# Drug Safety Initiative:

## Potentially Inappropriate Medications in Seniors:

## *A CME Monograph*


**Supporter:**
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## Accreditation:

**AMA:** The Georgia Academy of Family Physicians is accredited by the Medical Association of Georgia to offer continuing medical education to physicians. The GAFP designates this educational activity for a maximum of 1.0 AMA PRA Category 1 credit(s)™ toward the AMA Physician's Recognition Award. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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**Target Audience:** This activity is designed for family physicians, geriatricians, and other healthcare professionals who care for older adults.

## Objectives:

1. Understand and explain how certain drug combinations can cause patient harm
2. Recognize which drugs should be avoided in seniors and how to transition to safer alternatives
3. Perform medication reconciliation for patients in any setting

# Table of Contents

**Pharmacodynamics & Pharmacokinetics: Essential Issues in the Geriatric Patient** ..... 1
Armon B. Neel, Jr., Pharm.D, CGP, FASCP

**Potentially Inappropriate Medications (PIMs) in the Older Adult** ..... 4
James W. Cooper, RPh, PhD, BCPS, CGP, FASCP
Allison H. Burfield, RN, PhD

**High Risk Drug/Drug Interactions** ..... 9
Richard Ackermann, MD
Adrienne Mims, MD, MPH

**Medication Regimen Adherence Barriers in the Geriatric Patient** ..... 13
Monica W. Parker, MD
Adrienne Mims, MD, MPH

**Resource Tools-Best Practices** ..... 16
Harry Strothers, MD

**Self Assessment Post Test** ..... 19

**Activity Evaluation** ..... 21

## Introduction

Treating the geriatric population presents different and complex challenges when compared to the younger population. Many geriatric patients have multiple health problems and require more than one medication to manage their health conditions. The use of multiple medications introduces additional complications such as different pharmacologic behaviors in the older population as well as medications that are contraindicated in geriatric patients and increased risk of drug-drug interactions. With this population at higher risk for adverse events with prescription medication use, it is important that caregivers be equipped with the knowledge and tools to recognize potential problems and avoid these issues if possible. The amount of information is immense but recent technology advances can offer assistance for caregivers when managing medications in these patients. Understanding these areas of risk and the different types of systems available is key to improving the outcomes for these patients.

Physicians often have a hard time understanding that in today's medicine, with a rapidly aging population, two patient-care hats have to be worn. When dealing with patients up to 60 years of age, the physician has to wear a preventive care hat, yet when dealing with patients 60 years and older, the physician has to also add a palliative care hat. Caring for a 70 year old patient with 7 or 8 co-morbid problems requires a comprehensive understanding of all of the issues involved, not only in the patient's body but with the multiple drugs prescribed.

## Pharmacodynamics & Pharmacokinetics: Essential Issues in the Geriatric Patient

***Armon B. Neel, Jr., Pharm.D, CGP, FASCP***

The basic rules of chemistry are predictable in the young healthy patient. But as the body ages, the changes in body chemistry mean that the expected outcomes from drug therapy can change dramatically. A clinician must be familiar with both pharmacology and aging changes in order to predict the outcome from a drug therapy prescribed for a geriatric patient. Years of clinical practice with patients in this age group can also improve outcomes. For clinicians, all of these factors are important in providing a better quality of life for this patient group.

This article will address many types of pharmacodynamic (PD) and pharmacokinetic (PK) actions in the geriatric patient and how these changes affect various mechanisms and medications. Some drugs impact complete systems in the body and thus affect many or all drugs administered to that patient; some examples of these drugs will be reviewed as well. Physicians need to use PD and PK knowledge about medications in older patients to implement prescribing habits consistent with the patient's age.

## Pharmacodynamics (PD)

Pharmacodynamics is the study of the time course and intensity of a drug's effects on the body.[1] This also encompasses the pharmacologic effects when one drug influences or alters the effects of another drug. The net pharmacologic effects may be[1]:

- **Additive:** These are effects that enhance the desired therapeutic response which might be expected from a single drug. Patients who are administered benzodiazepine drugs for a desired therapeutic response of sedation might see an enhanced effect when combined with alcohol consumption in the geriatric population. This problem can be compounded in the geriatric patient with the concomitant use of anxiolytics, antidepressants and hypnotics.

- **Synergistic:** Drug synergism occurs when drugs can interact in ways that enhance or magnify one or more effects, or side effects, of those drugs. This is seen with combination drugs such as acetaminophen & codeine or acetaminophen & tramadol. There are many combinations in the antihypertensive/diuretic drug classes that have some synergistic activity. Although these drug outcomes are fairly predictive in the younger patient, this does not always hold true in the geriatric patient due to serious PK alterations which will be further discussed in the PK section.

- **Antagonistic:** In this type of pharmacological effect, the effect of two chemicals is actually less than the sum of the two drugs taken independently of each other. A very common example seen in today's treatment is the use of Alzheizmer's drugs or cholinesterase inhibitors, ***a cholinergic drug***, when given concomitantly with an antihistamine, which is an anticholinergic drug.[2] The contradiction between cholinergic and anticholinergic effects are seen here. The therapeutic activity of both are reduced or stopped.

## Pharmacokinetics (PK)

Pharmacokinetics is a discipline that uses mathematical models to describe and predict the time-course of drug concentrations in body fluids.[1] The pharmacokinetic issues are vast in treating the geriatric patient and must be considered with each drug ordered, condition changes, sex or race of the geriatric patient.

Concurrent administration of two or more drugs can result in the interference with any or all of the pharmacokinetic parameters. These parameters are[1]:

- **Absorption:** The pH of the stomach becomes higher with age and there is an inability to produce the necessary acid media as seen in younger patients. This lack of acid media may impair the absorption of a medication to the extent that the drug passes through the patient without being absorbed at all. Some drugs such as calcium carbonate may exacerbate rebound acidosis in the geriatric patient. Additionally, iron products are difficult to absorb. The use of citrate salts of calcium and sulfate salts of iron are more readily absorbed than other similar compounds. Also, the use of proton pump inhibitors keep the geriatric gut in a constant basic state, which then can exacerbate other problems such as Clostridium difficile diarrhea and anemia.

- **Distribution:** Age compromises the efficiency of the liver and kidneys as well as many other organs used in drug distribution in the geriatric patient. Most drugs are bound to albumin and without enough of this blood protein more unbound drug circulates throughout the body; this can cause unpredictable responses. Phenytoin is about 98% protein-bound as are many of the other antiepileptic drugs; therefore, geriatric patients who are nutritionally impaired may be at a higher risk for toxic drug therapy outcomes.

- **Metabolism:** The impact of metabolism on drugs is very important in the treatment of the geriatric patient. After age 60, many of the hepatic CYP 450 isozymes which are essential for the breakdown of various drugs are reduced; approximately 20% of geriatric patients stop producing CYP 2D6 which is also essential for metabolism of other drugs. The isozymes CYP 2C9 and 2C19 either are not available or in low supply, which may lead to fatal adverse reactions when prescribing warfarin drugs. In some situations, the INR values may vary from test to test; the clinician may consider discontinuation of the drug. For more predictable outcomes from drug therapy, clinicians should consider the use of drugs that are hepatically metabolized at the CYP 3A4 isozyme, which is more abundant in the geriatric population. For phenytoin, changes in PK activity in metabolism and elimination do not allow the drug to efficiently be removed from the patient.

- **Elimination:** Elimination is a major problem in the geriatric patient. Most medications are removed from the body through the kidney. Without the presence of any major chronic renal illness, the human body loses 1% of its renal function each year starting at age 30. Therefore by age 80, a patient typically only has 50% of normal renal clearance. Also beginning at age 30, all patients begin to develop sarcopenia, a wasting of muscle mass. Since creatinine is a by-product of muscle mass metabolism, the patient is losing both renal clearance and muscle mass at an equal pace. However, the overall serum creatinine will remain constant and may be deceptive when evaluating the renal clearance on a laboratory report. Contrary to popular belief, the use of the PK equation of the Modification of Diet in Renal Disease (MDRD) which is normally calculated on the laboratory report is less accurate when treating the geriatric patient. However, the Cockcroft-Gault equation is about 85% accurate when calculating the renal clearance for the geriatric patient. Due to the changes in the glomerular filtration rate (GFR), many drugs are inappropriate for use in the geriatric patient. Some drugs that require a robust degree of renal clearance such as nitrofurantoin, amantadine, memantine, many antibiotics, ACE & ARB drugs and some antidiabetic drugs can place the patient at risk of adverse events. Many of the medications mentioned can cause serious cognitive problems or stroke and can lead to falls and broken bones. Additionally, the previously discussed CYP isozyme losses can result in difficulties eliminating medications.

## Summary

In an effort to provide optimum therapeutic outcomes to geriatric patients, it is essential to evaluate the pharmacokinetics/pharmacodynamic potential risk with each drug prescribed and to ensure that drugs that are not acceptable in the geriatric patient are not prescribed. Comprehending the complexities associated with geriatric care requires much study and practice. Further information about the problems and challenges associated with age and drug therapy are cited.

## Additional Information

***The Sheiner-Tozer Equation is used for an accurate estimate for Phenytoin level:***

- Corrected Phenytoin = Measured Phenytoin Level / ( (adjustment x albumin) + 0.1)
- Adjustment = 0.2; In patients with Creatinine Clearance < 20, adjustment = 0.1.

***The formula for the Cockcroft-Gault equation:***

Estimated creatinine clearance, or GFR = [(140-Age) x IBW (in kg)] / [72 x Serum creatinine (in mg/dL)]

- If the patient is female, multiply the above by 0.85 If patient is over 65 years of age and Serum Creatinine value is less than 1, use 1 in the equation.

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# Potentially Inappropriate Medications (PIMs) in the Older Adult

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While an understanding the pharmacodynamics and pharmacokinetics of common medications prescribed in the geriatric patient is vital to the management of these patients, it is also important to have a practical understanding of the types of medications that can cause problems in this population

The last panel consensus on PIMs produced a list of medications that should potentially be avoided in the older adult [1]. There are two formats that were employed: one was to list drugs that may be inappropriate in all older adults; the second format was to list drugs that may be inappropriate for specific diagnoses. These lists form much of the basis for the Centers for Medicare and Medicaid Services (CMS) F-329 tag for Inappropriate Drugs in Long-term Care at **www.cms.hhs.gov**.

***Table 1*** lists some of the medications that can be considered PIMs and may be associated with unacceptable adverse effects on the older adult and shorten the patient's life expectancy [2-6]. The authors have added medications to these lists to update for newer drugs, per the latest literature and regulatory warnings on the use of these drugs in the older adult.

**Table 1- Potentially Inappropriate Medications (PIMs) for the Older Adult [1-6]**

| Drugs to Avoid | Alternative(s)* |
|---|---|
| **Analgesics** | |
| propoxyphene, pentazocine (Talwin), meperidine (Demerol), Ketorolac (Toradol) | APAP, Tramadol, codeine, hydrocodone, Fentanyl, oxycodone, morphine |
| All full-dose NSAIDs for prolonged periods(ie greater than 1-2 weeks) | Acetaminophen (APAP), topical NSAIDs for focal pain , short-term oral NSAIDs |
| indomethacin (Indocin) | APAP, topical NSAIDs |
| **Anxiolytics and Hypnotics:** Psychotropics, BZ=benzodiazepines, TCA= tricyclic antidepressants, LA=long-acting, SA=shorter-acting, SSRI= selective serotonin re-uptake inhibitors | |
| Longer-acting Benzodiazepines (LABZs): diazepam (Valium), chlorazepate (Tranxene), flurazepam(Dalmane), halazepam (Paxipam), chlordiazepoxide (Librium), alprazolam (Xanax), lorazepam (Ativan), | SSRIs or buspirone now preferred over BZs or TCAs, then oxazepam as the shortest acting-BZ, trazodone for hypnotic |
| Barbiturates- all except Phenobarbital for seizures | Newer antiepileptic drugs |
| meprobamate (Equanil/Miltown) | SSRIs or oxazepam, buspirone |
| **Antidepressant** | |
| amitryptyline in (Elavil) and in combination products such as Limbitrol and Triavil/Etrafon, doxepin (Sinequan), daily fluoxetine | sertraline, escitalopram, citalopram, weekly fluoxetine, buproprion or venlafaxine or desvenlafaxine if no HBP, mirtazapine |
| ****Antipsychotics: (in patients without the diagnosis of schizophrenia, or schizoaffective disorders)** | |
| thioridazine (Mellaril), mesoridazine (Serentil), and all other conventional antipsychotics, olanzapine (Zyprexa), ziprasdone (Geodon) aripiprazole (Abilify), quetiapine (Seroquel), paliperidone (Invega) | risperidone (Risperdal) for short periods of time (>2 weeks) **BUT GENERALLY AVOID ALL ANTIPSYCHOTICS IN DEMENTIA** |
| Multiple Psychoactive Drugs | Use fewest psychoactives as possible, and always carefully taper to fewest, lower dose and safer alternatives to lower morbidity and mortality risk |
| ****NOTE: metoclopramide (Reglan)- use lowest dose possible adjusting for renal function, it is a phenothiazine antipsychotic-derived drug** | |
| **Hormones** | |
| Oral estrogen | topical estrogen (patch, cream, ring) may be safer |
| Oral testosterone or derivatives | topical dosage forms,(patch, gel, cream) |
| **Cardiovascular Agents** | |
| disopyramide (Norpace) | NONE |
| amiodarone (Cordarone) | dronedarone (Multium |
| methyldopa (Aldomet), clonidine, reserpine (Serpasil), guanethidine, | Calcium channel blockers, angiotensin receptor blocker (ARB), angiotensin converting enzyme inhibitor (ACEI), Beta blockers |
| **Antidiabetic Agents** | |
| chlorpropamide (Diabenese) | metformin, acarbose, glitazones if no congestive heart failure (CHF), repaglinide, nataglinide |
| **Anti-nauseant/GI Motility Agents** | |
| trimethobenzamide (Tigan) | Promethazine |
| metoclopramide (Reglan) | Use lowest dose possible for renal function |
| **Vasodilator** | |

| Drugs to Avoid | Alternative(s)* |
|---|---|
| dipyridamole (Persantine) | Low-dose ASA (81-325 mg/day, clopidogrel or extended release (ER)-dipyridamole with ASA (Aggrenox) |
| **Amphetamines and other anorexic agents**<br>E.g. methamphetamine, pseudoephedrine | **AVOID altogether** |
| **Anti-infective Agents** | |
| Nitrofurantoin, erythromycin | Trimethoprim, other macrolides in place of erythromycin, eg clarithromycin, azithromycin |
| **Other Psychoactive Agents** | |
| **Antihistamines** | |
| diphenhydramine(Benadryl) and other sedating antihistamines, eg.chlor- or brompheniramine hydroxzine (Atarax/Vistaril), and its derivative cetirizine (Zyrtec) or levocetirizine (Xyztal), cyproheptadine (Periactin), meclizine (Antivert) | loratidine, fexofenadine desloratidine |
| **GI Antispasmodic Drugs** | |
| dicyclomine (Bentyl), hyoscyamine (Levsin/Levsinex),<br>Propatheline (ProBanthine), belladona alkaloids (Donnatal)<br>Clindinium-chlordiazepoxide (Librax) | AVOID ALL-especially in those with any cognitive impairment |
| **Urinary Tract Antispasmodics** | |
| ORAL oxybutinin | topical oxybutinin, lower doses of tolterodine (Detrol), fesoterodine (Toviaz), trospium(Sanctura), solfenacin(Vesicare), darifenacin (Enablex) IF no cognitive decline noted after starting any of these agents |
| **Cognition Enhancers** | |
| Tacrine (Cognex) | rivastigmine (Exelon patch only), donepezil (Aricept), or galantamine (Razadyne) and/or memantine (Namenda) |
| **Muscle Relaxants** | |
| methocarbamol (Robaxin), carisprodol (Soma), chlorzoxazone (Paraflex), metaxolone (Skelaxin), cyclobenzaprine (Flexaril), dantrolene (Dantrium), orphenadrine (Norflex, combo as Norgesic) | (BZ) Clonazepam in lowest possible dose and only for spasticity disorders or short-term for muscle injuries. OK in seizure disorders |

*As suggested by the authors, references and current guidelines see **www.fda.gov/medwatch** and **www.guidelines.gov** and **www.ahrq.gov** for more documentation.

## Medications That May be Inappropriate for Specific Diagnoses
**(Please see references and previously mentioned web sites for more information on the PIMs)**

**Table 2- PIMs by Diagnosis (HBP=high blood pressure MI=myocardial infarction)**

| Diagnos(is/es) | Potentially Inappropriate Medications (PIMS) | Alternatives |
|---|---|---|
| **Cardiovascular** | | |
| HBP, Heart Failure, MI | Full-dose NSAIDs, glitazones (rosa-and pio-), high sodium content drugs, all decongestants | APAP, metformin, insulins |
| Stroke, arrhythmias | Pseudoephedrine, all diet pills, CNS stimulants (e.g. methylphenidate), erythromycin, TCAs | AVOID ALL MEDS or herbals that stimulate heart or brain |
| Blood Clotting disorders or receiving anticoagulant therapy | Some combinations of ASA with clopidogrel, prasugrel, warfarin, or dabigatran, with heparin and heparin fragments or antithrombotic that may markedly increase GI and intracranial hemorrhage risk | Preferably single agents that affect intrinisic and/or extrinsic as well as common clotting pathways |
| **Gastrointestinal** | | |
| Gastroesophageal reflux disease, (GERD), peptic ulcer disease | ASA doses greater than 81mg/day, all NSAIDs, oral bisphosphonates (alendronate, risedronate, ibandronate) | Prefer-> ASA doses 5-81mg/day and IV bisphosphonates in place of oral agents given on any basis |
| Constipation | Mineral oil, stimulant laxatives | Prefer PEG or sorbitol 70% |
| **Genitourinary** | | |
| Bladder Outflow Obstruction (BOO) | Anticholinergics, antispasmodics, antihistamines, antipsychotics, TCAs, BZs, decongestants | Newer alpha blockers,eg tamsulosin, alfuzosin or silodosin then finasteride or dutaseride in males |
| Stress/urge incontinence or overactive bladder (OAB) | Older alpha blockers(eg prazosin,terazosin, doxazosin) diuretics, cholinesterase inhibitors (e.g. donepezil), LABZs | topical oxybutinin, lower doses of tolterodine (Detrol), fesoterodine (Toviaz), Trospium(Sanctura), solfenacin(Vesicare), darifenacin (Enablex) IF no cognitive decline noted after starting any of these agents |
| **Neurologic** | | |
| Parkinsonism, Tardive Dyskinesia | Most antipsychotics, metoclopramide, opioid analgesics, cholinesterase inhibitors except rivistigmine, memantine | ------- |
| Seizure disorders and insomnia | Above medications plus all CNS stimulants (e.g. methylphenidate, amphetamines), fluoroquinolones, buproprion, SNRIs, venlafaxine, desvenlafaxine, theophylline, pentoxyphylline, oral beta agonists, and decongestant sympathomimetics (e.g., pseudoephedrine) | ------- |
| **Psychiatric** | | |
| Depression | all BZs, TCAs, methyldopa, guanethidine, reserpine | SSRIs, SNRIs, mirtazapine |
| Dementia | All antipsychotics for prolonged use, BZs, all CNS stimulants | Acetaminophen for agitation suspected due to pain |
| Cognitive impairment | All psychoactive medications to include antipsychotics, BZs, TCAs, antihistamines, antispasmodics, muscle relaxants, metoclopramide, opioid analgesics, CNS stimulants | Use lowest possible total psychoactive “load” |
| **Pulmonary** | | |
| COPD | All BZs and hypnotics, all LA beta-agonists via oral or inhalation route without a prior LA-anticholinergic, cholinesterase inhibitors, theophylline, beta blockers via all routes, oral and topical | ------- |
| **Geriatric Conditions** | | |
| Anorexia, weight loss | All CNS stimulants, daily fluoxetine | ------- |
| Syncope | All antihypertensives, alpha-blockers, diuretics | ------- |
| Falls | All psychoactive medications to include all psychotropics, opioid analgesics, antihistamines, antispasmodics, muscle relaxants | ------- |

## Adverse Drug Withdrawal Effects

There are numerous studies that point to the need for careful tapering and withdrawal of many of the PIMs mentioned. The patient may insist on taking one of these medications, or their caregiver may not want to change their drug-taking behavior. It is usually imperative for the patient/caregiver to understand the risks of continuing these medications. Once they have agreed to the change in medications, it is critical that a therapeutic plan be agreed to in order to enable a smoother transition to the tapering and withdrawal process, and possible replacement of the PIM by a safer medication. Never order an abrupt discontinuance of most psychoactive medications and always suspect patient and/or caregiver noncompliance or nonadherence to medication orders when withdrawal adverse effects are reported or claimed by the patient or caregiver(s).

The authors and many others have successfully converted patients from PIMs to safer medications via a step-wise process. For example, the patient taking propoxyphene napsylate/acetaminophen (PN/APAP) four (4) times a day may be able to withdraw one PN/APAP per day each week and replace the PN/APAP with 500 mg of APAP.

To avoid withdrawal seizures, or tardive dyskinesia from abruptly stopping a benzodiazepine (BZ), antipsychotics, or metoclopramide, taper the daily dose 10 to 25% per week to every two weeks, depending on the drug half-life. Antidepressants withdrawn too quickly may also produce a myriad of adverse effects to include anxiety, paresthesias, serotonin syndrome, manic episodes, or panic attacks. The space limitations of this chapter preclude more extensive discussion of methods to avoid adverse drug withdrawal effects.

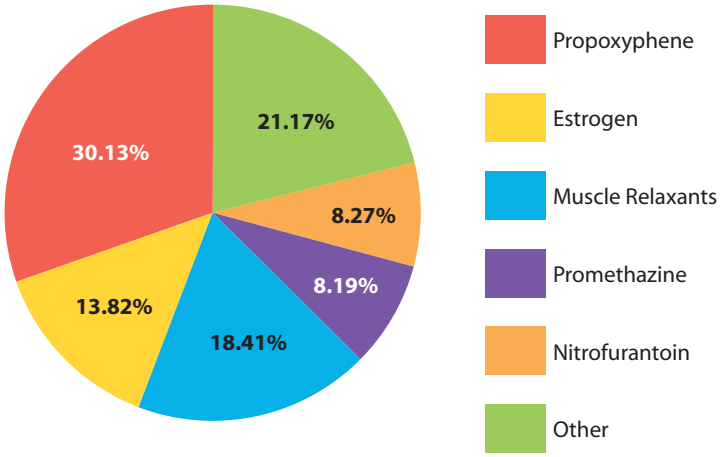
## PIMs and Health Care Morbidity and Mortality

The use of inappropriate drugs in the older adult within nursing homes has been shown to increase healthcare costs for ER visits, and hospitalization by 30-90% and an overall mortality rate by up to 1.9-2.5 times, when compared to patients who did not use these drugs [2,3]. Further studies found that the rate of falls, fractures, and both emergency room visits and hospitalizations are proportional to the total psychoactive drug load and may be reduced by decreasing this load to minimal to no psychoactive medications in the patient [4,5,6]. For example, the use of acetaminophen 500 mg 4 to 5 times a day has been shown to reduce both agitation episodes and the use of psychotropics and falls in older patients with dementia by 63 to 75%. [7]

## Summary

This article has briefly presented the potentially inappropriate medications that may be used in the older adult with some suggested alternatives when appropriate. Careful consideration of the removal of these medications from willing patients and their caregivers, as well as useful alternatives that address the problems or diagnosis(es) may help reduce medication associated morbidity and mortality. This is important for the geriatric patients and caregivers in the state of Georgia. Up to 24.45% of Georgians who are Medicare Part D enrollees have one or more PIMs prescribed. (Figure 1) In Georgia nursing homes, the use of PIMs may increase health care morbidity by up to 250%.[2] Awareness of the human and financial impact of PIMs on the population of this state can improve the level of care given by clinicians and improve the outcomes of these patients.

***Figure 1-Medicare: Potentially Inappropriate Medications Filled in Georgia***

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# High Risk Drug/Drug Interactions

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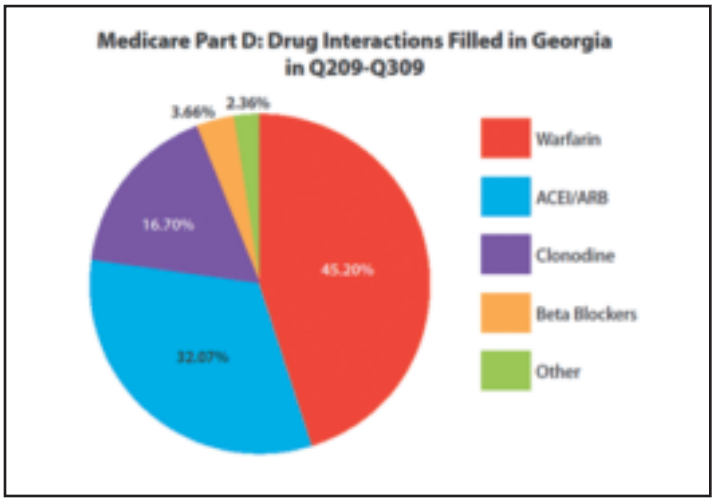
Adverse drugs reactions (ADRs) are common and are frequently either not recognized or attributed to another condition. Many ADRs are actually drug-drug interactions. This is a review of some drug-drug interactions that 1) are potentially harmful, 2) are frequent (a predictable consequence of two drugs together, and 3) result from drugs that are frequently prescribed to older adults. CMS data from Medicare Part D claims filled in Georgia demonstrate that there are opportunities to improve safe prescribing of drug combination in Georgia seniors (Table 4).[1] The percentage of Part D enrollees with at least one claim for a Part D drug, who have ≥1 DDI during a 12 month period is 9.06%.

In a case control study of Canadian older adults hospitalized with drug toxicity, Juurlink and colleagues[2] examined how many of these hospitalizations were due to drug-drug interactions. For older patients receiving the diabetic drug glyburide, those admitted with hypoglycemia were more than 6 times as likely to have been treated with trimethoprim-sulfamethoxazole in the previous week (odds ratio 6.6, 95% confidence interval 4.5 – 9.7). For patients admitted with digoxin toxicity, the odds ratio for having been prescribed clarithromycin (Biaxin) in the previous week was 11.7 (7.5 - 18.2). For patients taking ACE inhibitors who were admitted with hyperkalemia, the risk of having recently been treated with a potassium-sparing diuretic was more than 20 (OR = 20.7, 13.4 – 30.7).

***Figure 2 (Medicare Part D: Drug Interactions Filled in Georgia in Q209 – Q309)***




Many of these hospitalizations may have been avoided with either 1) the use of alternative medications or 2) closer patient monitoring. For example, for patients on glyburide who might need an antibiotic, using antibiotics such as amoxicillin or cefuroxime has no associated hypoglycemia for the patient. Using an ACE inhibitor along with a potassium-sparing diuretic may be appropriate with close monitoring of the potassium. However, choosing another diuretic that is not potassium-sparing may be prudent in these patients.

# Hypertensive Medication Drug-Drug Interactions

The thiazide diuretics such as hydrochlorothiazide (HCTZ) frequently cause hypokalemia especially if doses greater than 25 mg/day are used. To respond to this, clinicians often prescribe either K supplements or a combination of HCTZ with a potassium-sparing diuretic. These combination drugs use either triamterene or amiloride with HCTZ in a fixed-dose product, generally with 25 mg of HCTZ. The combination products triamterene-HCTZ (Dyazide, Maxzide, generics) or amiloride-HCTZ (Moduretic, generics) clearly reduce the risk of hypokalemia and are generally safer and better tolerated than combining HCTZ with potassium supplements.

However currently, there are usually better choices than Dyazide, Maxzide, or Moduretic in older adults. Most patients with essential hypertension need two or three drugs to control their blood pressure. One of these should clearly be a diuretic, and one of the others should usually be an ACE inhibitor. Further, in patients with systolic heart failure, evidence-based polypharmacy is the norm, with combinations of a diuretic, ACE inhibitor, and beta blocker being common. One should virtually never combine Dyazide/Maxzide/Moduretic with either an ACE inhibitor or an angiotensin receptor blocker (ARB), because of the substantial risk of serious hyperkalemia.

But it is NOT always wrong to combine a potassium-sparing diuretic with an ACE inhibitor or ARB.[3] Randomized controlled trials in patients with systolic heart failure have shown that adding either spironolactone (Aldactone) or eplerenone (Inspra) to patients already on diuretics and an ACE inhibitor (often also a beta blocker) can further reduce mortality. However, one should be careful of combining drugs that raise serum potassium, particularly in 1) older adults, 2) patients with renal insufficiency, and 3) patients with diseases like diabetes which predispose to hyperkalemia.[3] In general, for older adults with systolic heart failure, the clinician should start by getting volume under control with a diuretic and prescribing an ACE inhibitor. As a next step, the clinician should titrate up the ACE inhibitor and then add a beta blocker, all the while frequently checking electrolytes, especially the potassium levels. In selected patients, adding eplerenone or spironolactone could be a consideration.[3] In patients with systolic heart failure, there is almost never a reason to prescribe the old-fashioned Dyazide/Maxzide/Moduretic combination – this leads to complications with no increase in efficacy.

## Warfarin Drug-Drug Interactions

Major drug interactions with warfarin are likely the most important drug-drug interaction in older adults. Many drugs either increase or decrease the anticoagulant response, and either of these events may be adverse – if the anticoagulant response is increased, the patient may bleed, and if the anticoagulant response is decreased, the patient may not be adequately protected from embolism. The list of drugs[4] that interacts with warfarin is large and daunting, and no one clinician can realistically remember all of them. However, for older adults taking warfarin, every change in drug therapy should at least prompt consideration of an interaction.

Acetaminophen increases the INR in patients on warfarin.[5] The cause of this effect is not known, and the mere presence of this interaction should not cause the clinician to avoid the combination. Indeed, for older adults on warfarin, acetaminophen-containing pain medications are clearly preferable to NSAIDs, because NSAIDs increase bleeding by another effect, inhibiting platelet function.[6] For example, an 80-year old woman recovering from total hip replacement takes three Lortab-5 tablets (acetaminophen 500 mg and hydrocodone 5 mg) daily, in addition to warfarin, which was prescribed for thromboembolism prophylaxis. You would expect her INR to be increased, so 1) use lower doses of warfarin and 2) monitor the INR frequently. As her pain decreases and her use of Lortab-5 decreases and ceases, you can expect the INR to fall, so 1) you may need higher doses of warfarin and 2) you will need to keep monitoring the INR frequently.

Many antibiotics have been associated with an increase in anticoagulant effect among patients taking warfarin, but the most important predictable effects are probably seen with trimethoprim-sulfamethoxazole (Septra, Bactrim), metronidazole, erythromycins (the parent drug plus azithromycin and clarithromycin) or quinolones (especially ciprofloxacin, Cipro).[6] Try to avoid combining warfarin with one of these antibiotics, and if the combination is needed, consider lowering the warfarin dose and increasing the frequency of INR monitoring.

Before prescribing sulfa antibiotics, the caregiver should consider getting a culture and sensitivity, and ask if any antibiotic is truly necessary. If the clinician must use a sulfa drug, reducing the warfarin dose by one-half during the antibiotic administration as well as one week after antibiotic completion is a reasonable course of action. The INR should be periodically monitored, perhaps up to once or twice per week.

Similarly, clinicians should try to avoid using erythromycin, azithromycin (Zithromax) or clarithromycin (Biaxin) in patients taking warfarin.[6] These combinations have a high probability of raising the INR, and this effect is often delayed, lasting for days to weeks after stopping the antibiotic, especially for the long-acting drugs like azithromycin and clarithromycin. Is an antibiotic is clearly indicated for this patient? If a macrolide must be used, reducing the dose of warfarin, or monitoring the INR and adjusting the dose as needed are two potential preventative steps. When the physician stops an antibiotic like azithromycin or clarithromycin, the INR needs to be monitored more closely for the next week or two.

Many quinolones have also been associated with an increased warfarin effect, particularly enoxacin (Pentrex), ciprofloxacin (Cipro), norfloxacin (Noroxin), or ofloxacin (Floxin).[6] If antibiotics are truly needed in patients taking warfarin, there are antibiotic classes with less likelihood of warfarin interaction. If ciprofloxacin is used, the warfarin dose should be adjusted and the INR should be checked every second or third day.

Patients taking warfarin should also avoid drugs that increase the risk of bleeding, even though there may be no direct effect on the INR. For example, warfarin users should clearly avoid taking all non-steroidal anti-inflammatory drugs (NSAIDs) because they erode gastric epithelium and inhibit platelets, thereby dramatically increasing the risk of bleeding.[6] If a patient on warfarin develops pain or fever, acetaminophen (Tylenol) is a reasonable choice, even though acetaminophen may increase the INR as well. Low-dose acetaminophen for short periods does not seem to affect the INR.

Many patients taking warfarin will also have compelling reasons for taking cardio-protective, low-dose aspirin. This combination does increase the risk of bleeding, but the risk is not excessive.[7] However, if one adds a third drug like clopidogrel (Plavix), the risk goes up considerably.[8] Think twice, even three times, before authorizing such combinations. For patients taking anticoagulants, caregivers should advise avoidance of herbal supplements that can cause bleeding. These include the 4 G's (ginseng, ginkgo, garlic, and ginger),[9] as well as fish oil[10] and vitamin E.[11] In addition, patients on anticoagulants, especially on more than one, should be alert for early signs of bleeding, such as bruising, gingival bleeding, nosebleeds, or evidence of GI or GU bleeding. Selected high-risk patients should be treated with a proton pump inhibitor (PPI), although there are now concerns that combining clopidogrel (Plavix) with PPIs, especially omeprazole, may reduce the anti-platelet effect of the clopidogrel.[12]

## Drugs that interact with Warfarin

| Drug or Drug Class | Risk of Bleeding |
|---|---|
| **Antibiotics** | |
| Most agents, but especially co-trimoxazole, metronidazole, macrolides & quinolones | ↑ |
| Rifampin | ↓ |
| **Antifungals** | |
| Fluconazole, miconazole | ↑ |
| **Antidepressants** | |
| Selective serotonin re-uptake inhibitors (SSRI) | ↑ |
| **Antiplatlet agents** | |
| ASA, clopidogrel, ticlopidine | ↑ |
| **Anti-inflammatory agents** | |
| All, NASAID, including COX-2 inhibitors | ↑ |
| **Acetaminophen** | ↑ |
| **Alternative Remedies** | |
| *Gingko,* dong quai, fenugreek, chamomile, Pepto-Bismol® | ↑ |
| St. John's wart | ↓ |

** This is only a partial list of drugs that can interact with Warfarin.*

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## Antagonistic Drug-Drug Interactions

Some drugs have opposing mechanisms of action, and therefore their combination make no sense. For example, patients with Alzheimer's disease are often prescribed cholinesterase inhibitors (ChEIs) such as donepezil (Aricept), rivastigmine (Exelon), or galantamine (Reminyl). These drugs work by increasing the concentration of the neurotransmitter acetylcholine in the synaptic cleft.[13] It makes no sense to also prescribe to these patients a muscarinic (acetylcholine) receptor blocker, such as the drugs used to treat urge incontinence, like oxybutynin (Ditropan), tolterodine (Detrol), or tropsium (Sanctura). As the two drugs have exactly the opposite effect on acetylcholine, they should not be combined. The clinician should treat the condition, dementia or urinary incontinence that is more important or problematic for the patient. There are other anticholinergic drugs to avoid in patients taking ChEIs – this includes the directly anticholinergic drugs benztropine (Cogentin) and trihexyphenidyl (Artane), as well as tri-cyclic antidepressants, common medications for nausea, and anti-histamines.

Another example of prescribing drugs with opposing mechanisms of actions include prescribing a dopamine agonist such as carbidopa-levodopa (Sinemet) along with a dopamine-blocking drug such as an atypical antipsychotic like risperidone (Risperdal). Patients with Parkinson's disease have a deficiency of dopamine and are treated with Sinemet or a direct dopamine agonist like ropinorole (Requip) or pramipexole (Mirapex). These drugs increase the concentration of dopamine in the ailing striatum.[14] For patients like this, clinicians should not prescribe any drugs that block dopamine. This list includes both the older (typical) and newer (atypical) neuroleptics, but also drugs such as anti-nausea medicines like (Phenergan) or (Compazine), as well as the motility drug metoclopramide (Reglan).

## Clonidine Drug-Drug Interactions

The use of clonidine (Catapres) tablets or patches with the class of drugs known as beta- blockers can result in a serious drug to drug interaction. The medical literature supports three reasons that this combination is NOT recommended. The first reason is that non-selective beta-blockers can reverse the antihypertensive effect of clonidine, making it ineffective.[15] The second reason is that beta-blockers are known to affect sinus node function or AV nodal conduction and, when given in combination with clonidine, can produce additive effects such as bradycardia and AV block.[15] The third and final reason clonidine should not be used with beta-blockers is that beta-blockers can increase the severity of the withdrawal effect seen when clonidine is discontinued suddenly[15] if the patient stops taking it by themselves or forgets to take it. Symptoms of this withdrawal effect include nervousness, agitation, headache, and tremor followed by a rapid rise in blood pressure (known as "rebound" hypertension) and an increase in plasma catecholamine concentrations. This could lead to hypertensive encephalopathy, cerebrovascular accidents or even death.[16] It is important to counsel any patients on clonidine that they should not discontinue therapy without consulting a physician first. When discontinuing a patient's clonidine tablet therapy, the dose should be reduced gradually over two to four days.

## Summary

Drug-drug interactions are numerous and it is impossible for a clinician to remember all of them. However, with diligence and research when prescribing medications to the geriatric population, many of these interactions can be avoided with adjustments in dosage or class of medication.

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# Medication Regimen Adherence Barriers in the Geriatric Patient

***Monica W. Parker, MD and Adrienne Mims, MD, MPH***

Diminished and incorrect adherence to a prescribed medication regimen to treat multiple chronic diseases results in a significant public health problem for our nation's elderly. This important public health issue results in significant morbidity and mortality. Non-adherence to medications has resulted in $100 billion of healthcare costs from increased hospitalizations for adverse effects, ER visits, and nursing home placements.[1] Reasons for this are multifaceted. Medication costs, cognitive deficits, and a lack of knowledge about side effects associated with multiple drug regimens are the factors most cited. Prescription medication adherence, however, varies with the individual patient. Studies must be developed to more fully address this topic.

Medication expense for those with and without insurance is still an obstacle for many seniors in the United States. To improve financial access to medications, a voluntary enrollment program, Medicare Part D, was instituted in the US in 2006. Through this provision, 90% of US seniors have prescription coverage with Medicare Part D or Medicare Advantage Plans.[2]

***Figure 1:***
***Standard Medicare Prescription Drug Benefit, 2009***

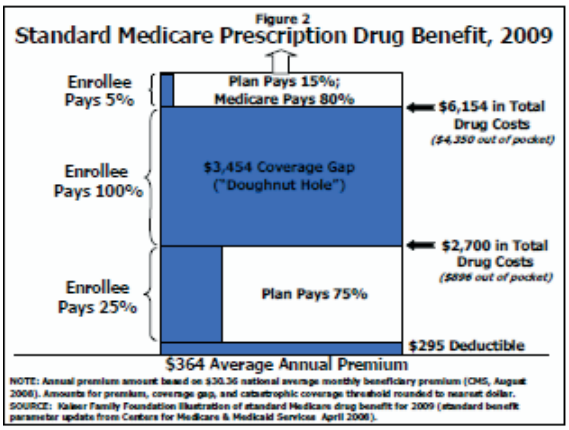
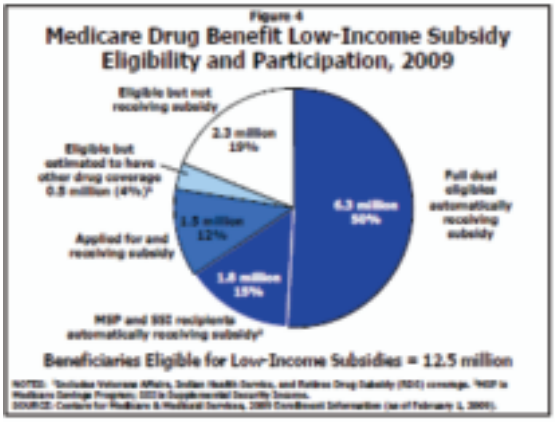



***Figure 2:***
***Medicare Drug Benefit Low-Income Subsidy Eligibility and Participation, 2009***




The standard benefit in 2009 had a $295 deductible and a 25% co-insurance up to an initial coverage benefit of $2,700 in total drug costs, followed by a coverage gap ( the donut hole ) where enrollees pay 100% of their drug costs until they have spent $4,350 out-of-pocket (Table 1).[3]

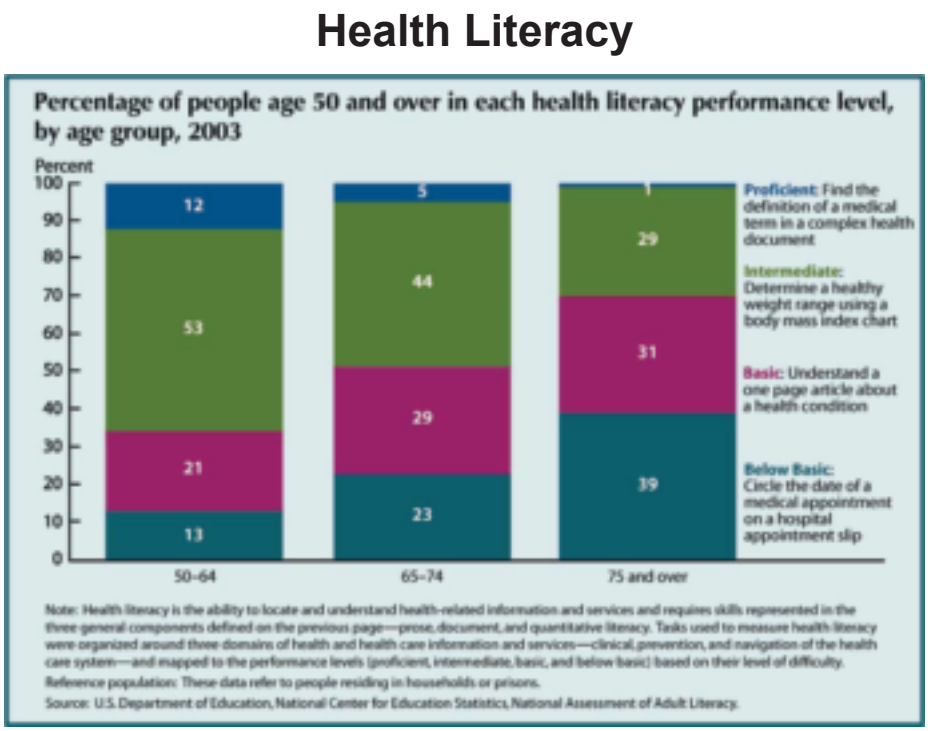
Seniors account for one third of all prescription drug use in the United States. Many Medicare beneficiaries have multiple chronic diseases for which they take multiple medications. Female gender, diagnoses of dementia, renal disease, diabetes, congestive heart failure and COPD are associated with exceeding the expense threshold and entering the donut hole early.[4] Persons with low incomes are dual eligible, eligible for both Medicare Part D and Medicaid, to assist with this gap in coverage (Table 2).[3] For persons, who are not dual eligible and without sufficient secondary insurance for prescription coverage, medication non-adherence may result from deliberate dose reduction (taking one pill instead of two, skipping doses) and not filling the prescription. Nearly 19% of all low income persons eligible for the subsidy do not receive it. Healthcare reform, via the Patient Protection and Affordable Care Act (PPACA) 2010, will eliminate the donut hole by 2020.

Seniors have high rates of chronic conditions, prescription medication use and many have more than one physician prescriber. However, drugs don't work in patients that don't take them as stated by C. Everett Coop MD, 13th Surgeon General. Nonadherence in a patient is defined as the individual has not filled a prescription, is not taking a drug, or is not using a drug as prescribed, whether intentional or unintentional. Older blacks have been found to have higher rates of nonadherence than whites (68% versus 42%; p. <.01).[4] When controlling for age, gender, number of chronic conditions and medications, education and presence of prescription drug coverage, blacks (OR 1.38; 95% CI 1.08-1.78) and Hispanics (OR 1.35; 95% CI 1.02-1.78) remained more likely to report cost-related nonadherence compared to whites.[5]

## Reasons for Nonadherence

Besides the lack of finances, there are several other reasons for nonadherence in this population. The higher rates of low health literacy with advancing age can impact the patient s ability to understand why a medication is used and how to use it. With 39% of those over age 75 having below basic health literacy skills (Figure 3)[6], the potential for unintentional nonadherence is higher.

***Figure 3: Health Literacy***




Regimen complexity can impact compliance with any medication regimen. Patients taking more medications were found to have lower odds of having refill adherence compared to those taking fewer medications (OR=0.77, 95% CI: .073 to 0.95).[7]

A failure to fill prescriptions is another cause of nonadherence. When surveyed, Medicare beneficiaries report low rates (4.4%) of not filling prescriptions. The most common reasons cited for failure to fill were: thought it would cost too much (55.5%), medicine not covered by insurance (20.2%), didn t think medicine was necessary for the condition (18.0%) and was afraid of medicine reactions/contraindication (11.8%).[8] Yet, higher rates for nonadherence are seen with e-prescribing. When controlling for clinician and patient characteristics, patients over age 65 have lower adherence with filling new electronic prescriptions (odds ratio .86 95% CI 0.76 to 0.98). When reported by chronic conditions, there is variation in non-adherence rates for filling e-prescriptions: hypertension (28.4%), hyperlipidemia (28.2%) and diabetes (31.4%).[9]

Elderly patients with memory loss should be routinely assessed for their abilities to follow a medication regimen to prevent significant drug related problems.[10] Memory Assessment tools employed in the outpatient setting usually include the MMSE (Mini Mental Status Exam). This screening test will not, however, allow the physician to assess the ability of a patient to follow a specific medication regimen.

Taking medicine properly requires the ability to understand why medications were ordered, how to routinely and repeatedly administer these medications and awareness of side effects. This requires intact executive function. As dementia severity increases, inadvertent non-adherence does too. The Medication Management Ability Assessment (MMAA) and the Drug Regimen Unassisted Grading Scale (DRUGS) are standardized tools for determining a patient's ability to manage their medications. Seniors with cognitive deficits are more likely to mismanage meds by skipping multiple doses, forget that they have taken their meds and retake them again.

The Steel Valley Seniors Survey was conducted in southwestern Pennsylvania to examine the relationship between verbal memory and executive function. Patients report of medication adherence was compared with actual medication vials. The study concluded that verbal memory functioning was associated with the ability to set up their own medication schedule while better executive function was associated with being fully adherent to prescription instructions.[11] Multiple medications and increased dosing frequency were associated with higher rates of non-compliance in this and other studies. Patients with dementia may have improved adherence rates if regimens were coordinated to coincide with daily routines (brushing teeth, evening meal) the number of drugs prescribed is minimized and if all medication dosing is simplified.[8] There is no evidence based information to definitively address medication adherence in patients with dementia.[12]

Lack of knowledge about medications can lead to nonadherence as well. Patients who are informed about their medication usage and likely side effects are more likely to adhere to a prescribed regimen. Routine review of all medications prescribed for the patient at each visit, will permit the provider and patient/caregiver to identify meds actually taken, problems encountered with specific medications, continued need for meds and duplications. This is especially important when patients are discharged from a hospital or rehabilitation facility. Generic medications are frequently substituted for named brands in hospitals. Elderly patients may take both generic medications prescribed at discharge and the name brand medications used before hospitalization.

## Medication Reconciliation

Medication reconciliation is a useful tool that can improve medication safety. It is a three step process that determines whether the providers known prescribed meds and the patient s list are in agreement. It is important that all medications being used by the patient are compared to the documented list of those prescribed by all treating physicians. The process can be performed by a physician or pharmacist and should be done in all settings of care. It is most important to provide the patient with a current (reconciled) list of medications at the end of each medical encounter.

**MEDICATION RECONCILIATION**

- Three Step Process
  - Compile a list* of current medications from patient history, list, bag (including OTC)
  - Compare list* to prescribed medications from chart, orders, consultant notes, hospital records
  - Resolve any discrepancies
- When to Perform
  - Hospital Admission
  - Hospital Discharge or transfer
  - New patient to your location
  - Patient's return from consultant care

* *Name, strength, dose, frequency, route, indication*

## Summary

Nonadherence may result from clinician s failure to consider a patient s knowledge of medications, financial, cognitive, or functional status. While from the patient s perspective, their beliefs and understanding of drugs and diseases may affect their medication use. Having a clear understanding of the patient s situation allows the prescribing clinicians to consider options to improve patient adherence and to perform medication reconciliation.

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# Resource Tools-Best Practices

***Harry Strothers III, MD, MMM***

While there are several challenges associated with the geriatric population and the medications they take such as nonadherence, drug-drug interactions and issues with potentially inappropriate medications, there are tools to assist in safe prescribing for seniors. Some of these tools are geared towards the caregivers and others are created to assist the patient. As with the use of any tool, the skill of the user and using the appropriate tool for the situation can vastly influence the outcome.

The increase in seniors taking multiple medications has increased the number of preventable adverse drug events (ADEs). Several studies have estimated that 2.4-3.6% of hospital admissions are caused by ADEs and up to 69% of those were preventable.[1] Preventable ADEs can also occur in the hospital. Although several medications from the Beers or Zhan lists are among the medications that can cause ADEs, the majority of ADEs are caused by anticoagulants, antidiabetes agents and medications with narrow therapeutic windows.[2]

In addition to single drug adverse events and drug-drug interactions, over the counter medications, supplements and food (like grapefruit juice) have the potential to create life-threatening interactions. Several studies[3] show 80 to 90% (varies with age range) of seniors use over-the-counter medications or dietary supplements. The caregivers of the patient need to be aware of these nonprescription medications which can have adverse interactions with prescription medications or even change the medication s action. Checking a patient's medication and supplements against what is charted (medication reconciliation) can prevent adverse drug events.

This careful review will minimize polypharmacy. Polypharmacy is the legitimate use of multiple medications for optimal disease management and inappropriate prescribing. This problem is costly and common in the elderly because of the number of chronic diseases managed by the use of multiple physicians, and lack of care coordination. Pharmacists are helpful consultants for patients and physicians. They can provide advice to physicians about simplifying regimens, medication adherence practice for patients, and adverse events. Pharmacists assist patients through direct counseling about medication use and provide written documents that list side effects and likely drug-drug interactions for each medication prescribed. One of the criteria for meaningful use electronic health records includes providing a list of medications to patients at the end of the visit. Thus, whether done in a paper based practice or those with electronic health records, medication reconciliation are imperative to excellent and safe care.

There have been dramatic changes in the technology used to identify and assess potentially harmful drug-drug interactions and other prescribing issues in the last 10 years. What was once a cumbersome chore of looking up medications in multiple pages of a book of drug interactions can now be done simpler. These ways include computerized physician order entry systems, Electronic Health Records, standalone prescribing or interaction programs on computers, handheld PDAs or Smartphones, and through web-based applications. Since the specifics of these types of software change rapidly, this article will give general descriptions and examples in each category.

## Computerized Physician Order Entry Systems (CPOE)

Several studies[4-7] show that a computerized order entry system with decision-support prescribing alerts and alternatives lowers the rate of potentially inappropriate medications or combinations. It is less clear what types of alerts work best and what types are soon ignored by the user. CPOE systems have several advantages over paper-based systems including:

- No handwriting interpretation problems
- Orders are easily linked to drug-drug interaction, food-drug interaction, condition-drug (i.e. renal impairment) interaction, drug-gender or age contraindications, and narrow therapeutic window drug warnings
- Orders reach the pharmacy faster
- Orders are less subject to errors associated with similar drug names
- Orders are more easily integrated into medical records and decision-support systems
- Fewer errors caused by use of apothecary measures or incorrect dosing
- Easier to identify the prescribing physician

With online prompts, CPOE systems can also link to algorithms to emphasize cost-effective medications, to reduce underprescribing and overprescribing, and to reduce incorrect drug choices. However, if poorly designed or implemented, CPOE systems can cause or exacerbate other problems or cause errors.[8,9] One solution is the recently released ISMP Guidelines for Standard Order Sets developed by the Institute for Safe Medication Practices (ISMP). (http://www.ismp.org/Tools/guidelines/StandardOrderSets.pdf).[10] ISMP has identified ten key system elements that influence medication safety: (i) access to patient-specific information; (ii) access to drug information; (iii) adequate communication; (iv) proper labeling, packaging, and nomenclature; (v) drug standardization, storage, and monitoring; (vi) medication delivery device use and monitoring; (vii) sufficient environmental support; (viii) staff competency and education; (ix) patient education; and (x) quality improvement and risk management programs. Using these guidelines can help organizations design CPOE order sets that reflect best practices.

CPOE systems with integrated Clinical Decision Support Systems (CDSS) can add a display of the patient's medical history and current test results, evidence-based clinical guidelines and condition-specific drug interactions or dosing warnings.[11] Since most of these systems are integrated into a system-wide pharmacy, they often restrict or prohibit prescription of drug combinations that the organization deems dangerous. Once a patient s medication list has been reconciled, the system keeps track of all medications and automatically runs interaction checks with any new medication addition, any dosage change, or any vital function change (i.e. renal function).

## Ambulatory Electronic Health Records (EHRs)

An EHR allows caregivers to automate clinical charting and maintain a comprehensive electronic health record for patients, eliminating paper charts. E-prescribing is one of many functions within an EHR.[12] Also known as Electronic Medical Records (EMRs), most Ambulatory EHRs do not have the tight integration with patients labs or conditions that the CPOE/CDSS systems mentioned previously possess. Otherwise, EHRs share many of the benefits of those larger systems. The AAFP s Center for Health Information Technology listed 93 EHRs in late March 2010.

Most EHRs have an integrated prescription writer and medication list. In a smaller number of systems, the software has the ability to provide information on formulary or tiered formulary medications, patient eligibility and authorization requirements from the patient s drug plan, and provide information on lower-cost, therapeutically appropriate alternatives. EHRs also have the ability to generate a complete medication list that incorporates data from pharmacies and Prescription Benefits Managers. This software also enables the user to update or correct the patient medication history, has the ability to transmit prescriptions electronically to the patient s preferred pharmacy using the appropriate standards, and receives refill requests from pharmacies directly on the computer sending approvals or denials back to the clinician electronically.

These systems have various levels of drug interaction checks and alerts which range from blocking the writing of the contraindicated prescription to warnings of various sizes and visual intrusion on the screen.

## Stand Alone E-prescribing or Prescribing/Interaction Programs

E-prescribing provides a way to electronically create and send prescriptions to a pharmacy. Several of the more advanced systems available provide real-time patient eligibility checks, provide real-time patient-specific formularies, patient medication history, drug and allergy interactions, and electronic connectivity to mail and retail pharmacies. These advanced systems support PC and Mac users as well as mobile users of iPhone, Blackberry, and iPaq.

## Medical Software Drug Database Physicians Reference

A stand-alone e-prescribing system allows the clinician to access a patient's prescription benefit coverage and prescription history in addition to bi-directional prescription routing of prescriptions and refills with the patient s preferred pharmacy.[13] Stand-alone e-prescribing systems are usually less costly and easier to implement than EHRs.

Stand alone prescribing and interaction checking programs are available for Android, Blackberry, iPhone, Palm, Windows and Windows Mobile devices; however, not all programs are available on all mobile platforms. Well known programs include those from Epocrates, The Medical Letter, Medscape Mobile, PEPID, and Tarascon. The programs enable caregivers to look-up medications and run drug-drug interactions, which give various levels of warning about potential interaction. Since they are not on a live link to an EHR or national prescribing database, each medication or supplement has to be entered every time the user wants to check an interaction.

## Web-based programs

A search of Google and other web search engines finds multiple web sites that will do drug-to-drug interaction checking. Some websites are oriented toward healthcare professionals while others are oriented toward the general public. A closer look finds that many use the same underlying data bases on several different web-sites. These sites commonly allow the input of several medications and then the site displays the interactions between them. As downsides, it can take significant amount of time to enter all the medications and these tools do not always take into consideration other issues like renal function or complementary or alternative treatments. Some websites, by supplying a username and password, enable users to store a medication list for future interaction tests. Examples of drug information and interaction websites include AARP.com, Drugs.com, Epocrates.com, and Medscape.com.

## Resources for Patients

It is helpful for patients to have both a written list of their medications and to bring the actual bottles of everything they take to every medical encounter. A wallet card of medications can be printed from the internet to facilitate this list. (http://www.gha.org/pha/Provider/patientsafety/medrec/pha_medcard.pdf.). To assist patients and families in medication administration, the use of a Pill Card can make medication administration easier. A simple format of this card has been developed by AHRQ (http://www.ahrq.gov/qual/pillcard/pillcard.htm).

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## CME Post Test

**AAFP:** This activity, Drug Safety Initiative Monograph of the Georgia Academy of Family Physicians, has been reviewed and is acceptable for up to 1 Prescribed credit(s) by the American Academy of Family Physicians. AAFP accreditation begins August 1, 2010. Term of approval is for one year(s) from this date, with option for yearly renewal.

**AMA:** The Georgia Academy of Family Physicians is accredited by the Medical Association of Georgia to offer continuing medical education to physicians. The GAFP designates this educational activity for a maximum of 1.0 AMA PRA Category 1 credit(s)™ toward the AMA Physician's Recognition Award. Physicians should only claim credit commensurate with the extent of their participation in the activity.

***Please record your answers on the key on the evaluation page.***

1) The issues of prescribing both a cholinesterase inhibitor and diphenhydramine in a patient with Alzheimer's disease are an example of a (n)_____ pharmacologic effect(s).

   a) Synergistic
   b) Additive
   c) Antagonistic
   d) Both synergistic and additive

2) Which of the following is not a pharmacokinetic parameter that may play a role in drug interactions in older adults?

   a) Absorption
   b) Distribution
   c) Elimination
   d) Additive

3) David C. is a 65 year old man who presents to your clinic as a new patient. He gives you his list of medications that he is currently taking. For which of the following medications should you not find a substitute?

   a) Alprazolam
   b) Amiodarone
   c) Labetalol
   d) Oral oxybutinin

4) Eleanor R. is a 73 year old woman with a history of heart disease (MIs X 2 and CHF), obesity and overactive bladder. During a routine work up, you notice an elevated fasting glucose and after further laboratory testing, you determine that she has type 2 diabetes. You have to select a medication to begin treating her T2DM. What medication(s) is (are) appropriate to begin treatment in this patient?

   a) metformin
   b) chlorpropamide
   c) rosiglitazone
   d) pioglitazone

5) Mitchell J. is an 80 year old man with high blood pressure and diabetes. He has been taking Dyazide for many years but it appears that the diuretic is not managing his blood pressure adequately any more. His doctor wants to add an additional medication to his medication regimen like an ACE inhibitor or ARB for kidney protection. What should his doctor keep in mind when prescribing a second medication?

a) Physicians should be not concerned about combining potassium-sparing medications in older adults
b) Patients with diabetes are not more prone to hyperkalemia unless they have high blood pressure as well
c) Patients with renal insufficiency only have problems with hyperkalemia when the creatinine goes above 2.0
d) Both Dyazide and ACE inhibitors are potassium-sparing agents

6) Denise M. is a 75 year old woman who suffered a mild stroke and was placed on warfarin one year ago. Her levels have been monitored and have remained in the therapeutic range during that time. Over the past week, she has developed a productive cough with greenish yellow sputum and a post nasal drip. The chest X-ray was nonspecific. You suspect bronchitis and decide to start an antibiotic. Which antibiotic class is likely to be the safest without an adjustment in warfarin dosage?

a) Erythromycins
b) Quinolones
c) Cephalosporins
d) Sulfa antibiotics

7) In a 2003 health literacy study by the US Department of Education, the percentage of people aged 65-74 who have below basic health literacy skills was _____.

a) 39%
b) 29%
c) 23%
d) 13%

8) The steps involved in medication reconciliation are compilation of a list of current medications, comparison of the list to all prescribed medications for all physicians and resolution of any discrepancies. When is the best time to perform medication reconciliation?

a) Admission to the hospital
b) New patient visit
c) Hospital transfer
d) All of the above

9) Advantages that computerized physician order entry systems (CPOE) systems have over paper-based systems include all of the following except

a) Orders reach the pharmacy faster
b) Orders are less subject to errors associated with similar drug names
c) Difficult to identify the prescriber
d) Fewer errors caused by use of apothecary measures or incorrect dosing

10) There are now tools available to assist in prescribing safer in seniors. Which type of system can display the patient's medical history and current test results, evidence-based clinical guidelines and condition-specific drug interactions or dosing warnings?

a) Electronic Health Records (EHRs)
b) Stand alone e-prescribing or prescribing/interaction programs
c) CPOE systems with integrated Clinical Decision Support Systems (CDSS)
d) All of the above



## CME Evaluation

The Georgia Academy of Family Physicians respects and appreciates your opinions. To assist us in evaluating the effectiveness of this activity, please take a few minutes to complete this evaluation form. Please note that a record of participation is issued only upon receipt of your completed evaluation form.

***Please use an evaluation rating of 5 as the highest and 1 as the lowest.***

❑ **Please send a letter of completion for activity** (non-AAFP members)

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# Author Biographies and Disclosures

**Faculty Disclosure Policy** - *It is the policy of the Georgia Academy of Family Physicians that faculty are required to disclose any commercial financial affiliations related to the content of their work to avoid a real or perceived conflict of interest. Each speaker is asked to disclose when any unapproved or off label use of pharmaceuticals or devices will be discussed. Acknowledgment will be made of any outside organization providing financial support for any component of an educational activity.*

**Richard Ackermann, MD**, is Professor of Family Medicine at Mercer University School of Medicine and the Founding Director of the Geriatrics Fellowship Program, and the Founding Medical Director of the Center for Palliative Care at the Medical Center of Central Georgia and Mercer School of Medicine. He has also served as a Certified Medical Director of a skilled nursing facility in Macon. Dr. Ackermann received his undergraduate degree (summa cum laude) from Furman University and his Medical Degree from Duke University School of Medicine. He completed his Family Practice residency at Naval Hospital, Charleston, South Carolina.

Dr. Ackermann is Past-President of the Georgia Geriatrics Society, a past board member of Georgia Medical Directors Association, and currently is the Chair of the Graduate Medical Education Committee at the Medical Center of Central Georgia. He is extensively published and his research interests include urinary tract infection, polypharmacy, pulmonary vascular control, health services utilization, and office procedures.

**Faculty Disclosure:** Dr. Richard Ackermann has no financial affiliation to disclose.

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**Allison Burfield, RN, PhD** is a native of Athens, Georgia, where she completed her undergraduate work at the University of Georgia and earned an Associate Degree in Nursing from Athens Technical Institute in 1995. She completed her BSN (2000) and MSN (2006) in Leadership and Management at the University of Central Florida, College of Nursing, along with a certificate in Nursing and Health Professional Education. She earned her PhD in 2009 from the same University. She was a Merritt Fellow for her Master's work and a Provost Fellow for her doctoral work due to her dedication to scholarship and ongoing research in the elderly. She currently is a Hartford Institute Geriatric Nursing Research Scholar (2010), and member of Sigma Theta Tau International and Phi Kappa Phi.

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**Faculty Disclosure:** Dr. Allison Burfield has no financial affiliation to disclose.

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**James Cooper, Jr., RPh, PhD**, received his BS in Pharmacy (1968) and PhD in Pharmaceutical Sciences and Clinical Pharmacy (1972) from the University of Georgia. Dr. Cooper currently serves as the President, Consultant Press, Director of Education and Research, SHCA, and Emeritus Albert W. Jowdy Professor of Pharmacy Care, College of Pharmacy, and formerly Honors, Graduate and Gerontology Faculties of the University of Georgia; formerly Assistant Clinical Professor, Department of Family Medicine, School of Medicine, The Medical College of Georgia. Dr. Cooper has offered consultative services to many hospitals, nursing homes, primary care centers, and a home health and hospice agency, and has served over 6,000 patients.

He has developed and/or taught in 69 courses in to over 4,000 pharmacy, nursing and medical students and Post Doctoral Fellowship and Residency Programs at URI and UGA. He currently serves on the editorial boards of Annals of Long-Term Care: Clinical Aspects of Aging, and the American Journal of Geriatric Pharmacotherapy and was the founding editor of the Journal of Geriatric Drug Therapy (1984-1999). Dr. Cooper has authored over 600 professional and research publications and made more than 1500 presentations, primarily on geriatric drug therapy. His research interests include: Geriatric Drug Therapy Efficacy, Toxicity, Pharmacoeconomics, Pharmacoepidemiology and Pharmacist Effect on Drug Related Problems and Disease Management in the Older Adult. He has had over 1.5 million in funding research, service and teaching. Dr. Cooper has served as a visiting professor throughout the United States and internationally.

**Faculty Disclosure:** Dr. James Cooper serves on the speaker's bureau for Forest Labs, Boehringer Ingleheim, and Pfizer.

**Adrienne Mims, MD, MPH** is a board certified family physician and geriatrician who practiced in the SW Atlanta area for 17 years. Originally from Washington D.C., Dr. Mims completed her undergraduate training at George Washington University; Medical school at Stanford University; Residency at Martin Luther King Jr./Charles Drew Medical Center; Geriatric Fellowship at the West LA VA and MPH at UCLA.

She was formerly with Kaiser Permanente where she served in various capacities including Chief of Geriatrics, Chief of Prevention and Health Promotion and Research, medical editor of the Partners in Health magazine and clinical lead for other health education resources and initiatives. She has published research on preventive health, smoking cessation, pneumococcal and influenza vaccination and obesity.

She was Medical Director for APS Healthcare s Georgia Medicaid Management Program from 2007-2009. There she provided oversight for statewide disease management services for more than 200,000 aged, blind and disabled Medicaid members.

Dr. Mims is now Medical Director for Medicare Quality Improvement for the Georgia Medical Care Foundation where she provides oversight to protect the Medicare trust fund and improve the quality of health for Georgia Medicare beneficiaries. She was elected to the Board of Directors for the American Geriatric Society, the trade organization for medical professionals specializing in the care of seniors. She is also a member of the Board of Directors of the Georgia Academy of Family Physicians.

She was in Leadership Atlanta class of 1995. She received the Pinnacle Award by Delta Sigma Theta and was recognized by Who s Who in Atlanta 2005 and 2006. She currently volunteers as the Medical Director for the CBWW Safety Net Clinic after having served on the Board of Directors for CBWW for 3 years.

**Faculty Disclosure:** Dr. Adrienne Mims serves as the Medical Director for Medicare Quality Improvement for the Georgia Medical Care Foundation (GMCF). Dr. Mims has no other financial affiliation to disclose.

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**Armon Neel, Jr., PharmD** graduated from the University of Georgia, School of Pharmacy in 1961, and received his Doctor of Pharmacy degree from the Rio Grande College of Pharmacy. He continued his education through internships at Athens General Hospital, Griffin Spalding County Hospital, and a residency in institutional pharmacy at Brook Army Medical Center.

After completing his residency, Dr. Neel returned to Griffin to enter his father s family pharmacy operation. In 1963, Armon opened Neel s Apothecary in Griffin. Three years later, he converted the Apothecary Shop into Georgia s first Pharmaceutical Center, a practice devoted to providing pharmacy services exclusively. He was the first pharmacist in Georgia to maintain patient profiles for his patients. His innovations in pharmacy services in long term care are numerous and continue to set the standard for accepted procedures and protocols today.

Dr. Neel founded Institutional Pharmacy Consultants in 1977, a pharmacy practice providing consultant services in pharmacy, computer services, medical management, system designs, nutritional support, pharmacokinetics and quality assurance. In June of 2000, he embarked on a new endeavor, merging with Restore Health Group, making it possible to expand services throughout the entire Southeast. After serving as Vice President of Clinical Services for Restore, he decided to get more involved in clinical drug therapy management by the development of an internet site where seniors could have available to them the services of a senior drug therapy specialist. The site is known as MedicationXpert.com. Along with a broad range of health care consulting, Dr. Neel continues to do research and publish.

Dr. Neel has received numerous awards throughout the years. Along with chairing numerous committees on national and state levels, he has written many articles published in professional journals and presented various papers on long term care, Alzheimer s disease, treatment of depression, anxiety, and dementia in the elderly, and performed numerous outcomes research studies relating to specific drug therapies.

Currently, Dr. Neel holds membership on several editorial boards and advisory panels. He also serves as a consultant for several companies. He continues to operate a private practice of pharmacy in Drug Therapy Management in Senior Care in an effort to improve quality of life for seniors.

**Faculty Disclosure:** Dr. Armon Neel is the owner of MedicationXperts. Dr. Neel has no other financial affiliations to disclose.

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**Harry Strothers III, MD, MMM** is Chairman and Professor of the Department of Family Medicine at Morehouse School of Medicine (MSM). He also serves as Geriatric team leader for the National Center for Primary Care at MSM and as Medical Director for the Georgia Enhanced Care program for APS Healthcare.

Dr. Strothers received his medical degree from the University of Maryland School of Medicine in 1982 and stayed for residency training in Family Medicine. He is board certified in Family Medicine, has a Certificate of Added Qualifications in Geriatrics, and a Certificate in Medical Management from the American College of Physician Executives and Tulane University. He finished his Masters in Medical Management at Tulane University School of Public Health and Tropical Medicine in May 2000.

Dr. Strothers started practice at a rural National Health Service Corps site in South Carolina. After leaving the rural health center, he was Director of Primary Care Services for Palmetto SeniorCare, a Program of All-Inclusive Care for the Elderly (PACE) from 2/90 through 4/91. After Palmetto SeniorCare, Dr. Strothers worked as Geriatrician and Quality Improvement coordinator for the SC Department of Mental Health. He taught Family Medicine and Geriatrics part-time 9 years for the University of South Carolina before moving to MSM in 1994.

At MSM, Dr. Strothers has served as Residency Director, Acting Medical Director, Interim Chairman and Associate Chairman for Academic Programs for the Department of Family Medicine. He and his team implemented the school s first Electronic Health Record in 2001. In 2000, he was named Family Practice Educator of the Year by the Georgia Academy of Family Physicians.

Dr. Strothers is currently President-elect of the Georgia Academy of Family Physicians. He completed two years as the Secretary-Treasurer of the Society of Teachers of Family Medicine and was appointed to the HHS Advisory Committee on Training in Primary Care Medicine and Dentistry.

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