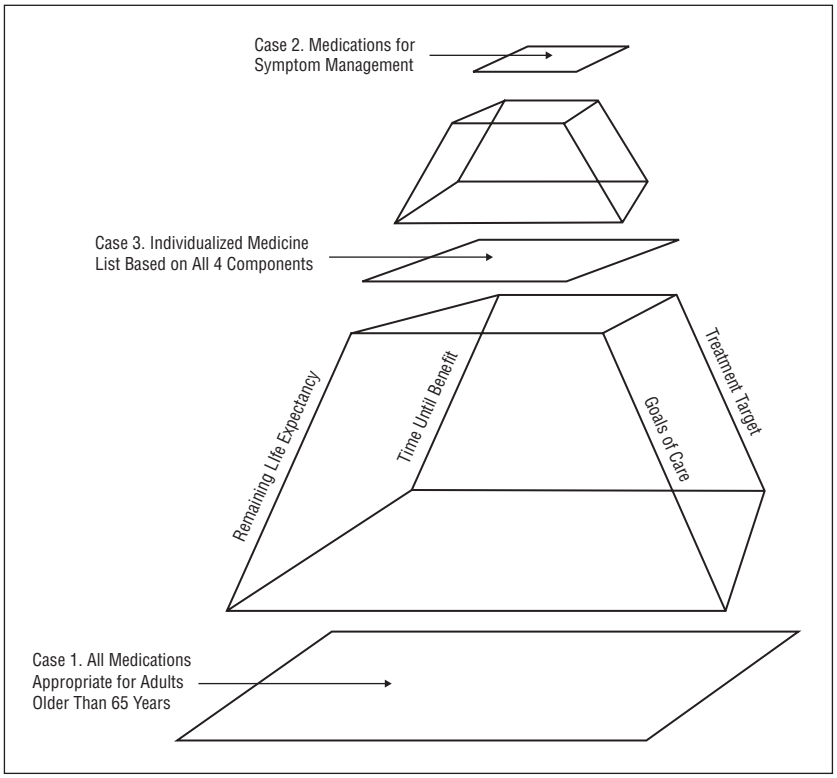

Figure 4. Use of the model in 3 distinct cases illustrates how it is used depending on the 4 components.

Remaining Life Expectancy. He has end-stage disease of 2 organ systems, consistent with an approximate life expectancy of 6 months.[13]

Time Until Benefit. Unless they provide significant symptom relief, medications to prevent heart failure mortality, like angiotensin-converting enzyme inhibitors, may have a longer time until benefit than medications to treat fluid overload, like loop diuretics. Similarly, in patients with emphysema, inhaled corticosteroids and theophylline may have a longer time until benefit than bronchodilators.

Goals of Care. The patient expresses a wish to avoid further diagnostic testing and hospitalization. His priority is to feel less short of breath and less anxious and to be home with his family. He is an appropriate candidate for hospice care.

Treatment Targets. Consider treatment targets that are mainly palliative, which is most consistent with life expectancy, benefits of treatment, and goals of care. Helpful medications might include analgesics, antianxiety agents, and medications to improve dyspnea, as well as bronchodilators if they provide relief. Applying our model indicates it is reasonable to discontinue use of medications, including pulmonary and cardiac drugs like inhaled corticosteroids and angiotensin-converting enzyme inhibitors, that may not contribute to the patient's goal of symptom relief.

Case 3

A frail 85-year-old man has hypertension, dementia, renal insufficiency, and stage C heart failure. Recent medication additions include furosemide and simvastatin.

Remaining Life Expectancy. Remaining life expectancy is approximately 2.2 years.[7]

Time Until Benefit. Medications with a time until benefit greater than about 2 years are not likely to be of benefit. Medications like furosemide may have a short time until benefit.

Goals of Care. The patient wishes to avoid invasive procedures, and his family's priority is to maintain his current status.

Treatment Targets. Treatment targets include symptom management,

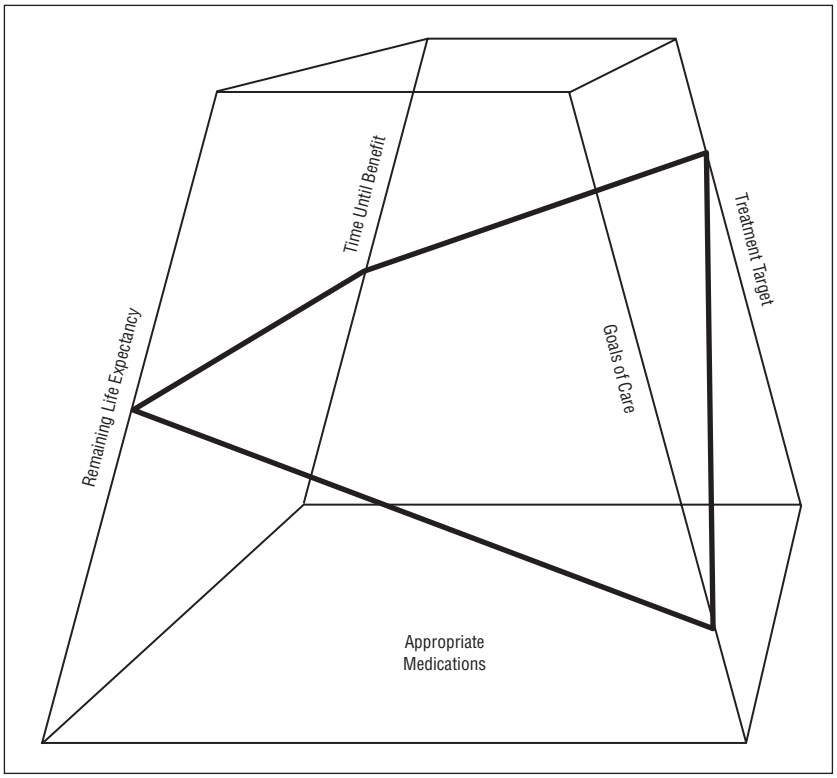

Figure 5. An example of a distorted model shows that all 4 components may not readily agree. Sometimes the time until benefit of a particular medicine will be considerably longer than a patient's estimated remaining life expectancy. Aggressive goals of care despite advanced disease may result in consideration of unrealistic treatment targets. When all 4 components are not consistent with each other, the resulting figure is a visually distorted, nonplanar slice of the model.

prevention of symptoms likely to occur from untreated disease, and treatment of acute disease or acute exacerbation of chronic disease. Furosemide would be part of a logical regimen; applying our model, one might reasonably either not start or discontinue the use of the statin because of its potential time until benefit exceeds the patient's remaining life expectancy.[14]

A benefit of this model is the possibility of recognizing a mismatch among the 4 components. When all 4 components agree, the resulting visual figure is a clear slice of the model in a single plane as depicted in Figure 4. However, if a frail older patient with a remaining life expectancy of 2 to 3 years expresses a desire to have aggressive care, including surgical management of vascular disease, primary and secondary prevention of diseases like diabetes mellitus and coronary artery disease, and other life-sustaining approaches, the resulting figure is visually nonplanar (**Figure 5**).

COMMENT

We propose a framework that may help guide the discontinuation or withholding of treatments otherwise indicated, appropriate, and recommended according to current guidelines. However, discontinuing or withholding medications proved safe and effective in well-designed studies can be challenging. Stopping the use of medications runs contrary to the directions that patients have received from their physicians to adhere to treatment. With more access to computerized medical information and more direct-to-consumer pharmaceutical advertising, patient requests for medications may affect decision making and promote medication overuse.[15] Despite these pressures, physicians still may overestimate patients' discomfort with stopping the use of medicines.[16]

Physicians have clinical inertia with regard to prescribing, an idea that is just as applicable when considering the effort required to stop the use of medications as it is to the problem of underuse in the elderly.[17] Unfortunately, the movement to overcome inertia by converting guidelines into performance measures and linking quality indicators to economic incentives for physicians may undermine efforts to individualize care.[18,19]

Our model addresses issues when one considers medication use late in life that are not adequately considered with existing models of medication appropriateness, thus our model could aid in the development of guidelines to reduce polypharmacy in older patients who may have a limited life expectancy. Nevertheless, our model has potential limitations.

First, this is a time-consuming way of approaching pharmacotherapy when patient visits are already pressured by many complex medical decisions. Second, goal setting has become increasingly challenging; patients and family members may have difficulty making decisions about complex clinical situations, and many physicians may have difficulty providing patients with the information needed to make decisions.[20] Third, providing rational pharmacotherapeutic recommendations in the elderly is hindered by their lack of adequate representation in clinical trials, despite overwhelming numbers with chronic medical conditions.[21]

In addition, trial duration may be inadequate, making the concept of time until benefit difficult to apply for many medications. Despite the lack of literature regarding the consequences of stopping the use of medications, it is reassuring that in one study[22] of drug discontinuation in elderly persons, most drugs were stopped without an adverse drug withdrawal event. Furthermore, despite these limitations, we believe that a framework such as the model we propose may help guide decisions about the use of medications that are more concordant with the possible benefits of medications in the context of patients' life expectancies and goals of care.

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