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General Principles of Geriatric Drug Therapy

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Ms. Gutierrez is a 74-year-old female with a history of atrial fibrillation, type 2 diabetes, and hypertension. She recently visited her primary care provider (PCP) due to trouble sleeping at night. Her PCP prescribed zolpidem 5 mg at bedtime as needed for sleep without inquiring about patient preference for treatment. Despite taking zolpidem nightly for several weeks, Ms. Gutierrez continued to have trouble sleeping, so she purchased an over the counter medication to help. While her sleep improved, she noticed she had some nighttime incontinence and fell twice in the last week getting out of bed. She returned to her PCP who prescribed her tolterodine for incontinence symptoms and told her to rise slowly from her bed each morning.

Several weeks later, her daughter came to visit and was very concerned about her mother's memory. She recommended that her mother be evaluated for Alzheimer's disease by a neurologist. What happens to Ms. Gutierrez next?

Ms. Gutierrez is considered an "older adult," and as a result, medication use for her presents a number of challenges that are not usually present in younger individuals. These include polypharmacy, multimorbidity, physiologic changes that affect medication use and the use of potentially inappropriate medications. The purpose of this article is to review basic principles of medication use in older adults and to emphasize medication-related problems that may occur in this population. While the United Nations defines older adult as any person over the age of 60, the terms "older adult" and "geriatric" are typically applied to adults aged 65 and over.[1] It is important to recognize that aging is an individual process, and some individuals well under the chronological age of 65 could qualify as frail. In contrast, some people beyond 65 can be quite healthy and vigorous. For the purposes of this article, the age of 65 is used to generally define "older adults."

Multimorbidity and Person-Centered Care

> "Is it quality of life or quantity of life? Truthfully, if my destiny is to feel great now and maybe shorten my future, I'd rather feel well now."
>
> --Nancy Richardson, 60, of Wayland, Mass., referring to risk versus benefit of estrogen therapy. Quoted in New York Times, December 18, 2006, article by Gina Kolata, "Breast Cancer News Brings a Range of Reactions"

Before a discussion on medication use in older adults can be described, it is important to recognize that many older adults suffer from multiple chronic illnesses commonly referred to as multimorbidity. The majority of older adults (67%) have two or more chronic conditions, and those over 85 have the highest prevalence (81.5%).[2] Ms. Gutierrez is a good example of an older adult with multimorbidity. She has three chronic conditions (atrial fibrillation, diabetes, and hypertension) that require management. While clinical practice guidelines and providers often focus on prolonging life in those with chronic disease and multimorbidity, maintaining or improving quality of life or functional status may be the goal of the patient. Therefore, patient preference should be the guiding principle in the care of older adults with multimorbidity and incorporated into medical decision-making, including prescribing medications.[3][4][5] The American Geriatrics Society definition of person-centered care includes eight key elements, which are included in Table 1.[4] Core to these elements is eliciting the patient's preferences on a regular basis and coordinating and communicating these preferences across the healthcare team.

This person-centered approach requires more than just reviewing medication prescribing against an algorithm or a clinical practice guideline and is not always in line with medical incentives.[6] For example, a medication that is "indicated" according to a guideline may not be consistent with a patient's preferences and may therefore be inappropriate for that patient. In the patient with multimorbidity, the cumulative burden (e.g. adverse effects, financial cost, etc.) of medications that are indicated for all the chronic conditions may be overwhelming for the patient.

Polypharmacy and Deprescribing

> *"As older patients move through time, often from physician to physician, they are at increasing risk of accumulating layer upon layer of drug therapy, as a reef accumulates layer upon layer of coral."*
>
> *-- Jerry Avorn, MD**

*Avorn, J. Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs. New York: Alfred A. Knopf, 2004.

Older adults frequently take multiple medications to treat chronic conditions and often see multiple specialists to manage their illnesses. This may lead to a "silo" approach where each prescriber is working with the patient, but not each other. The patient may also have medications started in different care settings (e.g., the hospital or rehabilitation center) and then the medication inadvertently fails to get discontinued when it is no longer needed. Using multiple unnecessary medications is often described as "polypharmacy." Polypharmacy in the older adult can lead to increased adverse drug events, morbidity and mortality.[9]

The medication regimen of the older adult needs a comprehensive review on at least an annual basis.[10] One purpose of this review is to identify and eliminate medications

that are no longer needed. This function is known as "deprescribing."[11] One survey of health professionals indicated that the most important medications to consider for deprescribing include benzodiazepines, atypical antipsychotics, proton pump inhibitors, typical antipsychotics and medications used for the treatment of sleep disorders.[12] However, it is often difficult for practitioners to successfully deprescribe medications because of the difficulty the prescriber may have making the decision to stop medications, challenges with stopping medications started by other prescribers, and lack of knowledge of how to properly stop medications.[13][14]

In the case of Ms. Gutierrez, she was prescribed a medication and no review occurred to evaluate if other medications may be contributing to her symptoms. In addition, her insomnia was undertreated and no provider assessed her response to zolpidem therapy. When Ms. Gutierrez added the over the counter medication, she inadvertently contributed to her own polypharmacy.

A comprehensive review of a medication regimen of an older adult taking ten, fifteen, or twenty or more medications can be very time-consuming. Few primary care physicians are able to take this time. The Board Certified Geriatric Pharmacist is the ideal person to fulfill this role (see sidebar).

Identification of the patient's medication-related problems involves exploring four important questions:

1. Is the medication indicated (appropriate)?

- Is the patient taking medications that are not indicated?
- Should the patient be taking a medication that is indicated but not prescribed?

2. Is the medication effective?

- Is the most effective drug product being used for the medical condition?
- Is the dose adequate to achieve the intended goals of therapy?

3. Is the medication safe?

- Is the patient experiencing an adverse event from the medication?
- Is the dose so high it could cause toxicity in the patient?

4. Is the patient able and willing to take the medication as intended (adherence, cost, patient preference, etc.)?

Potentially Inappropriate Medications

> *"Most of the nation's medical students finish their training without ever having set foot in a nursing home. Add the dearth of training in practical pharmacology, and for most graduates the proper use of medications in frail elderly patients becomes the overlapping of two voids, creating a particularly dense black hole in their clinical knowledge."*
>
> *--Avorn, Jerry. Powerful Medicines: the Benefits, Risks, and Costs of Prescription Drugs. New York: Alfred A. Knopf, 2004.*

A tenet of medication use is the balance of the potential benefit with the potential risk of the medication. Even without this evaluation, some medications have been recognized as potentially inappropriate for use in older adults. This is primarily because the risk of the medicine is greater than the benefit, or the expected benefits are minimal in this population.[15][16][17]

Several such lists of these potentially inappropriate medications (PIMs) have been compiled. The most commonly used list in the United States is the Beers list, named after geriatrician Mark Beers who coordinated the compilation of the first version of the list in 1991.[15]

The Beers list is intended for use by practicing clinicians.[16] These medications are generally considered best avoided in older adults because they have been found to be associated with poor health outcomes, including confusion, falls, and mortality. A similar but different criteria was developed to identify medications that should be avoided in older adults with certain diseases or syndromes (known as the STOPP criteria).[17]

The American Geriatrics Society has undertaken responsibility for periodic review and updating of the Beers list. The latest version of the Beers list can be found on its website and published in its journal.[16] Examples of most recent recommendations in the Beers list include:

- Avoid use of peripheral alpha-1 blockers (terazosin, prazosin, doxazosin) for hypertension due to high risk of orthostatic hypotension
- Avoid use of first-generation antihistamines (e.g. chlorpheniramine, diphenhydramine, etc.) due to high anticholinergic adverse effects. Of note, short-term use of diphenhydramine for acute treatment of severe allergic reaction may be appropriate
- Avoid nonbenzodiazepine, benzodiazepine receptor antagonists (e.g., zolpidem) due to risk of falls, hospitalization, emergency department (ED) visits, and car accidents with minimal effects on sleep latency

Some of the medications on the Beers list are there because of lack of demonstrated efficacy. Examples of Beers medications lacking efficacy include isoxsuprine and ergoloid mesylates.

Other noted changes to the 2015 version of the Beers list include medications listed as inappropriate for patients with renal dysfunction (e.g., direct acting oral anticoagulants), 13 combinations of medications known to cause harmful drug-drug interactions, and the addition of proton pump inhibitors for long-term use.

Another set of criteria for potentially inappropriate medications in the elderly, commonly used in Europe, is the STOPP (Screening Tool of Older People's Prescriptions) tool.[17] The actual STOPP criteria are found on the website version of this open access article and are available at http://ageing.oxfordjournals.org/content/44/2/213. STOPP criteria look at the patient's condition when considering which medication is or is not appropriate. For example, a patient with constipation should not be given hydrocodone or amitriptyline.

It is important to recognize that the PIM criteria do not dictate that these medications are always inappropriate in older adults but rather are potentially inappropriate. They may be appropriate in some situations, but they should generally be avoided if possible.

In the case of Ms. Gutierrez, the prescription she obtained for her sleep was likely inappropriate because it was not efficacious and likely led to her risk of falling. In addition, her self-treatment with an over the counter medication (likely diphenhydramine) is also inappropriate and made her risk of falls greater. The strong anticholinergic properties of the diphenhydramine contributed to urinary retention and bladder overflow secondary to over sedation at night. Her memory could certainly be impaired by the use of the zolpidem, tolterodine, and diphenhydramine together leading to her daughter's concerns of dementia. While not always the case, these potentially inappropriate medications appear to have contributed to actual and serious adverse effects for Ms. Gutierrez.

Prescribing Cascade

> *"Any symptom in an older adult should be considered a drug side effect until proved otherwise."*
>
> *--Jerry Gurwitz, MD*

One of the fundamental principles of geriatrics is: "Any symptom in an older adult should be considered a drug side effect until proved otherwise."[18]

In this situation, drug side effects are commonly misdiagnosed as new diseases or conditions, and the patient is given a new drug to treat this "new diagnosis." This practice is known as the prescribing cascade.

The adverse effects of medications may be easier to recognize when a patient is taking only one medication for one medical problem or condition. In the older adult with multiple chronic conditions, taking multiple medications, the new symptom may be attributed to "old age" or may be considered a symptom of one of the underlying chronic conditions.

An early example of the prescribing cascade was reported in the literature through evaluation of a Medicaid database. Patients started on metoclopramide, which causes extrapyramidal side effects, were found to be three times more likely to be diagnosed with Parkinson's disease and started on therapy with medication containing levodopa.[19]

In the case above, Ms. Gutierrez was prescribed tolterodine for urinary incontinence that may have been caused by the use of zolpidem and diphenhydramine. The use of these medications can cause over sedation and urinary retention leading to bladder overflow in this patient. In addition, diphenhydramine and zolpidem can also cause memory loss, which led to Ms. Gutierrez's daughter's concern about dementia. If the neurologist elected to test her mental state and determined deficits, it would be possible that the PCP would then prescribe a medication for dementia such as donepezil, which could worsen her bladder control.[20]

Underuse of Medications

Although more attention has been focused on the problem of medication overuse in the elderly, failure to prescribe indicated medications is also an issue that should be considered. An excellent example is the failure of many older adults to receive indicated vaccines, especially influenza, pneumococcal, and zoster vaccines.[21] It is not just medications and vaccinations that are underused, older adults receive just 56% of the recommended care for chronic conditions (e.g., preventative treatment for chronic conditions, screening for cataracts and colorectal cancer, etc.).[22]

To address these concerns, researchers have developed a tool for use in older adults. The Screening Tool to Alert doctors to the Right Treatment (START) includes a set of criteria to indicate when initiation of medication should be considered.[17] An example of START criteria would be to initiate a stimulant laxative in a patient who is on opioid therapy. The START criteria are found on the website version of the open access article and are available at: http://ageing.oxfordjournals.org/content/44/2/213.

Populations of older adults have been screened with the START criteria to evaluate frequency of omission of recommended medications. In a recent study of the START criteria, an associated increased risk of mortality and hospitalization in older adults was observed when they did not receive medications that were recommended in the START criteria.[23] In another study of adults aged 65 and over in Ireland, 42% of study participants were found to be missing one or more recommended medications. In this study, patients who triggered two or more START criteria were found to have significantly more ED visits and significantly more visits to their primary care physician.[24]

The Most Dangerous Drug Is?

When evaluating the impact of potentially inappropriate medications, it is important for the clinician to consider other dangerous drugs not included on the Beers list or other guidelines. In fact, the medications that cause the highest rate of ED visits and hospitalizations related to adverse events in older adults are warfarin, insulin, and digoxin.[25] All of these medications have a narrow therapeutic index and their toxicities may be more pronounced in older adults. In addition, patients over the age of 80 are most at risk for developing significant drug-related adverse events when compared to younger cohorts.[26] The high rate of adverse drug reactions (ADRs) linked to these medications may also be due to the fact that surveillance data used to evaluate drug-related ED visits and hospitalizations rely upon objective measures to determine the causal relationship to the ADR in a patient. For example, hypoglycemia from insulin and bleeding from warfarin can be measured. Regardless, it is important to use warfarin, agents that cause hypoglycemia and PIM cautiously in older adults.

Research in recent years has led to reconsideration of target therapy goals of chronic disease in older adults as risks of "tight" management (e.g. hypoglycemia) are evaluated. Many clinical practice guidelines for the management of chronic diseases now soften goals of therapy in older adults to reduce the over aggressive treatment of an older adult.[27][28] Many older adults do not need tight glycemic or blood pressure control due to short life expectancy or evidence of complications of the disease already present. In other situations, patients simply cannot tolerate the aggressive management of chronic disease. Some of these guidelines are controversial, and new research may indicate that tight blood pressure control in older adults is beneficial in certain populations.[29][30] As a result, an individualized approach is recommended when managing chronic illnesses in older adults.[27][28]

Adherence

In addition to addressing medication indication, effectiveness and safety, it is important for the pharmacist to evaluate patient adherence with medication therapy. As former U.S. Surgeon General C. Everett Koop once said, "Drugs don't work in people who don't take them."

With all populations, it is important to realize that adherence is a critical step in the medication review process. This is especially true in the older adult because poor adherence can lead to underuse of medications and can contribute to the prescribing cascade (prescribing more medications to improve an undertreated problem). As previously discussed, older adults are more susceptible to adverse events because of multimorbidity, physiologic changes, polypharmacy, and the use of potentially inappropriate medications. Therefore, addressing adherence in the older adult should include a comprehensive review of medication taking behavior. If an adherence program (such as auto refills, blister packs or using pill boxes) is applied without carefully reviewing the patient's medication taking behavior, it can be potentially dangerous.[31] An Australian study monitored 29 adults over the age of 75 for eight weeks. It gave pill organizers to half the adults and found that when pill organizers were introduced, adherence was improved. The group using the organizers, however, experienced five adverse events, compared to none in the control group.[31]

It is unclear if Ms. Gutierrez is adherent to her chronic medications for her atrial fibrillation, diabetes and hypertension. If she was not taking her medications for diabetes, it could lead to hyperglycemia, which may provoke her PCP to prescribe more medications to treat diabetes (leading to polypharmacy). If an adherence program was developed without understanding her medication underuse, that could lead to unintended hypoglycemia (an adverse event).

Summary

Like Ms. Gutierrez, many older adults have geriatric syndromes that are confounded by polypharmacy, the prescribing cascade and the use of potentially inappropriate medications. Ms. Gutierrez was a victim of the prescribing cascade and the use of potentially inappropriate medications. Zolpidem, prescribed for her sleep, was ineffective and increased her risk of falls. The use of diphenhydramine and zolpidem together led to over sedation and urinary retention and bladder overflow. The PCP prescribed an anticholinergic drug, tolterodine, for the urinary incontinence, further confounding the effects of zolpidem and diphenhydramine and ultimately leading to increasing healthcare utilization.

When caring for older adults, it is critical to be aware of their unique characteristics and medications to avoid (unless the benefit outweighs the risk), work toward medication deprescribing, and apply a comprehensive patient-centered approach to this diverse population. Because of the risk of adverse drug events in this population, pharmacists are in a particularly good position to make a significant impact on the quality of care delivered to older adults.

Sidebar

Board Certified Geriatric Pharmacist (BCGP) Credential

The Certified Geriatric Pharmacist credential was offered by the Commission for Certification in Geriatric Pharmacy (CCGP) from 1997 through 2016. CCGP merged with the Board of Pharmacy Specialties at the beginning of 2017. By the beginning of 2018, the geriatric pharmacy certification examination will be fully integrated into BPS, while 2017 is a year of transition between the two programs. Updated information about the transition of the geriatric credential can be found at: www.ccgp.org/bpstransition.

The BCGP credential is intended to recognize and identify pharmacists who have achieved a designated level of knowledge, skills, and abilities in geriatric pharmacy practice. A role delineation study (job analysis) is conducted every five years to define the scope of geriatric pharmacy practice. This serves as the basis for the certification examination. The next study is due to be conducted in 2017.

To be eligible for the BCGP credential, a pharmacist must hold a current active pharmacist license, have two years of experience as a pharmacist, and successfully pass the multiple-choice examination. The examination is offered in computer testing centers around the United States, Canada, and other countries. The exam will be offered in four test windows in 2017 and then in two test windows per year (Spring and Fall) beginning in 2018.

The CCGP website will be active through most of 2017 and has reference information about medication use in older adults—Key Resources in Geriatric Pharmacotherapy. Check this link: www.ccgp.org/GeriPharm. Links to many of the resources and references mentioned in this article can be found on this web page.

Table 1:

The American Geriatric Society Elements Essential to Delivering "Person-Centered Care"[4]

Key Element	Example
Individualized, goal-oriented care plan based on the person's preferences	In the case of Ms. Gutierrez, who has a complaint of insomnia, the primary care provider should determine the patient's desire to take a medication to treat the problem compared to her desires for a non-pharmacologic intervention. In addition, a plan to evaluate the effectiveness of the intervention should be developed.
Ongoing review of the person's goals and care plan	The primary care provider can evaluate the effectiveness of the current treatment plan for insomnia and if the patient desires change, adapted to meet those new needs.
Care supported by an interprofessional team in which the person is an integral team member	Comprehensive medication review by the pharmacist might reveal potentially inappropriate medications that the patient is taking (including over the counter medications) and determine the reasons why the patient is not responding to treatment for insomnia. In this scenario, the patient is a key member of the team who drives many decisions.
One primary or lead point of contact on the healthcare team	In this scenario the primary care provider, nurse or pharmacist could all serve as the contact person for the patient.
Active coordination among all healthcare and supportive service providers	If Ms. Gutierrez sees a specialist for her sleep or is admitted to the hospital for an acute condition, the above mentioned contact person can and should coordinate communication across the team members.
Continual information sharing and integrated communication	Active listening to Ms. Gutierrez and her needs as well as using the electronic health record or other mechanisms to share the evolving care plan with each team member and the patient is essential.
Education and training for providers and, when appropriate, the person and those important to the person	Providers should receive team based and person centered care training and should provide resources to the patient to ensure they are aware of their role.
Performance measurement and quality improvement using feedback from the person and caregivers	Outcomes should be measurable and focus on the person-centered goals that were developed. In addition, the transitions between care settings should be minimized and evaluated.

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