Interventions to decrease inappropriate prescribing and medication use in older adults: a clinical review

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Interventions to Decrease Inappropriate Prescribing and Medication Use in Older Adults:

A Clinical Review

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Introduction

Researchers, for many years, have focused on the pharmacology of medications and how each reacts in the body. Unfortunately, not until the 1990s has the specific pharmacology of certain medications been studied in older adults (Cavanaugh & Blanchard-Fields, 2006). With this research, we now know that certain age-associated factors affect how medications can be used in older adults. Many aspects specific to each older adult, such as disease states, body habitus, physical function, and cognition, must be considered before prescribing medications to the older adult population, making this population difficult to treat. As a result, older adults are at a higher risk of adverse reactions due to inappropriate prescribing and medication use. It is essential that the importance of this issue be explored.

Prescription drug use in the older adult population has increased over the years. From 1988-1994, 73.6% of older adults (aged 65 and older) consumed at least one prescription drug. This number greatly increased to 84.7% of older adults consuming at least one prescription drug from 1999 and 2002 (National Center for Health Statistics, 2007). In fact, this number is now approaching greater than 90% in some older adult populations (Gallagher, Barry, Ryan, Hartigan, & O'Mahony, 2008). This may not seem alarming since adults tend to develop more illnesses with age, necessitating pharmacologic treatment. But, older adults react to medications much differently than their younger counterparts and the risk an older adult will suffer an adverse reaction from medications is greatly increased. As a result, many die each year from medication-related problems, potentially making this the 5th leading cause of death if it were ranked as a disease (Simonson & Feinberg, 2005). Therefore, it is not surprising to see why prescribing and medication use in older adults has become a large research topic over the last 2 decades.
This clinical review will explore much of this research in order to identify many important topics regarding prescribing and medication use in older adults. The specific vulnerabilities of older adults that make this population more susceptible to adverse drug reactions will be addressed first. These vulnerabilities will include, but are not limited to, comorbid conditions, physiologic, physical, and cognitive differences of older adults. Many researchers studied these vulnerabilities in order to create criteria to be used by prescribers when prescribing medications to older adults. These criteria will be identified in this review. In addition, common drug classes from the criteria will be discussed, including the specific pharmacology of each medication class that contributes adverse drug reactions. The high general incidence of adverse drug reactions will also be a topic of discussion, which will include facts about the preventability of this issue. As a result, this review will end with a review of interventions found to decrease inappropriate prescribing and medication use in older adults.

The purpose of including the above topics in this clinical review is to educate clinicians about the importance of inappropriate prescribing and medication use in older adults. Additionally, it is reassuring to know this problem can be prevented, making this an even more important clinical review topic for health care professionals, particularly those who prescribe medications. Therefore, with the newly established prescriptive authority of physician assistants (PAs), this topic is becoming more relevant to PAs. The PA profession was intended to expand the delivery of quality medical care during the shortage and uneven distribution of primary care physicians (American Academy of Physician Assistants, 2008). Therefore, “as part of their comprehensive responsibilities, PAs conduct physical exams, diagnose and treat illnesses, order and interpret tests, counsel on preventive health care, assist in surgery, and write prescriptions. Within the physician-PA relationship, physician assistants exercise autonomy in medical
decision making and provide a broad range of diagnostic and therapeutic services” (American Academy of Physician Assistants, 2008). Regardless of the specialty, older adults will be frequent visitors to all medical practices. Inevitably, PAs are going to see older adults in their practice. Consistent with their role, PAs are given more time to analyze medication regimens and educate their patients. As a result, it is important that PAs are knowledgeable about prescribing to older adults since they may be the sole provider analyzing and prescribing medications to these patients. Additionally, all other healthcare professionals who prescribe medications and are involved in the administration of medications should boast the same knowledge. The following clinical review will provide these medical professionals with a solid foundation to provide excellent pharmacologic care and education to older adults.
Methodology

A MEDLINE and PubMed database search was conducted for the following terms: medication errors, Beers criteria, inappropriate medication use, patient compliance, adverse drug reactions, and medications and elderly. All search options were limited to subjects 65 years and older. Articles congruent with the subject matter of the clinical review article were selected. Intervention articles were limited to include only prevention and control articles recent as of 2000. Lastly, the majority of relevant articles were hand-searched from the bibliographies of selected articles from the search mentioned above. These articles were searched for in MEDLINE and PubMed using the first author’s last name.
Older Adults

The longevity of Americans is increasing. Older adults, age 65 and older, now make up approximately 12% of the US population (Administration on Aging, 2006) and, by 2030, it is projected older adults will make up 20% of the U.S. population (Administration on Aging, 2007). Despite older adults living longer and making up a larger portion of the U.S. population, older adults are very sensitive. Illnesses accumulate with age, increasing in both severity and number. This results in various comorbid conditions, defined as a disease that worsens or impacts a primary disease (Comorbid disease, 2001). Hajjar et al. (2003) found multiple chronic illnesses present in 26.5% of older adults discharged from the hospital. In addition, the average older patient has 6 medical conditions (Doucette, McDonough, Klepser, & McCarthy, 2005). As a result, older adults are likely to take many prescription and over-the-counter (OTC) medications to treat comorbid conditions.

Older adults, on average, consume over 2.5 times more prescription medications than the rest of the population combined (Stagnitti, 2007). Almost every older adult is on at least one medication. Ninety-one percent and 94% of ambulatory older males and females, respectively, reported using one or more medications, including prescription, OTC, vitamins, herbals and supplements. Seventy-one percent and 81% of ambulatory older males and females, respectively, reported using at least one prescription medication (Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002). Similarly, 95% of older adults acutely admitted to the hospital were on at least one prescription medication (Gallagher et al., 2008). In general, older adults consume between 0 and 13 medications with the average older adult consuming about 5 prescription medications (Barry, O'Keefe, O'Connor, & O'Mahony, 2006; Gallagher et al., 2008). From the outside, it may
appear beneficial for patients to take many medications when suffering from multiple comorbid conditions. However, it can actually cause harm, especially in older adults.

Older adults are physiologically very different from their younger counterparts. Therefore, medications react much differently in their bodies compared to younger adults. Researchers have conducted studies for many years to identify multiple physiologic differences in older adults that alter the way medications work. One must understand the specific mechanism of a medication and the physiology of the older adult to understand the pharmacokinetics and pharmacodynamics of each medication. Pharmacokinetics refers to the changes associated with altered drug concentrations at sites of action in the body (Turnheim, 1998) or simply what the body does to the drug. Pharmacodymics refers to the physiologic effects of the drug on the body (Ali Raza & Movahed, 2002). The particular pharmacokinetic and pharmacodynamic changes seen in older adults will now be discussed.

**Pharmacokinetics**

Several pharmacokinetic factors have been studied in depth, including the absorption, distribution, metabolism and excretion of drugs in older adults. The absorption of medications refers to “the passage of a substance though some surface of the body into body fluids and tissues,” (Comorbid disease, 2001) most commonly involving the passage of medications into the bloodstream. The fate of orally administered medications when given to an older adult is well known compared to other routes of administration. There is an increase in the pH and motility of the older adult’s stomach, which increases the speed at which medications are passed into the intestines (Hämmerlein, Derendorf, & Lowenthal, 1998). However, intestinal motility and blood flow is diminished, indicating decreased absorption (Ali Raza & Movahed, 2002; Hämmerlein et al., 1998). Despite these few minimal changes of the gastrointestinal (GI) tract, overall the
epithelium of the GI tract does not change significantly with aging (Hämmerlein et al., 1998; Turnheim, 1998, 2003, 2004). As a result, the intestinal absorption of medications remains relatively unchanged (Hämmerlein et al., 1998; Kapoor, 1994; Turnheim, 2003, 2004) or may be slightly delayed (Ali Raza & Movahed, 2002) into older adulthood. Overall, the absorption of orally-administered medication is minimally altered in older adults.

Other routes of administration have been studied less. There have been few glimpses of significance in studies involving transdermal (through the skin) and intramuscular (IM; into the muscle) injections. Transdermal absorption may be reduced due to decreased perfusion of the tissue and atrophy of the epidermis and dermis (Trautinger, 2001; Turnheim, 2003, 2004). A few studies indicate IM injections have a reduced rate of absorption in older adults (Hämmerlein et al., 1998). Others have shown erratic absorption from IM sites (Turnheim, 2004). Therefore, the general rule is to avoid IM injections in older adults since it is relatively unknown how the medication will be absorbed (Turnheim, 2004).

Medication distribution refers to the volume of apparent space in the body available to contain a drug (Katzung, 2007). Medication distribution throughout the body greatly depends on the physical composition of the older adults. Older adults tend to have a high proportion of body fat, less lean body mass and less total body water. As a result, certain medications will be distributed throughout the body differently depending on the medication’s chemical make-up. Body water falls by 10-15% until the age of 80 (Turnheim, 1998, 2004). This decreased body water may not only be a “normal” pharmacokinetic change with aging, but may also be due to decreased fluid intake resulting from a reduced sensation of thirst in older adults (Turnheim, 1998). Water-soluble drugs (such as atenolol, an anti-hypertensive β-blocker, and alcohol) tend to have a small volume of distribution, meaning these drugs will reach fewer tissues, leading to a
higher peak plasma concentration (Mangoni, 2005; Turnheim, 1998; Vestal, 1997). A large plasma concentration increases the chance for toxic effects from water-soluble drugs.

Body fat increases 18-36% in older men and 33-45% in older women (Vestal, 1997). Lipid (or fat)-soluble drugs (such as halothane, benzodiazepines, amiodarone, and verapamil) tend to have a large volume of distribution in older adults due to the increase in body fat. The half lives of lipid-soluble drugs, especially sedatives, increase by 50-150% (Katzung, 2007) and will stay in the body longer. Since these drugs take longer to reach a steady plasma concentration (Turnheim, 1998), they should be given in lower doses and titrated up accordingly. This allows more time to reach a therapeutic level in order to avoid reaching toxic levels in older adults.

The ease of distribution highly depends on a patient’s cardiovascular status, tissue perfusion and plasma protein concentration. Older patients tend to have a declined cardiovascular status and poor tissue perfusion (Hämmerlein et al., 1998). As mentioned already, dermal perfusion affects the absorption of transdermal medications. In addition, certain organs that facilitate the elimination of drugs, such as the liver and kidney, have decreased perfusion into older adulthood, causing these organs to work less well in eliminating certain drugs from the body. Poor cardiovascular status may result in the decreased distribution of drugs to areas of the body with poor perfusion. For example, blood supply to the brain may be altered due to atherosclerosis, narrowing of the arteries. This may ultimately cause neuronal loss and altered sensitivity to certain central nervous system (CNS) drugs, such as benzodiazepines, tricyclic antidepressants and opiates (Hämmerlein et al., 1998).

Serum proteins are also needed to distribute drugs throughout the body. Many drugs (e.g., salicylate) bind to proteins, allowing them to be distributed through the body in an inactive form. However, the amount of protein, particularly albumin, in an older adult may be unchanged or
decreased by 15-20% (Hämmerlein et al., 1998; Vestal, 1997). As a result, the amount of
protein-bound drug will be less. Ultimately, the free-drug concentration, or active form of the
drug, may increase. This also causes the potential for drug toxicities in older adults.

Drug metabolism is the elimination of drugs through the liver. Many drugs, such as
theophylline, benzodiazepines, morphine, and indomethacin, are metabolized by the liver.
Depending on the drug, it can be metabolized to an active or inactive form. Therefore, the effect
of aging on the metabolism of drugs is very drug specific. Older adults tend to have a small,
poorly-perfused liver (Benedetti, Whomsley, & Canning, 2007; Vestal, 1997). Autopsy studies
have shown a 20-50% decline in liver weight in older adults, with ultrasound studies showing a
25% decline in liver volume (Vestal, 1997). Blood perfusion to the liver is decreased by 10-15%
in older adults (Vestal, 1997). A combination of these factors cause older adults to have
decreased liver metabolism regardless of having a medical condition affecting the liver, making
aging effects on metabolism particularly more significant in older adults with liver failure.
Physiologic changes in the liver alone have caused drugs eliminated by liver conjugation, such as
theophylline, to have a 20-25% decreased clearance rate (Vestal, 1997). As a result, these drugs
stay in the body longer, causing the potential for toxic effects. On the contrary, drugs activated
by the liver will take longer to reach therapeutic levels.

Drug excretion refers to the elimination of a drug through the kidneys. Kidney function
has been studied in depth and is known to decrease with age. In fact, there is an age-related
equation created by Cockercroft and Gault (1976) that calculates the estimated glomerular
filtration rate (GFR) or creatinine clearance according to age and is still widely used today. This
equation is illustrated in Appendix A. As a result, drug excretion is considered by some to be the
most important pharmacokinetic change in older adults (Turnheim, 1998, 2003, 2004) since most
all older adults undergo this change. Studies have shown renal mass to be decreased 25-30\% into older adulthood (Turnheim, 1998). Renal blood flow and creatinine clearance decreased 1-2\% per year after age 40-50 (Ali Raza & Movahed, 2002; Turnheim, 1998; Vestal, 1997). However, blood flow to the kidneys is reduced by up to 50\% in older adults (Hämmerlein et al., 1998). The glomerular filtration rate (GFR) in older adults decreased approximately 25-50\% by the age of 90 in healthy individuals (Turnheim, 2003; Vestal, 1997). These changes result in an overall decrease in kidney function to only 50-60\% of that of a healthy 20 year old (Turnheim, 1998). As a result, many drugs eliminated through the kidneys, such as ACE inhibitors, furosemide, metformin and gentamicin, are cleared from the body at a much slower rate. Older adults should be give such medications at a lower dose, as these drugs will stay in the blood stream longer, causing the potential for toxic effects from drug build-up.

**Pharmacodynamics**

Less is known about the pharmacodynamic changes in older adults. Pharmacodynamic changes are drug specific and occur at the level of the receptors and homeostatic mechanisms, with older adults having a reduced response to both (Hämmerlein et al., 1998; McLean & Le Couteur, 2004; Turnheim, 2003, 2004). Receptors are thought to become more “sensitive” to medications due to the down-regulation of the number of certain drug receptors. Older adults, therefore, respond less well to medications targeting these receptors. Additionally, older adults may experience physical changes as a result of the down-regulation of receptors. For example, the beta-adrenergic (\(\beta\)) receptors are down-regulated in older adults (Burton, Allen, Bird, & Faragher, 2005; Turnheim, 1998, 2004). This results in decreased sensitivity to medications acting at \(\beta\) receptors. In addition, older adults may experience late-onset asthma or reduced bladder compliance due to decreased \(\beta\) function (Burton et al., 2005).
Other receptors are down-regulated due to effects of aging, which cause other physiologic effects seen in older adults. The adenosine A1 and muscarinic receptors can contribute to cardiovascular changes in older adults. The decreased function of adenosine A1-receptors can lead to the loss of cardioprotective effects in older adults (Turnheim, 2003). The decreased muscarinic activity can lead to a decreased tachycardic response in older adults (Turnheim, 1998). The down-regulated activity of muscarinic receptors can also cause effects on the central nervous system (CNS). Decreased muscarinic receptor activity can lead to impaired memory in older adults (Hämmerlein et al., 1998), with other CNS effects seen with decreased dopamine receptors. The down-regulation of dopamine receptors to a certain threshold contributes to extrapyramidal symptoms commonly seen in the older adult population (Turnheim, 2003). Extrapyramidal side effects of medications are drug-induced parkinsonism symptoms characterized by muscular rigidity, bradykinesia, tremor and difficulty walking (Extrapyramidal side effects of medications, 2001). Additionally, medications targeting these receptors are less effective, making receptor changes an important pharmacodynamic change affecting how medications can be used in older adults.

Older adults also have a reduction in ability to maintain homeostasis. An older adult’s homeostatic mechanism is slower to respond to the physiologic changes brought about by certain medications or stressors. In other words, more time is required for an older adult to regain equilibrium. For example, older adults are slower than younger adults to return to their normal baseline blood glucose level after a sugar load despite having similar fasting blood glucose levels as younger adults (Turnheim, 1998). This is just one general example of the decreased homeostatic mechanism in older adults. However, these changes occur with nearly all autoregulatory systems in the older adult, including responses that occur with medication use.
The specific pharmacodynamic changes responsible for altered responses to common medications used by older adults cannot be generalized across the older adult population. These changes are very drug specific. Each drug affects specific receptors and affects the body’s homeostatic mechanisms in a unique way. In particular, blood pressure lowering drugs are greatly affected by ability of the older adult’s body to maintain homeostasis (Ali Raza & Movahed, 2002; Turnheim, 1998). This example and the pharmacodynamics of other common drugs used by older adults will be discussed in a later section.

The pharmacokinetic and pharmacodynamic changes mentioned above occur at a microscopic level and affect how medications are indicated for use in older adults. In addition to these hard-to-see changes, other gross physical changes affect how medications can be used in older adults. The functional ability of an older adult, including one’s cognitive and physical ability, greatly affects how an older adult takes his or her medication in the first place. Therefore, these changes can indirectly affect the microscopic changes that take place. The cognitive and physical changes in older adults affecting medication use will be discussed in the following section.

Cognitive and Physical Changes

Older adults have several cognitive and physical limitations making them susceptible to non-compliance in regards to medication use. The cognitive abilities of older adults must be considered when prescribing multiple medications and instructing older adults about medication use. Older adults tend to have a decreased short-term memory compared to younger adults (Cavanaugh & Blanchard-Fields, 2006). An impaired short-term memory can result in an older adult forgetting that he or she already took his or her medication and consequently take it again or maybe not taking it at all. This can lead to sub-therapeutic or toxic drug levels in the body. In
addition, older adults process information slower and, therefore, have a decreased working memory capacity (Cavanaugh & Blanchard-Fields, 2006).

These cognitive factors affect an older adults’ ability to understand instructions regarding medication administration. Considering many older adults take several medications each day at different times, remembering when to take which medication can be a very difficult task (Bangalore, Kamalakkannan, Parkar, & Messerli, 2007). Older adults do not seem to have trouble accessing multiple pieces of information, they just have difficulty juggling all the pieces once they are accessed (Oberauer, Wendland, & Kliegl, 2003). This may result in older adults, who take multiple medications, having a difficult time in remembering which medication they are supposed to take three times a day, which one at night, which one with food, etc.

Taking medications incorrectly also has the potential to cause detrimental effects in an older adult. Since older adults are very sensitive to medications due to their physiologic differences, taking a medication dose too close together may cause too high of a drug concentration or taking a medication dose too far apart may result in sub-therapeutic levels. This may cause the patient’s condition to not improve or worsen. However, it has been shown that the use of external memory aids is useful for improving older adults’ cognitive performance. Such aids to improve medication usage in the elderly will be discussed in the interventions section.

Older adults may also exhibit physical changes that affect an individual’s ability to take a medication properly. Regardless of whether an older adult remembers to take his or her medications, a problem exists if he or she cannot physically perform the tasks necessary to administer a medication. First of all, older adults obtain much of the information regarding their medications straight from the pill bottle (Wolf et al., 2007). However, increasing age increases the probability of macular degeneration, therefore decreasing visual acuity (Cavanaugh &
Blanchard-Fields, 2006). As a result, older adults may have a harder time reading pill bottles. This may cause them to misinterpret the medication label leading to inappropriate medication usage. Additionally, these visual changes may cause older adults to misidentify their medications. Older adults often rely on the appearance (size, shape and color) of a pill to identify what it is used for and when to administer it (Ballentine, 2008). However, with decreased visual acuity and increased risk of macular degeneration, older adults may become less able to decipher the color and fine print on pills used to identify each medication. This may cause older adults to confuse medications with one another or be unable to see the dosage written on a medication. This may, in turn, lead to the administration of the wrong medication, wrong dose or doubling of the same medication, causing the potential for adverse events.

Aging is also associated with decreased manual dexterity. One study by Olafsdottir and colleagues (2007) found that older adults have a decreased feed-forward adjustment of multi-finger synergies, a neural organization of elemental variables that stabilizes a performance variable over repetitive trials. Another study focused on older adults’ decline in the ability to manipulate objects (Danion, Descoins, & Bootsma, 2007). Although, older adults have an increased grip strength compared with younger adults, they are unable to modulate their grip force in a feed-forward direction (i.e., through a predictive control mechanism) (Danion et al., 2007). The combination of these factors may prevent an older adult to be able to produce the force necessary to open a pill bottle. This will decrease the chance an older adult will take his or her medication.

Overall, older adults are a very vulnerable population. They commonly experience changes that affect the way drugs can be used or the way drugs work in the body. Particularly, it is important to keep the pharmacokinetic changes that take place with aging in mind when
prescribing medications. The proper method of drug administration must be chosen, in that orally-administered drugs seem to be the best option for older adults. In addition, underlying illnesses, including, liver and renal failure must be taken in account when choosing drug options for older adults. Since most changes that occur in the older adult cause abnormally high drug concentrations, the solution for this tends to be “go low and go slow.” By starting at a low dose in older adults, a practitioner can be sure the patient is tolerating the medication correctly before slowly increasing the dose in order to avoid the potential for toxic drug levels. However, the mild cognitive and physical changes older adults exhibit with age is yet another barrier one must consider when prescribing to older adults. These changes affect how medications are used by older adults. Therefore, with all the factors that must be considered when prescribing medications to older adults, it is clear this can be a difficult task leaving room for much error. As a result, the next section will focus on the prevalence and importance of inappropriate prescribing in older adults.
Inappropriate Prescribing

Inappropriate medications can consist of any medication including prescription, over-the-counter (OTC), vitamins, herbals and supplements that have the potential to cause a significant risk of adverse drug reactions when more effective, lower-risk alternatives are available (Beers, 1997; Beers et al., 1991; Gallagher et al., 2008). These include medications that generally have altered pharmacokinetics and pharmacodynamics in the older adult and have the potential for drug-drug interactions or drug-disease interactions. In addition, administering a medication when safer options are available, prescribing a drug for a longer period of time or at a larger dose than therapeutically necessary or failing to prescribe a medication when it is indicated for a particular disease can also be considered inappropriate prescribing of medications. Several researchers have already taken these issues into account to create drug utilization criteria on proper prescribing in older adults. In particular, the Beers criteria and the Improved Prescribing in the Elderly Tool (IPET) are two widely used drug utilization review criteria (Beers, 1997; Beers et al., 1991; Fick et al., 2003; McLeod, Huang, Tamblyn, & Gayton, 1997; Naugler, Brymer, Stolee, & Arcese, 2000).

The Beers criteria was originally created in 1991 as a formulary for nursing home patients (Beers et al., 1991) and has been updated twice to include all older adults (Beers, 1997; Fick et al., 2003). This set of criteria was most recently updated in 2003. This most recent update used expert opinion to identify 48 medications that should generally be avoided in older adults and certain medications that should be avoided in patients with 20 specific medical conditions such as heart failure, hypertension, depression, etc. (Fick et al., 2003). The criteria for potentially inappropriate medication use in older adults, independent of diagnosis, are listed in Appendix B. The IPET model is based on McLeod’s criteria (McLeod et al., 1997). This set of drug utilization
criteria identifies 37 agents explicitly contraindicated or likely to cause drug-drug interactions or
drug-disease interactions in older adults (Naugler et al., 2000).

Barry and colleagues (2006) compared the Beers and IPET drug utilization criteria. Using
the Beers criteria, they found 34.6% of older adults were taking at least one inappropriate
medication. While using the IPET model and the same sample of patients, they only identified
22% of older adults taking at least one inappropriate medication. A matched odds ratio was used
to compare each method. They concluded the updated Beers criteria is more effective in
identifying inappropriate prescriptions than the IPET (Barry et al., 2006). Unfortunately, the
IPET model is heavily weighted toward certain drug classes (e.g., cardiovascular, NSAIDs,
psychotropics) and under-represents many other, smaller drug classes.

Due to the superiority of the Beers criteria, many studies have utilized this set of criteria
to assess the prevalence of inappropriate medication use in older adults. Many different older
adult populations have been studied for inappropriate prescription use. Inappropriate
prescriptions can range from 12-24% in community-dwelling ambulatory patients (Curtis et al.,
2004; Fu, Liu, & Christensen, 2004; Hanlon et al., 2002; Maio et al., 2006; Viswanathan,
Bharmal, & Thomas, 2005), 32% in acutely ill patients (Gallagher et al., 2008) to near 40% of
nursing home populations (Laroche, Charmes, Nouaille, Fourrier, & Merle, 2006). Surprisingly,
15-17% of older adults take 2 or more inappropriate medications and 2-4% take 3 or more
inappropriate medications (Curtis et al., 2004; Gallagher et al., 2008; Maio et al., 2006). Of all
the inappropriate medications used, nearly 70% are considered high risk according to the Beers
criteria (Maio et al., 2006; Viswanathan et al., 2005).

Inevitably, the more medications a patient takes, the more likely he or she is to have an
inappropriate medication on board. Polypharmacy, defined as the concomitant use of several
drugs to treat multiple chronic illnesses, is a growing problem among the older adult population. Most times, researchers consider the concomitant use of five or more medications to be polypharmacy (Steinman et al., 2006). Considering the average older adult takes approximately 5 medications (Barry et al., 2006; Gallagher et al., 2008), it is clear polypharmacy is prevalent among nearly half of all older adults (Kaufman et al., 2002). In fact, 9-12% of the population has a high rate of polypharmacy, considered to be the use of 10 or more medications (Gallagher et al., 2008; Kaufman et al., 2002). There are risks involved with polypharmacy being quite prevalent in the older adult population.

Polypharmacy patients are at an increased risk of taking an inappropriate medication that could potentially cause adverse effects (Gallagher et al., 2008; Steinman et al., 2006). Steinman and colleagues (2006) considered medication misuse according to the Beers criteria in polypharmacy patients (i.e., subjects taking more than five medications). Thirty-seven percent of the polypharmacy patients were taking at least one inappropriate medication. After making all considerations, including underuse and overuse using different criteria, only 13% of polypharmacy patients were taking the correct medications (Steinman et al., 2006). There is, in fact, a positive correlation between the number of medications prescribed to an older adult and the likelihood that at least one medication is inappropriate. Patients prescribed greater than 5 medications are 3.3 times more likely to receive a potentially inappropriate medication (Gallagher et al., 2008). The prevalence of inappropriate medications increases as polypharmacy increases. Patients taking 5-6 medications only average 0.4 inappropriate medications, whereas patients taking greater than 10 medications consume an average of 2 inappropriate medications (Steinman et al., 2006).
These inappropriate medications, however, most often fall under common medication classes used by older adults. These classes of medications, include, but are not limited to, psychotropic, cardiovascular and analgesic medications. Not only are these medications crucial in treating an older adult, they also pose a large problem when prescribing to older adults. Therefore, the following section will focus on the prevalence of inappropriately prescribing common medication classes to older adults and the effects of these medications.
Specific Drug Classes and Effects

Over 90% of older adults take at least one medication (Gallagher, Barry, & O'Mahony, 2007; Kaufman et al., 2002). The most commonly prescribed medications in older adults are cardiovascular drugs, analgesics, psychotropics (i.e. drugs acting in the central nervous system, including sedatives, hypnotics and anxiolytics), respiratory drugs and GI drugs (Barry et al., 2006; Gallagher et al., 2007; Higashi et al., 2004; Viswanathan et al., 2005). Of these, the most inappropriately prescribed drug classes listed in the Beers criteria (Fick et al., 2003) are psychotropics, cardiovascular agents and analgesics (Fu et al., 2004; Hanlon et al., 2002; Laroche, Charmes, Nouaille, Picard, & Merle, 2007; Viswanathan et al., 2005). These drug classes are frequently mentioned throughout the literature and are commonly associated with adverse drug reactions (ADRs) (Field, Mazor, Briesacher, Debellis, & Gurwitz, 2007; Laroche et al., 2007). Therefore, the focus of this section is to identify the common drugs in these specific classes, including the particular pharmacodynamics contributing to altered drug actions and ADRs.

Psychotropics

The psychotropic drug class includes a wide range of drugs, including sedatives, hypnotics, anxiolytics and antidepressants. Psychotropics are the second most commonly prescribed drug class in older adults, with 35-52% of older adults taking at least one psychotropic medication (Barry et al., 2006; Gallagher et al., 2008). However, Gallagher et al. (2008) noted approximately 50% of these patients were on multiple psychotropics at one time. The Beers list of medications to avoid in older adults includes many psychotropic medications. These include benzodiazepines, amitriptyline (Elavil ®; an antidepressant), doxepine (an antidepressant), meprobamate (an anxiolytic) and fluoxetine (Prozac ®; an antidepressant)(Fick
et al., 2003). In fact, of all inappropriate medications dispensed, 41% are prescriptions for psychotropic medications (Curtis et al., 2004).

Benzodiazepines are the most commonly prescribed medication class among the psychotropics, belonging to the sedative subclass. Approximately 20-35% of community-dwelling older adults are on a benzodiazepine (Barry et al., 2006; Pierfitte et al., 2001; Tu, Mamdani, Hux, & Tu, 2001). However, these medications are considered high risk according to the Beers criteria list of medications that should generally be avoided in persons age 65 or older (Fick et al., 2003). As a result, benzodiazepines have been found by many researchers to be a common inappropriately prescribed medication (Barry et al., 2006; Hanlon et al., 2002). Depending whether researchers considered long-acting (half life >24 hours), short-acting (half life ≤ 24 hours) or both types of benzodiazepines, these drugs accounted for 23-67% of inappropriate medications (Barry et al., 2006; Laroche et al., 2007). In addition, many other psychotropic medications are listed on the Beers criteria. Of these, amitriptyline and doxepine (antidepressants) account for 23% of inappropriate medications (Curtis et al., 2004). However, due to the higher prevalence of inappropriate benzodiazepine use, the benzodiazepine drug class will be used to exemplify the effects of psychotropics in older adults.

The central nervous system is a sensitive target in older adults. Atherosclerosis, a common condition in older adults characterized by narrowing of the arteries, may cause diminished blood flow to the brain contributing to neuronal loss and increased sensitivity to psychotropic drugs (Hämmerlein et al., 1998). As mentioned above, many psychotropic drugs are sensitive to pharmacokinetic changes. In particular, most benzodiazepines are metabolized by the liver and succumb to aging effects on the liver, causing them to have a low hepatic clearance (Hämmerlein et al., 1998). In addition, most benzodiazepines are lipid-soluble which causes
them to have an increased volume of distribution (Hämmerlein et al., 1998) due to the general
increase in body fat seen in older adults. Both low clearance and increased volume of distribution
cause benzodiazepines to have an increased half life and stay in the body longer. Consequently,
the pharmacodynamics of these drugs is altered. The concentration of drug needed to reach
therapeutic effects is 2-3 times lower in older adults than younger adults (Hämmerlein et al.,
1998) and half of the effective concentration (EC50) in an older adult is reduced by 50% (Bowie
& Slattum, 2007; McLean & Le Couteur, 2004). These results indicate the need for a lower
therapeutic dose in older adults than is therapeutically necessary in younger adults. If a lower
dose is not used, older adults are more prone to adverse reactions from these drugs.

Benzodiazepines are frequently associated with psychomotor depression, increased
drowsiness, motor vehicle accidents (MVAs) and cognitive and mobility impairment (Gray et al.,
found 47% of older adults with no prior disability using benzodiazepines had impaired mobility,
meaning they were unable to walk a half mile or climb stairs unassisted despite being able to do
so before starting the medication. This increase correlates to a 23% greater risk of impaired
mobility with benzodiazepine use (Gray et al., 2006). Psychomotor depression can increase the
frequency of ataxia and immobility which can contribute to falls in older adults. Therefore, falls
resulting in hip fractures are commonly associated with benzodiazepine use (Cumming, 1998;
The use of benzodiazepines was associated with a 50-60% increased risk of falling (Leipzig,
Cumming, & Tinetti, 1999), correlating to a doubled risk of hip fracture with benzodiazepine use
(Turnheim, 1998; Wang et al., 2001). However, when considering all older adults with hip
fractures, only 4.8% of hip fractures were found to be attributable to benzodiazepine use (Wang et al., 2001).

Some studies show long-acting benzodiazepines (half life > 24 hours) put patients at more risk of hip fractures and other ADRs than short-acting benzodiazepines (half life ≤ 24 hours) (Cumming & Le Couteur, 2003). Others have failed to show a significant difference in the incidence of adverse reactions between short- and long-acting benzodiazepines (Gray et al., 2006; Leipzig et al., 1999; Wang et al., 2001), with both types showing an increase in adverse reactions. Furthermore, few studies have failed to find a correlation between any benzodiazepine use, except in the case of lorazepam, and the risk of falls and hip fracture (Pierfitte et al., 2001).

Benzodiazepine duration and dose has also been studied to see if there is a correlation with adverse events. Studies have shown ADRs, particularly falls and hip fractures, to be correlated with duration of benzodiazepine use. Wang and colleagues (2001) found the risk of hip fracture was 60% higher in the first 14 days of therapy and 80% higher after 28 days of therapy. However, there was a decrease in risk between 14 and 28 days of therapy (Wang et al., 2001). In addition, Hebert and colleagues (2007) found an increased correlation of MVAs with infrequent use of long-acting benzodiazepines. This parallels the increased risk of ADRs in the first 14 days of therapy that Wang and colleagues (2001) found.

When considering the dosage of benzodiazepines and other psychotropic medications, Campbell and colleagues (1999) showed that reducing the dose of psychotropic medications reduced the risk of falling by 66%, indicating higher doses of benzodiazepines are associated with an increased incidence of ADRs. The risk of hip fracture was increased by 50% with high doses (≥3 mg/day) of benzodiazepines (Wang et al., 2001). However, Gray et al. (2006) showed an increase risk of impaired mobility from benzodiazepine use irrespective of dose. These results
indicate ADRs are very detrimental events correlated with all types of benzodiazepine use at various doses and durations. Hip fractures, in particular, lead to independence and even secondary mortality of 21% within a year (Katelaris & Cumming, 1996). Overall, benzodiazepine use is risky in older adults, particularly at the dosage and duration mentioned above. It is also important to reiterate these risks are evident even at low dose benzodiazepine use. However, in the end, it is reassuring to know the prevalence of benzodiazepine use is slowly decreasing among older adults (Tu et al., 2001).

Cardiovascular Agents

When considering cardiovascular disease is the leading cause of death in older adults (Centers for Disease Control and Prevention, 2008), it is expected that many older adults are prescribed various cardiovascular drugs. In fact, cardiovascular agents are the most commonly prescribed medications in older adults with 64-78% of older adults taking at least one cardiovascular drug (Barry et al., 2006; Gallagher et al., 2008). However, cardiovascular agents should be used with caution in older adults because the cardiovascular system has a decreased response to these drugs with age (Hämmerlein et al., 1998; Turnheim, 1998). As a result, many cardiovascular agents are considered inappropriate in older adults (Fick et al., 2003).

The Beers criteria contains several cardiovascular drugs. These include antihypertensives (e.g., guanethidine, guanadrel, cyclandelate, isoxxsurpine, doxazosin, and clonidine) and antiarrhythmics (e.g., disopyramide, amiodarone and digoxin). According to this criteria, these drug classes contain medications with high severity risks associated with them (Fick et al., 2003). In particular, disopyramide may induce heart failure in elderly patients and guanethidine, guanadrel and clonidine have the potential for orthostatic hypotension. The antihypertensive and
antiarrhythmic drug classes have been mentioned most in the literature and will be discussed in this section.

**Antihypertensives**

Most of the literature concerned with adverse effects of antihypertensive medications in older adults focuses on the broad class of antihypertensive medications, including, but not limited to, those agents listed in the Beers criteria. This broad category includes β-blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, diuretics, and other antihypertensives.

Pharmacodynamic changes in older adults are especially important with antihypertensive drug use. As mentioned above, nearly all homeostatic mechanisms are altered and become insufficient in older adults. In particular, older adults require more time to regain equilibrium in part due to a decreased baroreceptor response. Baroreceptors, located in the aortic arch and carotid sinuses, sense a change in arterial pressure and send messages to the central nervous system to alter the blood pressure, either through a change in cardiac output or peripheral vascular resistance. Upon standing, moderate volumes of blood pool in the lower extremities of older adults, which decreases venous return leading to hypotension (Kapoor, 1994). The insufficient baroreceptor reflex in older adults causes a slowed response to raise blood pressure. Increased vascular resistance is slowed, which contributes to the increased susceptibility of older adults to orthostatic hypotension (Mangoni, 2005; Pugh & Wei, 2001) and in response to antihypertensive medications (Ali Raza & Movahed, 2002; Turnheim, 1998). Orthostatic hypotension is defined as a reduction in blood pressure (>20 mmHg systolic or >10 mmHg diastolic) in response to a change from supine to an upright position.
Drug-induced orthostatic hypotension is fairly common among the older adult population. In fact, drug-induced orthostatic hypotension increases with age and affects 5-33% of older adults (Verhaeverbeke & Mets, 1997). The resultant sudden drop in blood pressure increases the risk of syncope or falls (Verhaeverbeke & Mets, 1997). However, syncope was only attributable to drugs in 11% of older adults experiencing syncope (Kapoor, 1994). The fall risk associated with orthostatic hypotension carries the same risks with it as mentioned above with the benzodiazepines. These patients have a higher chance of sustaining hip fractures, therefore increasing rates of morbidity and mortality in older adults.

Although orthostatic hypotension is the most significant adverse event associated with antihypertensive therapy, other adverse effects have been studied. Diuretic therapy, in particular, may exacerbate the pharmacokinetic changes caused by the physiologic reduction in body water content (Ali Raza & Movahed, 2002; Turnheim, 2004). Loop diuretics, specifically, have a very short-half life and more significantly contribute to a decrease in total body water, therefore increasing dehydration in older adults (Mangoni, 2005). When combined with decreased thirst, fluid intake and cardiovascular reflexes, significant dehydration causes a deficit in hemoperfusion of vital organs (Turnheim, 1998; Verhaeverbeke & Mets, 1997; Vestal, 1997). This significantly increases the chances of toxic effects, contributing to an increased risk of electrolyte disturbances, metabolic changes and prerenal failure (Mangoni, 2005; Turnheim, 1998).

In addition, patients on antihypertensive therapy were reported to achieve lower scores on intellectual/cognitive tests (Amenta, Mignini, Rabbia, Tomassoni, & Veglio, 2002; Turnheim, 2003). However, untreated hypertension is also associated with cognitive impairment (Amenta et al., 2002), therefore indicating the cause of cognitive impairment is unknown since both
untreated hypertension and antihypertensive therapy have been shown to contribute to cognitive impairment (Amenta et al., 2002). Amenta and colleagues (2002) have reported hypertension to be associated with impairment of cognitive function and that antihypertensive therapy provides a protective effect on cognitive function, particularly in reducing the incidence of stroke and vascular dementia. This suggests the cognitive benefits of antihypertensive therapy outweigh the risks of therapy and the risks of untreated hypertension.

Antihypertensive agents are generally well tolerated in older adults and do, in fact, contribute to a reduced risk of stroke and transient ischemic attack in older adults (Mangoni, 2005). Most of the antihypertensive agents listed on the Beers criteria are $\alpha$-adrenergic agonists, which seem to have a higher incidence of orthostatic hypotension than other antihypertensive agents (Verhaeverbeke & Mets, 1997). Therefore, if orthostatic hypotension is an issue, $\beta$-blockers, ACE inhibitors and selected calcium channel blockers should be used instead of agents that interfere with $\alpha$-adrenergic function (Verhaeverbeke & Mets, 1997). In general, many effects of antihypertensive medications can be predicted due to the general pharmacokinetic changes in older adults mentioned above. As a result, the general consensus throughout the literature encourages the use of antihypertensives when they are indicated since they have protective effects (Mangoni, 2005). However, it is recommended that these medications be started at lower doses and doses be adjusted as needed (Ali Raza & Movahed, 2002; Mangoni, 2005; Williams & Kim, 2003).

**Antiarrhythmics**

Amiodarone, disopyramide and digoxin are three antiarrhythmic medications found on the Beers list of potentially inappropriate medications to use in older adults (Fick et al., 2003). Amiodarone, in particular, makes up 10% of inappropriately prescribed medications (Barry et al.,
2006) and is commonly used to treat atrial fibrillation and ventricular and supraventricular arrhythmias. Despite being used as an antiarrhythmic agent, amiodarone is associated with severe cardiac events, such as prolonged QT intervals, torsades de pointes (a type of ventricular tachycardia), hypotension, atrioventricular (AV) blocks and bradycardia (Ali Raza & Movahed, 2002; Fick et al., 2003; Lim, Pak, Ahn, Song, & Kim, 2006). It is, therefore, considered by the Beers criteria to have a lack of efficacy in older adults and is consequently associated with a high severity rating (Fick et al., 2003). However, if amiodarone is chosen for therapy in older adults, the lowest maintenance dose necessary to achieve the desired antiarrhythmic effects (100-200 mg/day) should be used to minimize potential adverse effects (Ali Raza & Movahed, 2002; Williams & Kim, 2003). Regardless of dose, close cardiac monitoring should be carried out when older adults are taking amiodarone.

Amiodarone is also associated with non-cardiac adverse events. This drug is highly lipophilic and has an increased volume of distribution due to the physiologic increase of body fat in older adults (Ali Raza & Movahed, 2002; Williams & Kim, 2003). Since it is lipophilic, amiodarone tends to accumulate in fatty organs, such as the liver, lung, skin and other tissues. As a result, amiodarone has been shown to induce thyroid disease (Franklyn & Gammage, 2007), pulmonary injury (Fung, Chan, Chu, & Yue, 2006), hepatic disease (Rizzioli et al., 2007), corneal deposits, photosensitivity and neuromuscular symptoms in older adults (Ali Raza & Movahed, 2002; Kang et al., 2007; Williams & Kim, 2003).

Zimetbaum (2007) has evaluated the prevalence and relative severity of these non-cardiac ADRs of amiodarone. The most severe and potentially fatal non-cardiac event is pulmonary toxicity, which occurs in approximately 1.9% of patients on the usual 200 mg dose of amiodarone therapy (Fung et al., 2006). However, the incidence of pulmonary toxicity can
increase to 20% with an increased doses of 400 mg of amiodarone (Fung et al., 2006). In the event that pulmonary problems arise while taking amiodarone, therapy should be discontinued immediately. Altered thyroid function is also a fairly common reaction occurring in over 20% of amiodarone users. The associated hypo- or hyperthyroidism is rarely life threatening. As a result, altered thyroid function does not warrant the discontinuation of amiodarone therapy and should be treated accordingly with glucocorticoids or levothyroxine (Franklyn & Gammage, 2007). Hepatic toxicity, on the other hand, is quite rare and is commonly seen at low doses of amiodarone (Rizzioli et al., 2007). Liver function tests should be monitored while on this medication and if hepatic disease occurs, it can be reversed with discontinuation of amiodarone therapy (Zimetbaum, 2007). Corneal microdeposits are, by far, the most common adverse event seen in almost all patients on long-term amiodarone therapy. These deposits are rarely clinically significant and do not necessitate a change in amiodarone therapy (Zimetbaum, 2007).

Digoxin is another antiarrhythmic medication considered to be inappropriate for use in older adults (Fick et al., 2003). Despite being inappropriate, Kaufman and colleagues (2002) found 9% of ambulatory older adult men and 5% of older adult women were taking digoxin. This medication is used in the management of atrial fibrillation, heart failure and supraventricular tachycardia (Hanratty, McGlinchey, Johnston, & Passmore, 2000; Williams & Kim, 2003). Digoxin is water-soluble and binds to lean muscle tissue (Hanratty et al., 2000). The physiologic decrease in total body water and lean body mass causes reduced digoxin-tissue binding and increased serum levels of digoxin (Hanratty et al., 2000; Williams & Kim, 2003). In addition, digoxin is primarily eliminated unchanged by the kidneys, so the physiologic decrease of renal function in older adults is a large contributor to increased digoxin toxicity (Hämmerlein et al., 1998; Hanratty et al., 2000; Turnheim, 2003). In fact, the renal clearance of digoxin is decreased
by up to 65% in the average older adult (Hanratty et al., 2000) causing digoxin to have an increased half-life.

The factors mentioned above contribute to digoxin having a low toxic-therapeutic window in older adults. This increases the likelihood older adults will develop digoxin toxicity. As a result, digoxin must be carefully administered at an individualized titrated dose for rate control and doses should be further decreased in patients with renal impairment (Williams & Kim, 2003). Since digoxin carries such a high risk, it is necessary that digoxin serum levels and kidney function (creatinine clearance) are closely monitored while older adults are on digoxin therapy (Hämmerlein et al., 1998; Hanratty et al., 2000). Finally, digoxin interacts with several drugs that consequently increase its sensitivity and toxicity. Therefore, digoxin should be used with caution when older adults are taking other antiarrhythmics, ACE inhibitors, verapamil, diuretics, warfarin and antibacterials (Hämmerlein et al., 1998; Hanratty et al., 2000).

Due to the associated fatal arrhythmic effects of antiarrhythmics, it is reassuring to know the use of several antiarrhythmic agents in all ages is decreasing (Fang, Stafford, Ruskin, & Singer, 2004). A significant downward trend was noted for digoxin. Particularly, digoxin use in all populations for ventricular rate control has decreased from 64% in the early 1990s to 37% in 2000. Unfortunately, amiodarone use is increasing in all populations (0.2% to 6.4% of cases) for the maintenance of normal sinus rhythm (Fang et al., 2004). These trends are likely similar for the older adult population.

*Analgesics*

The prevalence of pain is significantly higher in older adults. Pain increases with each decade of life and 67-80 % of adults older than 65 years of age complain of pain (Davis & Srivastava, 2003). The cause of pain can vary significantly in older adults. Older adults often
suffer from many comorbid illnesses that cause pain, such as osteoarthritis, neuropathies, peripheral vascular disease, coronary artery disease and diabetes (Davis & Srivastava, 2003). However, older adults are often undertreated for pain due to inadequate recognition, assessment and management of pain in this population (Cavalieri, 2005). Older adults then have difficulty performing activities of daily living (ADLs) and an increased risk of depression. Despite the risks associated with untreated pain, many dangers also exist with the use of pain medications in older adults.

Common analgesics include non-steroidal anti-inflammatory drugs (NSAIDs) and opioid narcotics. These drugs can be found OTC or as a prescription medication and frequent the list of the top forty most commonly used prescription and OTC drugs created by Kaufman and colleagues (2002). However, these medications should be used with caution in older adults because this population has an increased response to analgesics, resulting in faster peak serum concentrations (Vestal, 1997). Consequently, the Beers criteria considers propoxyphene (Darvon®), an opioid analgesic, a medication that should always be avoided in older adults because safer alternatives are available. In addition, the Beers criteria discourages the use of NSAIDs in older adults, particularly if the patient has a history of peptic ulcers or bleeding disorders, as these medications may exacerbate existing ulcers, produce new ulcers, or increase the potential for bleeding (Fick et al., 2003). Both medications are associated with a high severity risk if used in older adults (Fick et al., 2003).

NSAIDs are one of the most widely used medications for pain. Overall, older adults use 3 times more NSAIDs than younger adults (Hämmerlein et al., 1998), with 26% of older adults using NSAIDs (Johnson, 1998). NSAIDs make up 4-9% of all prescriptions (Johnson, 1998). In addition, most NSAIDs are available OTC, making ibuprofen the most frequently used NSAID
with 7% and 8% of male and female older adults, respectively, taking it on a regular basis (Kaufman et al., 2002). Unfortunately, NSAIDs are known to produce many adverse effects. NSAID use in older adults carry a higher risk of peptic ulcer disease, GI bleeding, hypertension, renal failure and congestive heart failure than in younger adults (Davis & Srivastava, 2003; Hämmerlein et al., 1998; McLean & Le Couteur, 2004; Turnheim, 1998). For example, renal impairment is doubled in older adults taking NSAIDs (Field et al., 1999) and antihypertensive therapy increases 1.7-fold when associated with NSAID use (Johnson, 1998).

This study indicated NSAIDs may induce hypertension, therefore necessitating the use of antihypertensive therapy. However, Frishman (2002) found patients on antihypertensive therapy had a much larger rise in blood pressure when started on NSAIDs, indicating NSAIDs may adversely interact with antihypertensives to increase blood pressure. Twelve to fifteen percent of hypertensive older adults concurrently take an antihypertensive medication with an NSAID (Johnson, 1998). Despite the mechanism behind the hypertension, Hanlon and colleagues (2002) found the most common drug-disease interaction involved the use of NSAIDs with hypertension. NSAIDs cause increased sodium reabsorption in the renal tubules, therefore increasing water retention (Frishman, 2002; Johnson, 1998). Water retention contributes to the small rise in blood pressure (usually <5 mmHg systolic pressure) seen in older adults using NSAIDs (Frishman, 2002).

Other severe adverse effects associated with NSAID use in older adults involve the gastrointestinal tract (GI). NSAID use causes 3-4% of older adults to experience intestinal bleeding compared to only 1% of younger patients (Davis & Srivastava, 2003; Turnheim, 2003). However, if an older adult has a history of peptic ulcer disease, this frequency increases to 9% (Davis & Srivastava, 2003). With increasing age being a known risk factor for GI events when
taking NSAIDs, safer alternatives have been established. The alternative therapy includes using cyclooxygenase-2 (COX-2) selective inhibitors, or coxibs, as opposed to NSAIDs, which are non-selective COX inhibitors. Coxibs and NSAIDs have the same analgesic characteristics, however GI bleeding with coxibs is only half of that compared to NSAIDs (Bombardier, 2002). However, renal impairment is the same (Bombardier, 2002; Harris, 2002) with a doubled risk of renal impairment in older adults taking regular NSAIDs and coxibs (Field et al., 1999). Therefore, it is recommended to use coxibs when possible in older adults instead of NSAIDs to reduce the risk of GI adverse effects (Turnheim, 2003). Better yet, acetaminophen (Tylenol ®) is preferred over COX inhibitors. Acetaminophen is a weaker analgesic, but has low GI and renal toxicity (Davis & Srivastava, 2003).

Opioids are second line analgesics for mild to moderate pain when pain is unresponsive to NSAIDs or other analgesic therapy. Propoxyphene, an opioid analgesic, can be found alone or mixed with other analgesics such as acetaminophen (known as Darvocet ®). As a result, this medication is readily available and is prescribed to approximately 7-10% of older adults (Kamal-Bahl, Stuart, & Beers, 2005; Kamal-Bahl, Stuart, & Beers, 2006; Singh, Sleeper, & Seifert, 2007). It consequently ranks among the top five inappropriately prescribed medications (Gallagher et al., 2007). Specifically, propoxyphene has been found to be the most commonly inappropriately prescribed medication (Zhan et al., 2001), accounting for 20-23% of all inappropriately prescribed medications (Barry et al., 2006; Gallagher et al., 2008). In fact, 24% of older adults receiving propoxyphene had noticeable symptoms attributable to opiate side effects, including acute confusion, severe constipation and drowsiness (Gallagher et al., 2008). Therefore, older adults on propoxyphene should have frequent follow-ups with his or her practitioner to monitor for side effects.
Frequent adverse drug reactions related to propoxyphene and other opioid use can vary in older adults. Propoxyphene is thought to inhibit its own hepatic metabolism in older adults (Kamal-Bahl et al., 2006). This leads to a slower metabolism, 3-5 times greater serum levels and more adverse effects (Goldstein & Turk, 2005; Kamal-Bahl et al., 2006). As a result, propoxyphene and other opioids are commonly associated with constipation, oversedation, nausea, respiratory depression, reduction in protective reflexes, and delirium (Davis & Srivastava, 2003; Goldstein & Turk, 2005; Kamal-Bahl et al., 2006; Turnheim, 1998). Respiratory depression induced by propoxyphene use is quite severe, however occurs in only <1% of propoxyphene-using older adults (Goldstein & Turk, 2005). Central nervous system (CNS) adverse effects are much more common and include symptoms such as drowsiness, dizziness, confusion and euphoria. Twenty-three percent of propoxyphene users experience CNS effects, whereas NSAID use is less frequently associated with CNS effects, with 12% of NSAID users experiencing CNS effects (Goldstein & Turk, 2005). These CNS effects can cause falls. Hip fractures may result as a rare adverse effect in <1% of propoxyphene-using older adults, which corresponds to up to a 2-fold higher risk than in non-users (Kamal-Bahl et al., 2006).

Lastly, the most common adverse effects associated with propoxyphene use are nausea and constipation. These symptoms are thought to exist because of opioid-induced gastroparesis (Davis & Srivastava, 2003). In fact, constipation is often considered to be the classic adverse event associated with opioid use and is often the cause for discontinuation of therapy.

Many adverse reactions associated with medication use can contribute to a patient’s self discontinuation of therapy. However, most adverse reactions can go unnoticed and occur at the microscopic level so patients cannot physically detect them until it is too late. Therefore, prescribers should be aware of the above adverse reactions that can occur in an older adult taking
the specific medications mentioned above. But, these reactions do not account for all ADRs older adults suffer. Therefore, the focus of the next section will be to identify the prevalence, severity and preventablity of ADRs seen in older adults from inappropriate prescribing and medication use.
Adverse Drug Reactions

Older adults are a very vulnerable population due to the physiologic, cognitive and physical differences outlined above. The fact that older adults have many comorbid conditions and take many inappropriate medications increases their susceptibility to adverse drug reactions (ADRs) compared to younger adults. An ADR is defined as a reaction that is noxious, unintended and occurs at doses normally used in humans for prophylaxis, diagnosis or therapy (Hajjar et al., 2003). ADRs are prevalent in 5% of ambulatory older adults (Gurwitz et al., 2003) and 6.5 – 19% of acutely admitted older adults (Joanna Briggs Institute, 2006; Laroche et al., 2007). Fortunately, less than 1% of ADRs result in death (Gurwitz et al., 2003). However, this number is significant if generalized across the older adult population. Approximately 180,000 to 200,000 older adults die each year from medication-related problems, which would make it the 5th leading cause of death if it were ranked as a disease (Gurwitz et al., 2003; Simonson & Feinberg, 2005).

Several factors make older adults at a high risk of ADRs. The leading risk factor for ADRs in older adults is polypharmacy (Hajjar et al., 2003; Hanlon et al., 1997). Thirty-five percent of polypharmacy patients experience ADRs (Hanlon et al., 1997). Of patients experiencing ADRs, 83% are found to be taking more than 5 medications (Hajjar et al., 2003). Polypharmacy makes patients 3-6 times more likely to experience an ADR than the average older adult (Laroche et al., 2007). In addition to polypharmacy, other significant risk factors making older adults more susceptible to ADRs include multiple chronic medical problems (comorbidities), prior ADRs and dementia. These risk factors are found in 10-26% of patients experiencing ADRs (Hajjar et al., 2003).
ADRs can vary in severity. Gurwitz et al. (2003) categorized ADRs as significant, serious, life-threatening or fatal. Significant reactions, such as rashes, falls without associated fracture and hemorrhage without associated transfusion, are present in 62% of ADRs. Serious reactions, such as urticaria, falls with fractures, hemorrhage needing transfusion and delirium, are present in 28% of ADRs. Life-threatening reactions, such as hemorrhage with hypotension, hypoglycemic encephalopathy, hyponatremia and renal failure, are present in 9% of the ADRs. Fatal reactions occurred in less than 1% of ADRs (Gurwitz et al., 2003). Consequently, 11-12% of hospital admissions are linked to ADRs (Hanlon et al., 1997; Mannesse, Derkx, de Ridder, Man in ’t Veld, & van der Cammen, 2000).

Despite the high prevalence of ADRs, it is reassuring to know that 27.6% of ADRs are considered preventable (Gurwitz et al., 2003). ADRs occur due to preventable errors at many levels of patient care. This includes errors at the level of the prescriber (regarding prescribing and monitoring) and patient. Of ADRs deemed preventable, the monitoring phase of patient pharmacologic care at the level of the provider most commonly contains preventable errors (Gurwitz et al., 2003; Higashi et al., 2004). Thirty-six percent of preventable ADRs are due to the clinician failing to act on clinical or laboratory findings of drug toxicity. Equally prevalent is general inadequacy of monitoring (Gurwitz et al., 2003). Medication monitoring was appropriately carried out 64% of the time, with proper dose adjustments occurring only 22-25% of the time with anti-depressant therapy (Higashi et al., 2004).

Prescribing errors are also very common preventable errors present in 58% of preventable ADRs (Gurwitz et al., 2003). The most common prescribing error involves prescribing the wrong therapeutic choice 27% of the time and wrong dose errors 24% of the time (Gurwitz et al., 2003). Higashi and colleagues (2004) found slightly higher incidences, in that medications were only
prescribed 50% of the time when they were indicated. For example, proton pump inhibitors (PPIs) are prescribed only 11% of the time when they were indicated for gastrointestinal conditions in older adults. More favorably, inappropriate medications are the culprit in only 6-10% of ADR cases (Higashi et al., 2004; Laroche et al., 2007).

Less common areas of prescribing errors involves the clinician providing inadequate patient education and prescribing drugs with well known drug-drug interactions. Overall, physicians provided adequate education, continuity and documentation in 81% of cases (Higashi et al., 2004). The documentation of GI bleeding and ulcer history in patients using NSAIDs was the most prevalent failed documentation, present only 10% of the time when it should have been (Higashi et al., 2004).

Patient adherence contributes the least to only 21-23% of preventable ADRs (Field et al., 2007; Gurwitz et al., 2003). However, when considering all drug-related issues, preventable or not, patient adherence is the most common, accounting for 25.9% of drug-related issues (Doucette et al., 2005). Adherence errors most commonly involve patient failure to modify a drug regimen when advised to do so and improper administration of medications (Field et al., 2007). Seventy to seventy-five percent of patient non-adherence was intentional with omission accounting for up to 90% of forms of non-adherence (Vestal, 1997). Since a large proportion of adverse drug reactions are preventable, certain interventions should be used more frequently to ensure older adults do not suffer from unnecessary consequences.
Interventions

The previous sections highlight the significance of inappropriate prescribing and medication use in older adults. In general, older adults are a hard population to treat when considering the physiologic, physical and cognitive changes they undergo with age. Additionally, older adults accumulate illnesses over time and tend to have many comorbid medical conditions. As a result, older adults consume many medications. This increases the risk of inappropriate prescribing and medication use in older adults and, subsequently, increases the risk of adverse drug reactions (ADRs) even from the most commonly-used medications. These reactions are generally not life-threatening, however, have the potential to become fatal in about 1% of the cases (Gurwitz et al., 2003). Regardless, this risk should not be taken. Instead, interventions to ensure medications are being prescribed properly and that older adults are using their medications as indicated should be established.

It is important that healthcare providers, pharmacists, patients and all parties involved with an older adults’ healthcare are aware of the dangers of inappropriate prescribing and medication use in older adults. These individuals can then take steps to be certain older adults are pharmacologically treated properly and are compliant. On the bright side, as mentioned in the previous adverse reactions section, researchers have found approximately 30% of medication errors are attributable to preventable causes (Field et al., 2007; Gurwitz et al., 2003; Higashi et al., 2004). Therefore, it is important the cause of an ADR is sought out to prevent ADRs from occurring due to careless prescribing and medication usage errors. As a result, the focus of this section will be to identify specific interventions to help decrease the frequency of many of the preventable medication errors found by the above researchers.
There is quite a bit of literature on interventions proven to identify and decrease inappropriate prescribing and medication use in older adults. Most preventable medication errors take place at the level of the healthcare provider and patient. In general, the healthcare provider assumes the largest responsibility of assuring they are prescribing the correct medications, educating their patients and monitoring patients for compliance. Therefore, many interventions to decrease prescribing errors will be discussed first. And, secondly, interventions to decrease medication use errors will be discussed. Pharmacists can play a role in aiding with both prescribing and medication use interventions.

**Prescribing Interventions**

Healthcare providers with prescriptive authority have a large responsibility when prescribing to older adults. These “prescribers” assume a large role in assuring they are treating older adults with the correct medications at the correct doses since older adults respond to medications differently than younger adults. Unfortunately, prescribing errors occur much too frequently in the care of older adults. In fact, to emphasize study results mentioned previously, approximately one-quarter to one-third of older adults take an inappropriate medication (Barry et al., 2006; Curtis et al., 2004). Of older adults taking an inappropriate medication, many experience adverse drug reactions (ADRs), of which 27.6% are preventable (Gurwitz et al., 2003). However, Gurwitz and colleagues (2003) found that prescribing errors accounted for 58% of preventable ADRs. Of these errors, wrong drug/therapeutic choice errors accounted for 27% of preventable prescribing errors. In addition, wrong dose errors and drug-interaction errors accounted for 24% and 13% of preventable prescribing errors, respectively. It is evident by the high incidence of these preventable prescribing errors, something should be done to decrease prescribing errors in older adults. Consequently, many interventions to minimize inappropriate
prescribing and medication use in older adults begin with each visit to a healthcare provider. Many interventions a healthcare provider can utilize to ensure they are prescribing the correct medication have been studied and will be discussed here.

*Prescriber medication assessment*

The first step in prescribing a new medication to an older adult is to carry out a thorough medication assessment. Before a new prescription can be written, information about an older adult’s current medication regimen needs to be obtained. A medication assessment enables healthcare providers to review an older patient’s list of chronic illnesses and current medications to check for inappropriate medications, drug-drug and drug-disease interactions. Then, an appropriate medication that fits nicely in an older adult’s current medication regimen can be chosen that will not interact with other medications or cause further harm to an existing medical condition.

Prescribers can assess an older adult’s medication regimen using several methods. The medication assessment must involve proper communication between the healthcare provider and older patient, while maintaining adequate documentation. Medication assessment methods include interviews, medication list/regimen reviews and medication container evaluations. There is very little research on the accuracy of these methods of medication assessment. Regardless, it is necessary these assessments are carried out with care so an accurate medication history is obtained.

Many healthcare providers rely on a patient interview to obtain a medication history. This method involves very little preparation, but relies much on patient memory and recall. However, as mentioned previously, older adults undergo many cognitive changes with aging. They may have difficulty recalling the name of a medication and, particularly, the doses and frequency of
administration. As a result, an inaccurate medication history may be obtained from an interview solely obtained from older patient recall. Therefore, healthcare providers may ask their older patients to keep a written medication record, including dosing and administration information.

A written medication record is another common method of medication assessment. A written record may be in list form or in grid form according to the administration schedule (Muir, Sanders, Wilkinson, & Schmader, 2001). These two methods will provide much of the same information, but the grid may provide additional visual information to the complexity of a medication regimen. A written medication record may be more useful in creating an accurate medication history, but an older adult may not be able to provide much more information regarding a medication based on its name. Older adults have a hard time recalling their medications and information about their medication by name and often recognize their medications by appearance (Ballentine, 2008). Therefore, other medication assessment methods based on medication appearance may be beneficial and are commonly used.

The commonly termed “brown bag” approach is a popularly used medication assessment method. With this approach, a patient is asked to bring in all of his or her medication bottles so each medication can be assessed individually. The use of telephone reminders before appointments can be helpful in stressing the importance of the “brown-bag” and in reminding older adults to bring their “brown-bag” to their next appointment (Bergman-Evans, 2006). This medication assessment is especially helpful at a first visit to establish an accurate medication history from the beginning, but should be used at all visits to monitor medication usage. Since older adult recognize their medications better by appearance (Ballentine, 2008), it may be easier to discuss indications and administration schedules when all the medications are present. In that case, older adults may be more likely to remember any new or important information regarding a
medication. Additionally, the physical presence of medication bottles allows refill dates to be determined and compliance, which will be discussed later, to be indirectly assessed.

The use these medication assessment methods will provide an easy way for healthcare providers to maintain an accurate medication record of older patients from visit to visit. With an accurate medication record, prescribing healthcare providers are able to assess the appropriateness of current medications and the addition of new medications. However, medication prescribing errors still occur and the prescriber is ultimately responsible for these errors. However, other healthcare providers are responsible for performing their own medication assessment which involves checking the medications already prescribed to an older adult. Therefore, an interdisciplinary approach is needed to carry out a proper medication assessment. Specialty healthcare providers, including emergency, outpatient, inpatient and nursing home providers, should also assume a role in medication assessment (Ballentine, 2008). Additionally, pharmacists are specifically trained to know the effects of medications and can be helpful by performing medication assessments. As a result, researchers have studied the effectiveness of medication assessments carried out by pharmacists.

**Pharmacist medication assessment**

Pharmacists play an important role in helping prescribers identify medication prescribing errors. In particular, one group of researchers from Norway investigated whether a pharmacist interview of hospitalized patients about their medications would result in the identification of more drug related problems than those found by usual care procedures (Viktil, Blix, Moger, & Reikvam, 2006). Ninety-six patients were interviewed, with the average interview lasting 20 minutes. The remaining patients were not interviewed and were used as the “usual care” group. The usual information from each medical record was collected, with the interview group having
the information obtained from the interview as one piece of additional information. The available patient information was assessed by a healthcare team, including physicians, nurses, pharmacists and members of other professions. Drug related problems were placed into 13 different categories, including, but not limited to, the need for additional therapy, unnecessary drugs, non-optimal drugs, non-optimal doses, drug-drug interactions, unnecessary drug and a patient experiencing an adverse drug interaction. Once the data was analyzed, significantly more drug related problems (4.4 per patient) were found in the interview group compared with the usual care group (2.4 problems per patient) (Viktil et al., 2006). Forty percent of the problems found in the interview group were found during the interview procedure, of which two-thirds were considered to be of major clinical significance (Viktil et al., 2006). Based on these results, Viktil and colleagues (2006) were successful in emphasizing pharmacist interviews are effective in identifying more medication errors than the usual care procedures.

Doucette and colleagues (2005) performed a similar study involving pharmacist interviews of Iowa Medicaid patients with ≥ 4 chronic medications and ≥1 disease states. Pharmacists in this study interviewed and reviewed the records of 150 community-dwelling patients to identify drug-related issues classified as inappropriate adherence, adverse drug reaction, needs additional therapy, dosage too low or high, wrong drug or unnecessary drug. Pharmacists found 886 drug-related issues involving 109 physicians during the 2-year period. This correlated to an average of 5.9 drug-related issues per patient (Doucette et al., 2005). This number appears to be significant, although there was no control group in this study. However, Doucette and colleagues (2005) went on to identify and compare other interventions used by pharmacists to identify and prevent prescribing errors.
Pharmacist education

After performing a thorough medication assessment, healthcare providers must be able to identify errors in a medication record in order to resolve them. Unfortunately, the high incidence of prescribing errors found by pharmacists may indicate prescribers are careless or do not have the adequate knowledge to identify such errors. This may prove to be particularly difficult when prescribing to older adults since there is much literature describing the specific prescribing criteria and medications that should be generally avoided in older adults (Beers, 1997; Beers et al., 1991; Fick et al., 2003; Zhan et al., 2001). As a result, prescribers may need to rely on the help of educational materials and recommendations from pharmacists to further decrease the incidence of prescribing errors.

Doucette and colleagues (2005) continued the above study to assess the use of pharmacist recommendations and education on resolving drug-related issues. After pharmacists assessed and classified drug-related issues as defined previously, the pharmacist made recommendations to prescribers. Pharmacists recommended the prescriber add, discontinue or switch drugs or increase or decrease the dosage of a particular drug. After the intervention, prescribers’
responses were scored as no response, agreed, agreed but no action taken or disagreed. Pharmacists made recommendations to alter a patient’s drug therapy in 74.4% of the drug-related issues. Of these recommendations, prescribers accepted the recommendation 47.5% of the time. Most of the accepted recommendations involved stopping or replacing a medication, with starting a new medication being the least common accepted change. In the end, these results corresponded to approximately one-third of the drug-related issues being resolved by pharmacist medication assessment and recommendations.

This study by Doucette and colleagues (2005) was very helpful in identifying where prescribing errors are made and methods that can be used to resolve them. However, this study did not look at older adults specifically and only looked at one pharmacy in Iowa. It included a fairly large study population and adults of all ages, with an average age of 54.4. Additionally, the patients in this study took an average of 9.3 medications and had an average of 6.1 medical conditions. A large proportion of older adults, however, fit this profile since most are known to have several comorbid illnesses and consume a large number of medications. It is realistic, then, that this study can be generalized to older adults. It can be assumed prescribing errors in older adults will be identified using a pharmacist medication assessment and prescribers will generally accept pharmacist recommendations about medication changes in older adults.

Kaufman and colleagues (2005) also used the help of pharmacists to carry out a trend analysis to study the effects of prescriber education on the use of medications contraindicated in older adults. The researchers formulated a list of 7 inappropriate medications from the Beers criteria (Beers, 1997; Fick et al., 2003) and the criteria created by Zhan and colleagues (2001). This intervention involved the use of pharmacy services to identify the older adults who received one or more prescriptions for a potentially inappropriate medication. Once an inappropriate
medication was identified, the prescribers of these medications were then identified and were mailed a letter, called by a clinical pharmacist and received an article entitled “Inappropriate Prescribing in the Elderly.” The frequency of inappropriate prescribing was assessed at the end of each quarter of the 4-year study period. The researchers then carried out a trend analysis without a control group. They found a statistically significant downward trend for both the percentage of older adults who received prescriptions for inappropriate medications and the percentage of older adults who received one or more of the 7 inappropriate medications identified. This indicates the use of prescriber education can help decrease the incidence of inappropriate prescribing in older adults.

Aside from the help of pharmacist recommendations, other educational methods may be used to decrease the prevalence of inappropriate prescribing in older adults. Another group of researchers examined the effectiveness of the use of an intervention involving educational brochures to change physician prescribing behavior and decrease the use of potentially inappropriate medications (Fick et al., 2004). This intervention included 355 primary care physicians. Each physician in the treatment and control groups were mailed an educational brochure and a copy of the Beers list of inappropriate medications (Fick et al., 2003). The intervention group of physicians additionally received 3 items: a detailed educational brochure listing the potentially inappropriate medications (PIMs), a list of alternative medications, and a personally addressed letter describing each of the physician’s patients who were determined to have 1 or more PIMs. All physicians in the intervention group were invited to comment on any prescribing changes using a fax-back form. Seventy-one percent of the physicians who prescribed PIMs returned the form, but only changed a PIM in 15.4% of the cases. However, after the 6-month study period, the number of older adults receiving a PIM significantly
decreased by 1.5% (19.4% to 17.9%) (Fick et al., 2004). This indicates the use of education materials at an attempt to influence physician prescribing behavior is successful in decreasing the number of inappropriate medications prescribed to older adults.

In general, prescribers seem to be responsive to the input from pharmacists and others methods to change prescribing behavior. However, these studies did not assess outcome data, or how patients fared with or without a medication change, so it is hard to know if patients saw an added benefit (e.g., through a decrease in adverse drug reactions) to prove these interventions are indeed beneficial to the patient. However, these studies confirm the idea that reducing the number of prescribing errors is a complex issue that one intervention cannot solve. A large amount of time and effort must be put forth by multiple pharmacists and staff to carry out the above-mentioned interventions. One must judge whether the benefit is worth the time and may want to consider an alternative method, such as a computerized prescribing alerts.

**Computerized Aides**

Many drug-drug and drug-disease interactions exist and the list of inappropriate medications for older adults continually gets longer. Therefore, healthcare providers may find it difficult, at times, to recall these numerous interactions and inappropriate medications for older adults, which may lead to prescribing errors. As a result, healthcare providers often rely on the help of other professionals and methods to identify particular interactions and problem medications. However, healthcare providers may not solely rely on the help of a pharmacist to catch prescribing errors, but they may also rely on electronic aides to do so. In some cases, both computerized alerts and pharmacist recommendations may be used in combination.

Raebel and colleagues (2007) studied the use of a computerized alert system in 21 pharmacy’s computer systems in identifying inappropriate medications based on a patient’s age.
The computerized system was set to alert the pharmacist if one of 11 potentially inappropriate medications based on the Beers (Beers, 1997; Fick et al., 2003) and Zhan (Zhan et al., 2001) criteria was prescribed to ambulatory patients aged 65 years or older. The pharmacist responded to the alert by either deeming the indication acceptable and dispensing the medication or consulting the prescribing physician. During the consultation, the physician and pharmacist decided to dispense the medication as written, dispense an alternative medication or stop the medication. The results of this study showed 1.8% of the intervention patients and 2.2% of the usual care patients were newly dispensed one or more of the 11 inappropriate medications (Raebel et al., 2007). Although these numbers seem small, they indicate only the percentage of newly prescribed inappropriate medications, not all of the inappropriate medications a patient is taking. Although this difference may seem insignificant, it correlates to a significant 16% relative risk reduction in the intervention group.

This study included a very large population of 59,680 older adults at 21 different pharmacies (Raebel et al., 2007). Therefore, this study is able to be generalized over a large older adult population. Also, unlike the other studies involving pharmacist interventions and recommendations, this intervention is less time consuming and does not interfere much with the day-to-day workings of a pharmacy or physician office. As a result, other researchers have studied the use of similar computerized alert systems in clinical sites.

Simon and colleagues (2006) also used a computerized alert system to reduce the use of potentially inappropriate medications in older adults. Unlike the previous study, this study involved the use of computerized alerts at the time of prescribing, not dispensing. Fifteen clinical practices were provided with the capabilities to use a computerized medication system. This system was set to provide drug-specific and age-specific alerts when an inappropriate medication
was prescribed. The researchers concluded the age-specific alerts were associated with sustained improvement in the dispensing of potentially inappropriate medications for older adults. However, without a control group, one is unable to determine the cause of this trend or if it would continue. Also, the researchers only assessed the prescribing step of these drugs. It is possible the pharmacist intervened, consulted the prescriber, and did not dispense the medication. Regardless, the authors indicated that real-time reminders are effective in changing a prescriber’s behavior. Therefore, more research on this topic may show the use of computerized alerts for physicians at the time of prescribing may be effective in decreasing prescribing errors.

A future topic of research may include the use of a universal electronic computerized medication alert system used by all healthcare providers and pharmacists. In fact, preliminary research has been conducted in Denmark regarding the use of a nationwide on-line prescription record for hospitalized patients (Glintborg, Poulsen, & Dalhoff, 2008). Additionally, a group of researchers from the Netherlands have shown promising results with an inter-hospital computerized physician order entry (CPOE) system (van Gijssel-Wiersma, van den Bemt, & Walenbergh-van Veen, 2005). They have shown prescribing errors to decrease from 50% to 20% with the CPOE system (van Gijssel-Wiersma et al., 2005). In the future, these universal systems may enable real-time medication alerts and immediate, automatic updates for all providers to access.

Interphysician communication – Discharge summary

The success of these studies in using the help of pharmacists and electronic aides support the idea that an interdisciplinary approach is helpful in decreasing prescribing errors. Because older adults have multiple comorbid illnesses and are more likely to seek care from multiple specialists, it is important that interphysician communication be well-established. Medications
can change frequently and when this occurs, all parties involved in an older adult’s care should be notified. Healthcare providers can use medication summaries to fulfill that objective. Although there is little research about medication summaries used in the general ambulatory care of older adults, there have been studies published using medication summaries at the time of hospital discharge.

The transition of inpatient care to outpatient care is a vulnerable time for older adults. Forster and colleagues (2005; 2003) found that approximately 20% of adults of all ages experienced an adverse event when discharged from the hospital. This percentage is likely higher for older adults since they accounted for 70% of hospitalized patients (Halasyamani et al., 2006). Of these adverse events, 66% were adverse drug events (Forster et al., 2003). In fact, the average older adult was found to have two medication errors when transitioned from the hospital to primary care (Midlov, Bergkvist, Bondesson, Eriksson, & Hoglund, 2005). Of the adverse events occurring at discharge, 62% were considered preventable or ameliorable (Forster et al., 2003).

Forster and colleagues (2003) went on to identify four principle aspects of the discharge system that required improvement, two of which dealt with medication use. These included improvements in the areas of patient education regarding medications and monitoring of drug therapies after discharge. As noted in a previous section, these aspects were also found by Gurwitz and colleagues (2003) to be the cause of a large percentage of preventable adverse drug reactions in ambulatory older adults. As a result, to improve the quality of care of older adults and decrease the incidence of medication errors having the potential to cause adverse drug events at discharge, several studies have looked at the use of discharge summaries and checklists.

It is important to examine the general content of a discharge summary or checklist before discussing the benefit to using discharge summaries as an intervention to decrease inappropriate
prescribing and medication use in older adults. Halasyamani and colleagues (2006) performed a literature review and consulted experts to create a discharge checklist targeting older adults that includes elements “required for optimal handoff” from inpatient to outpatient care (Halasyamani et al., 2006). This checklist contained a “discharge medication” section, including a written medication schedule. This schedule included the purpose and caution for each medication and a comparison with pre-admission medications. The specific description of the patient’s past and present medications, with specific attention to high-risk medications, provided a better understanding of discharge medications. By designating medications as “new,” “modified,” or “discontinued,” there should be no confusion whether to stop or continue taking an old medication. In this particular checklist, these elements were written at a 6th grade reading level to improves a patient’s understanding of the follow-up plan after hospital discharge. Additionally, Wolf and colleagues (2007) support the idea that patients understand instructions better when written at a 6th to 8th grade reading level. Although Halasyamani and colleagues (2006) did not study the effectiveness of their discharge checklist in detecting and preventing medication errors, other researchers have studied the effectiveness of similar discharge summaries.

Midlov and colleagues (2008) studied the use of a medication report in reducing the number of medication errors in older adults at the time of discharge from a Swedish hospital. The intervention group of patients received a medication report at discharge from the hospital, as opposed to the control group who were not given a medication report. Like the discharge checklist created by Halsayamani and colleagues (2006), the medication report created by Midlov and colleagues (2008) included a detailed list of the patient’s medication changes throughout the hospital stay, including discontinued medications, dosage changes and new medications. The discharge medication report, in this case, allowed discharge practitioners to
focus on which medications they were discharging a patient on and catch errors in order to
communicate effectively to the next level of care and patient. As a result, only 32% of the
intervention group experienced medication errors compared with 66% of the control group. The
most common error was the erroneous addition of a medication (commission error). The
intervention group had only 0.64 commission errors per patient and the control group had 1.29
commission errors per patient. The erroneous change in dosage and omission errors accounted
for fewer errors. Additionally, the relative risk of experiencing an error with moderate or high
clinical risk, as evaluated by two physicians, was 0.46 in the intervention group. This correlates
to the control group having almost twice the risk of having an error with a moderate or high
clinical risk, although over half the intervention and control groups had errors without clinical
risk. This data generated by Midlov and colleagues (2008) supports the idea that discharge
summaries decrease the incidence of medication errors in older adults by nearly 50%.

The previous studies reviewed the content of the discharge summary and the usefulness
of the discharge summary in minimizing the incidence of medication prescribing errors. Few
studies, however, have evaluated outcome effects of the discharge summary on adverse drug
events. One study by van Walraven and colleagues (2002), in fact, studied the effects of
discharge summaries on health outcomes. After collecting data from a large population of
inpatients from a teaching hospital in Ontario, Canada, they found a discharge summary
decreased the prevalence of readmission to the hospital, a positive health outcome. However,
they did not specify the cause of readmission. They mentioned many readmissions are due to the
progression of disease rather than medical error, but we cannot assume the favorable results
found in the study are associated with medication errors or other preventable causes. Regardless,
this study provides promising preliminary work to future research looking into the cause of
readmission. Whether discharge summaries provide a significant decrease in the incidence of adverse drug events and inappropriate prescribing and medication use is yet to be studied.

Overall, the studies looking at the use of discharge summaries are hard to generalize away from many local issues since each study only looked at patients from a single medical facility. Instead, studies should be carried out across a variety of medical settings. Additionally, Midlov and colleagues (2008) only studied nursing home and home-health patients since it is easier to control their medication administration because it is well-documented in these patients. This makes it harder to generalize to ambulatory older adults. Also, these studies could not control whether follow-up physicians actually read the discharge summary or whether they received interim information from other sources in addition to the discharge summary. This interim information could have instead affected how follow-up physicians treated older adults. However, these studies have used large patient populations and collected objective information with enough background and demographic information to control for confounding factors. Therefore, the results can be safely generalized across a large population, but may best be used as a template for future research to better achieve a flawless transition of care for hospitalized patients.

The favorable results achieved by the research on discharge summaries, makes it reasonable to assume this method would also work in outpatient medicine. In that case, sending a patient home from an office visit with a detailed medication summary, will allow patients to bring that report with them to all visits to a healthcare provider. As a result, it is likely the number of medication errors due improper interphysician communication could be reduced. In addition, a medication summary can provide older adults with an official medication record to refer to in order to double-check their medication regimen. This can indirectly increase patient
compliance and, as a result, be the first intervention discussed to help reduce medication use errors brought on by poor patient compliance.

Medication Use Interventions

Medications can be prescribed correctly by a healthcare provider and distributed correctly by a pharmacist, but can still be inappropriately used by an older patient. Therefore, interventions to decrease medication errors are not only found at the level of the prescriber, but also at the level of the patient. Patient adherence accounts for 21% of preventable adverse drug reactions (ADRs) (Gurwitz et al., 2003). Patient education errors account for 18% of preventable prescribing ADRs (Gurwitz et al., 2003). These facts alone indicate interventions to decrease the incidence of medication use errors starts at the level of the healthcare provider, adding yet another role a healthcare provider must fulfill to ensure his or her patients are being treated properly. Healthcare providers must monitor and educate their older patients about medication usage in order to decrease medication use errors.

Many of the prescribing interventions mentioned above, particularly medication assessment tools, can be used by healthcare providers to monitor if medications are being used correctly by older patients. Compliance, by using the brown-bag method, can be assessed by checking refill dates on bottles and performing a pill count (Ballentine, 2008). For example, a healthcare provider can assume an older adult is taking too little of a medication if he or she has not refilled a medication by its refill date or have too many pills remaining in the bottle. A healthcare provider can then intervene by appropriately reminding his or her patient about the proper usage of his or her medication. However, this reminder should not come as new information to the patient. The first step healthcare providers must take in assuring medications are used correctly by older adults, is to properly educate them about medication usage.
Patient education

Unfortunately, physicians are lacking in their patient education and communication skills. Tarn and colleagues (2006) studied physician communication when prescribing a new medication. These researchers evaluated previous research to formulate a list of 5 expected elements of communication when initiating a new prescription. These elements of communication included: the name of the medication, purpose of the medication, duration of intake, directions for use (number of tablets and/or frequency of intake) and adverse effects associated with the medication. Physicians fulfilled 3.1 out of the 5 expected elements when initiating a new prescription. Of the expected elements, the name of the medication and the purpose were mentioned most frequently 74% and 87% of the time, respectively. However, the duration of intake and adverse effects were mentioned least 34% and 35% of the time, respectively. Although this study involves persons of all ages, it can be generalized to include older adults since they consume over 2.5 times more medications than the rest of the population combined (Stagnitti, 2007). Additionally, Wilson and colleagues (2007) found that 32% of older adults have not talked to their physician about their medications in the last 12 months, with over 50% of older patients with ≥3 medical conditions admitting to some type of non-adherent behavior. Thus, the results of these studies suggest the need for continued physician interventions through patient education to minimize non-compliance in older adults.

Once prescribed a medication, an older adult faces the difficult task of comprehending and integrating all the information he or she receives to fit the new medication properly into his or her medication regimen. Since physicians do a poor job of communicating information with their patients about a new medication, older patients often rely on the drug label to provide them
with the necessary information they need to use their new medication properly. Various studies have looked at drug labels and patient compliance.

Medication labels

Pharmacists distribute multiple pieces of information each time a patient fills a prescription. If the patient has any questions regarding a medication, they could potentially obtain the answers to all their questions and more by reading the FDA-approved medication guide they receive with each prescription. Unfortunately, these materials are only looked at by 23% of patients because they are written at too high of an education level (Wolf, Davis, Shrank, Neuberger, & Parker, 2006). As a result, these information leaflets may appear intimidating to patients and patients may interpret the information wrong. In fact, approximately 35% of patients experience increases anxiety after reading a drug information leaflet, which causes a 10% decreased adherence rate (Vinker, Eliyahu, & Yaphe, 2007). It is, therefore, recommended that these medication guides be written at a 6th to 8th grade level in order for patients to understand and should include a summary section with the most important information. However, these guides are still rarely read and patients may rely solely on the information provided to them on the medication label. The medication label is, therefore, a good area where healthcare providers and pharmacist can intervene in order to improve patient compliance.

In one study, Wolf and colleagues (2007) studied misinterpretations of prescription drug labels. Forty-six percent of adult patients (18 years and older) misunderstood at least one prescription label (Wolf et al., 2007). Although this prevalence is higher in patients with lower literacy levels (63%), misinterpretation was still present in 38% of patients with an average literacy level. Although these numbers do not specifically reflect the older adult population, lower literacy was associated with age (Wolf et al., 2007). As a result, the misinterpretation rate
is likely to be higher in older adults. Also, patients managing multiple medication regimens made more misinterpretation errors (Wolf et al., 2007). This further supports the idea that the prevalence of misinterpretation would be higher in older adults since the polypharmacy rate is higher in older adults. As a result, several specific interventions can be carried out to increase a patient’s comprehension of drug labels since they are often the sole, tangible source for specific drug dosage and usage instructions.

One intervention can be achieved through a joint effort from healthcare professionals and pharmacists. This is to improve the “label language” on prescription drug labels (Wolf et al., 2007). Seventy-two percent of patients misunderstood repetitive phrases of dosage and frequency, such as “take two tablets by mouth twice daily.” To achieve a solution to this discrepancy, research experts suggest using numeric symbols rather than written words (e.g., “2” versus “two”) to further increase the ease of reading. In addition, the complexity of instructions should be explicit in nature rather than implicit in nature. Older adults have a hard time making inferences (Park, Morrell, Frieske, Blackburn, & Birchmore, 1991), so patients should be told exactly when to take a medication (e.g., “take two tablets by mouth in the morning and two tablets by mouth at 5 pm”) rather than vague instructions (e.g., “take two tablets by mouth twice daily”) which leave older adults guessing when they should take a medication. Drug labels should also include the indication of a particular medication (e.g., “take for diabetes”) to minimize any confusion about an indication in order to increase the chance a patient will take a medication when he or she knows what it is for.

These changes made to drug labels will enable older adults to interpret the labels much easier. Explicit instructions will not leave older adults inferring what the label is instructing them to do. Therefore, by creating drug labels with clear language according to the tips mentioned
above, older adults will better comprehend instructions to help decrease inappropriate medication use in older adults.

Reducing medication regimen complexity

Once older adults are able to understand the administration schedule of a particular medication, they still face the difficult task of integrating all of their medications into one large medication regimen. Therefore, one problem resulting in medication use errors is a complex medication regimen. A complex medication regimen is determined by the number of medications a patient takes (polypharmacy) and the number of doses each day a medication must be taken. Consequently, complex regimens are associated with decreased patient compliance and more adverse drug reactions (Stewart & Cooper, 1994). This adds other potential interventions a healthcare provider should utilize to decrease medication use errors due to inadequate patient compliance.

Medication grids. As discussed previously, a medication grid can be helpful in performing a medication assessment. A medication grid can also provide a visual representation of a medication regimen to assess its complexity. One study by Muir and colleagues (2001) provided medical residents with a medication grid including names of all medications and times of administration for one week. This study included 836 polypharmacy patients (>5 medications). The intervention group had 368 patients, in which the number of medications per patient decreased by 0.92 as opposed to a 1.65 medication increase in the control group (Muir et al., 2001). In addition, the average number of doses per day decreased by 2.47 per patient compared to an increase by 3.83 doses per day in the control group. Ultimately, the use of a medication grid was successful in decreasing the complexity of medication regimens.
This study by Muir and colleagues (2001) contained various limitations, however. It was not specific to older adults, but did include patients who were taking 5 or more medications. Because a large majority of older adults are polypharmacy patients, this study can be generalized across the older adult population. Also, this study shows some bias between the intervention and control group. Fifty percent of the intervention groups had a pharmacist in the group and only 42% of the control groups contained a pharmacist. Also, of the 2nd & 3rd year residents studied, the control group contained 62% 2nd year residents and the intervention group only contained 46% 2nd year residents. Therefore, the intervention group contained more pharmacists and 3rd year residents, who are assumed to have more experience treating patients. The experience of the pharmacist and 3rd year resident may affect the results. Additionally, this study only included long-term medications. Otherwise, if short-term medication were included, the regimens might have appeared more complex and may have, in turn, undergone more medication changes. Lastly, the residents were not blinded, so the results of the study may be due to the residents knowing they were part of the study. Regardless, this intervention required less time than a chart review and showed promising results supporting the use of medication grids as an intervention to reduce medication complexity.

Fixed-Dosing Drug Regimens. Healthcare providers can also use fixed-dose combination medications as an intervention to reduce the complexity of medication regimens. Bangalore and colleagues (2007) performed a literature review to study the use of a fixed-dose combination therapy compared to free-drug component regimens. They found that patient compliance significantly improved if dosing regimens were simplified to a single fixed-dose combination pill instead of 2 separate pills given at different times. In fact, non compliance rates decreased by 24-26% with the fixed-dosing therapy (Bangalore et al., 2007).
Connor, Rafter and Rodgers (2004) found similar results in their literature review. Adherence behaviors significantly improved using fixed-dose combinations. However, one concern with this method involves the efficacy of a fixed-dose combination pill compared to the free drugs. Bangalore and colleagues (2007) found that fixed-dose combination therapies were equally, if not more, efficacious than free-drug therapies. This simplified dosing regimen is a beneficial way to reduce the pill burden and increase compliance in this population of patients.

**Medication organizers**

Older adults may still have a hard time complying with a medication regimen despite efforts to reduce the complexity of medication regimens. The use of external cognitive supports, such as medication organizers, blister packs and unit-of-dose packaging, may aid older adults in remembering when to take their medications. Although current literature on this topic is scarce, some studies have shown promising results about the effect of these methods on patient adherence.

Huang and colleagues (2000) studied the difference between the two medication organization methods blister packs and pill organizers on patient compliance. These organization systems were filled with vitamins, so the researchers could measure serum levels to test for compliance. In addition, pill counts were used as a measure of compliance. The patients using blister packs were more likely to be compliant based on pill count. In fact, the percentage of participants who took >90% of their pills was 87% for the pill organizer group and 93% for the blister pack group (Huang et al., 2000). However, when looking at the vitamin serum levels, neither organizational system showed an improvement in compliance. This discrepancy may indicate patients were “pill-dumping” because they knew they were being studied. Regardless, both medication organization systems showed increased adherence compared to no
organizational system. Therefore, by using a medication organizer, patients were likely to have increased compliance.

Several older studies by Park and colleagues (1991; 1992) looked at the use of only medication organizers. In the 1991 study, the researchers studied adults with arthritis aged 35 or older taking ≥3 medications. They compared several types of organizers: a 7-day with times (morning, noon, evening and bed) organizer, a 7-day without times organizer, and a one-day wheel with hour-by-hour time slots. Patients were asked to load each organizer with their medications and the researchers studied the number of errors made. They found the use of a 7-day with times organizer lead to <2% loading errors, with the one-day wheel and 7-day without times leading to approximately 6% and 14% errors, respectively (Park et al., 1991). Therefore, the 7-day with times organizer seems to be the easiest to organize and may have the best potential to improve patient compliance.

In 1992, Park and colleagues created another study looking at adherence behaviors in older adults. The older adults were assigned to no intervention, a 7-day with times organizer, an organizational chart describing medication events on an hourly basis for one week, or both. An overall compliance rate of 89% was found for all groups (Park et al., 1992). The patients did best with both interventions. This indicates the two aids together are effective at reducing the cognitive stress of organizing the medications and remembering when to take them. However, if only one intervention were used, the patients in the medication organizer group were almost twice as compliant as the organizational chart group (Park et al., 1992). This supports the idea that multiple interventions are best in improving patient compliance.

Another study looked at the use of multiple interventions through a pharmacy care program aimed at improving medication compliance of hypertensive and hyperlipidemic patients
(Lee, Grace, & Taylor, 2006). This program used multiple intervention methods already discussed. These included patient education, pharmacist interviews, and blister packs dispensed for each day, both morning and evening. Medication adherence in these patients increased from 61% to 97% after the 6-month program. Not only did these patients exhibit improved adherence, but they also showed significant health improvements shown by decreased systolic blood pressure and LDL cholesterol. However, it is hard to tell which intervention was mostly correlated with the improved compliance seen in this study since each intervention was not studied individually. Patients in this study may have been compliant solely because they knew they were being studied or just discarded their medications. Regardless, this study shows the combination of multiple interventions can significantly increase patient compliance. This increased compliance, in turn, can significantly improve health outcomes. As a result, it is necessary health care professionals and older patients use multiple interventions to decrease inappropriate prescribing and medication use in older adults.
Conclusion

Researchers have made considerable strides in the area of prescribing and medication use in older adults. This is a large accomplishment because the specific effects of medications on older adults was not looked at until the 1990s (Cavanaugh & Blanchard-Fields, 2006). However, there is still much ground to cover. Since Beers created his prescribing criteria for nursing home patients in 1991, many other researchers have made valuable contributions to this area of research. Various sets of criteria have been established (Beers, 1997; Beers et al., 1991; Fick et al., 2003; McLeod et al., 1997; Naugler et al., 2000), but these criteria must be regularly updated to reflect new information and new medications. No updated prescribing criteria, however, were found in the literature since the last update of the Beers criteria in 2003 by Fick and colleagues and some researchers agree these criteria need updating (O'Mahony & Gallagher, 2008). The Beers criteria and other sets of criteria are widely used in research, however have not made it into mainstream medical practice…yet.

Older adults only make up 12% of the U.S. population (Administration on Aging, 2006) yet consume over 2.5 more prescription medications than the rest of the population combined (Stagnitti, 2007). But, 12-24% of community-dwelling older adults (Curtis et al., 2004; Fu et al., 2004; Hanlon et al., 2002; Maio et al., 2006; Viswanathan et al., 2005) and 32-40% of acutely ill and nursing home patients (Gallagher et al., 2008; Laroche et al., 2006) consume an inappropriate mediation according to the published prescribing criteria. Therefore, it is clear that inappropriate prescribing in older adults remains a large problem.

Inappropriate prescribing and medication use in older adults seems to be an unavoidable issue. It is inevitable that the aging process and physiologic changes that take place in older adults will cause them to develop chronic medical conditions requiring pharmacologic therapy.
As a result, the general rule “go low and go slow” is often used when prescribing medications to older adults in order to avoid toxic effects. However, it is not always bad to prescribe multiple medications in this population and it is important that healthcare professionals know where the balance is.

The published criteria provide prescribers with a good baseline to consider when prescribing to older adults. These criteria often do not address all aspects of prescribing, such as duration, dosage and medication omissions. However, some studies considered these aspects when determining the appropriateness of a medication. Many times the specific criteria used to determine appropriate medications were not specified and studies were done outside the United States where there are different prescribing laws. Regardless, many studies still added the use of an expert opinion to determine whether medications were appropriate or another medication should have been added to an older adult’s regimen. Furthermore, these criteria generally apply to older adults age 65 and older. However, not all adults age the same way and at the same rate. An older adult’s chronological age does not equal his or her functional or physiologic age. For example, two 20-year-olds are much more similar functionally and physiologically than two 80-year-olds (Ballentine, 2008). As a result, older adults will have a wide range of drug responses. Prescribers must use their clinical experience and take into account an older adult’s functional age when prescribing medications. Therefore, these criteria should not supersede the clinical judgment of a healthcare professional.

Healthcare professionals should rather use these criteria as a guideline for medications to use with caution in older adults. The updated Beers criteria (Fick et al., 2003), for example, includes many specific drugs (e.g., doxazosin and clonidine) from various drug classes (e.g., alpha-blocker, alpha2-agonists). However, several other drugs from each class are not included
in the criteria despite having a very similar mechanism of action. Additionally, many researchers studying the pharmacology of medications in older adults seem to focus on the general class of medication as opposed to each specific medication. Prescribers should, therefore, be aware of which medication class each individual drug in the published prescribing criteria belongs to. As a result, if a prescriber is considering a particular medication from these classes for therapy in an older adult, he or she should proceed with caution. The practitioner should use his or her clinical expertise over a list of criteria, keeping in mind that no list of criteria is perfect. However, the clinical judgment of a prescriber may also contain flaws, therefore necessitating intervention.

It is hard to conclude which intervention worked best since most of the intervention studies mentioned in this review demonstrated promising results. Some results were more significant than others, but many intervention studies were not blinded, meaning the study participants knew they were being studied. Although, this may have contributed to the significance of the results, it is also evident that many prescriber and patient factors must go into consideration before deciding which intervention is best. For example, many interview and computerized interventions require many financial resources, time, and effort. However, other interventions, such as fixed-dosing or combination regimens require relatively no time to achieve considering a prescriber must fill out a prescription anyway. Interventions, such as the medication assessment, patient education and a medication summary of changes should be expected at most office visits, however are not always done (Tarn et al., 2006). Medication organizers are relatively cheap and improve patient compliance a great deal, but depend on the cognitive ability of the older adult patient. Therefore, one specific intervention will not be helpful for all healthcare providers and older adults.
Prescribing and medication use interventions are very individual specific. The prescribing interventions depend greatly on the resources and personnel available to healthcare professionals. In turn, prescribers must take individual patient factors into account when deciding which intervention would be best to increase a patient’s compliance. This is the same idea that no single medication will provide the same outcome for all older adults, so prescribers must choose one medication among many that works best for an individual patient. Although, most of the individual intervention studies showed mildly promising results, Lee and colleagues (2006) were on the right track by combining several interventions (education, blister packs and pharmacist interviews) to achieve a 97% patient compliance rate. Few studies came close to achieving these same results. Additionally, this particular study did not take into account whether the older adults were taking appropriate medications according to prescribing criteria. This may indicate multiple interventions are needed to achieve a near 100% appropriate prescribing rate.

In conclusion, inappropriate prescribing in the older adult population remains highly prevalent today. Healthcare professionals and patients need to take multiple steps to decrease the prevalence of inappropriate prescribing and medication use. However, it is difficult to make generalizations when considering older adults and each situation must be looked at individually. It is hard to generalize which medications or interventions will work best for an older adult if all cognitive, physiologic and functional aspects of that individual are not addressed. The clinical judgment of a healthcare professional carries much value when deciding the appropriate treatment(s) and intervention(s) for an older adult. The published prescribing criteria discussed in this review, however, provides healthcare professionals with solid foundation on which they can build their knowledge of appropriate prescribing in older adults. With this knowledge and by
strategically using the interventions mentioned above, healthcare professionals can take part in decreasing the prevalence of inappropriate prescribing and medication use in older adults.
References


Appendix A

Cockcroft and Gault equation to estimate the creatinine clearance or GFR (Cockcroft & Gault, 1976):

Creatinine Clearance for men  =  \[
\frac{(140 - \text{age}) \times (\text{lean body weight in kg})}{72 \times \text{serum creatinine}}
\]

Creatinine Clearance for women  =  \text{above equation} \times 0.85
### Table 1. 2002 Criteria for Potentially Inappropriate Medication Use in Older Adults: Independent of Diagnoses or Conditions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concern</th>
<th>Severity Rating (High or Low)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propoxyphene (Darvon) and combination products (Darvon with ASA, Darvon-N, and Darvocet)</td>
<td>Offers few analgesic advantages over acetaminophen, yet has the adverse effects of other narcotic drugs.</td>
<td>High</td>
</tr>
<tr>
<td>Indomethacin (Indocin and Indocin SR)</td>
<td>Of all available nonsteroidal anti-inflammatory drugs, this drug produces most CNS adverse effects. Narcotic analgesic that causes more CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs. Additionally, it is a mixed agonist and antagonist.</td>
<td>High</td>
</tr>
<tr>
<td>Pentazocine (Talwin)</td>
<td>One of the least effective anisesthetic drugs, yet it can cause extrapyramidal adverse effects.</td>
<td>High</td>
</tr>
<tr>
<td>Trimebuterzamide (Tigan)</td>
<td>Most muscle relaxants and antispasmodic drugs are poorly tolerated by elderly patients, since these cause anticholinergic adverse effects, sedation, and weakness. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.</td>
<td>High</td>
</tr>
<tr>
<td>Muscle relaxants and antispasmodics: methocarbamol (Robaxin), carisoprodol (Soma), chlorzoxazone (Paraflex), metaxalone (Skelaxin), cyclobenzaprine (Flexeril), and oxybutynin (Ditropan)</td>
<td>Do not consider the extended-release Ditropan XL.</td>
<td>High</td>
</tr>
<tr>
<td>Flurazepam (Dalmane)</td>
<td>This benzodiazepine hypnotic has an extremely long half-life in elderly patients (often days), producing prolonged sedation and increasing the incidence of falls and fractures. Medium- or short-acting benzodiazepines are preferable.</td>
<td>High</td>
</tr>
<tr>
<td>Amitriptyline (Elavil), chlor diazepoxide-amitriptyline (Limbritrol), and phenzepoxide-amitriptyline (Travil)</td>
<td>Because of its strong anticholinergic and sedation properties, amitriptyline is rarely the antidepressant of choice for elderly patients.</td>
<td>High</td>
</tr>
<tr>
<td>Dextoxic (Sinequan)</td>
<td>Because of its strong anticholinergic and sedating properties, dextoxic is rarely the antidepressant of choice for elderly patients. This is a highly addictive and sedating anxiolytic. Those using dextoxic for prolonged periods may become addicted and may need to be withdrawn slowly.</td>
<td>High</td>
</tr>
<tr>
<td>Meprobamate (Miltown and Equanil)</td>
<td>Because of increased sensitivity to benzodiazepines in elderly patients, smaller doses may be effective as well as safer. Total daily doses should rarely exceed the suggested maximums.</td>
<td>High</td>
</tr>
<tr>
<td>Doses of short-acting benzodiazepines: doses greater than lorazepam (Ativan), 3 mg; oxazepam (Serax), 60 mg; alprazolam (Xanax), 2 mg; temazepam (Restoril), 15 mg; and triazolam (Halcion), 0.25 mg</td>
<td>These drugs have a long half-life in elderly patients (often several days), producing prolonged sedation and increasing the incidence of falls and fractures. Short- and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.</td>
<td>High</td>
</tr>
<tr>
<td>Long-acting benzodiazepines: chlor diazepoxide (Librium), chlor diazepoxide-amitriptyline (Limbritrol), clonidium-chlor diazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorzepate (Tranxene)</td>
<td>Of all antianxiety drugs, this is the most potent negative inotrope and therefore may induce heart failure in elderly patients. It is also strongly anticholinergic. Other antianxiety drugs should be used. Decreased renal clearance may lead to increased risk of toxic effects.</td>
<td>High</td>
</tr>
<tr>
<td>Digoxin (Lanoxic) (should not exceed &gt;0.125 mg/d except when treating atrial arrythmias)</td>
<td>May cause orthostatic hypotension.</td>
<td>May cause orthostatic hypotension.</td>
</tr>
<tr>
<td>Short-acting dipryidamol (Persantine)</td>
<td>Do not consider the long-acting dipryidamole (which has the longer-acting in older adults) except with patients with artificial heart valves.</td>
<td>May cause bradyarrhythmia and exsorberorheal depression in elderly patients.</td>
</tr>
<tr>
<td>Methyldopa (Aldomet) and methyldopa-hydrochlorothiazide (Aldomet)</td>
<td>May cause bradyarrhythmia and exsorberorheal depression in elderly patients.</td>
<td>May cause bradyarrhythmia and exsorberorheal depression in elderly patients.</td>
</tr>
<tr>
<td>Reserpine at doses &gt;0.25 mg</td>
<td>May induce depression, impotence, sedation, and orthostatic hypotension. It has a prolonged half-life in elderly patients and could cause prolonged hypoglycemia. Additionally, it is the only oral hypoglycemic agent that causes SIADH. G1 antispasmodic drugs are highly anticholinergic and have uncertain effectiveness. These drugs should be avoided (especially for long-term use).</td>
<td>May induce depression, impotence, sedation, and orthostatic hypotension.</td>
</tr>
<tr>
<td>Chlorpropanolide (Diabinese)</td>
<td>SI antispasmodic drugs are highly anticholinergic and have uncertain effectiveness. These drugs should be avoided (especially for long-term use).</td>
<td>SI antispasmodic drugs are highly anticholinergic and have uncertain effectiveness. These drugs should be avoided (especially for long-term use).</td>
</tr>
<tr>
<td>Gastrinonteral antispasmodics: dicyclobeine (Bentyl), hyoscyamine (Levin and Levinson), propantheline (Pro-Banthine), belladonna alkaloids (Donnatal and others), and chlor diazepoxide (Librox)</td>
<td>All nonprescription and many prescription antihistamines may have potent anticholinergic properties. Nonanticholinergic antihistamines are preferred in elderly patients when treating allergic reactions.</td>
<td>High</td>
</tr>
<tr>
<td>Anticholinergics and antihistamines: chlorpheniramine (Chlor-Trimeton), diphenhydramine (Benadryl), hydroxyzine (Vistaril and Atarax), cyproheptadine (Periactin), promethazine (Phenergan), triprolidine, deschlorpheniramine (Polaramine)</td>
<td>May cause confusion and sedation. Should not be used as a hypnotic, and when used to treat emergency allergic reactions, it should be used in the smallest possible dose.</td>
<td>May cause confusion and sedation. Should not be used as a hypnotic, and when used to treat emergency allergic reactions, it should be used in the smallest possible dose.</td>
</tr>
<tr>
<td>Ergot mesylate (Hydromine) and cyclandelate (Cyclospasmol)</td>
<td>Have not been shown to be effective in the doses studied. Doses &gt;325 mg/d do not dramatically increase the amount absorbed but greatly increase the incidence of constipation.</td>
<td>Have not been shown to be effective in the doses studied. Doses &gt;325 mg/d do not dramatically increase the amount absorbed but greatly increase the incidence of constipation.</td>
</tr>
<tr>
<td>Ferrous sulfate &gt;325 mg/d</td>
<td></td>
<td>Doses &gt;325 mg/d do not dramatically increase the amount absorbed but greatly increase the incidence of constipation.</td>
</tr>
<tr>
<td>All barbiturates (except phenobarbital) except when used to control seizures</td>
<td>Are highly addictive and cause more adverse effects than most sedative or hypnotic drugs in elderly patients.</td>
<td>Are highly addictive and cause more adverse effects than most sedative or hypnotic drugs in elderly patients.</td>
</tr>
<tr>
<td>Drug</td>
<td>Concern</td>
<td>Severity Rating</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Meperidine (Demerol)</td>
<td>Not an effective oral analgesic in doses commonly used. May cause confusion and has many disadvantages to other narcotic drugs.</td>
<td>High</td>
</tr>
<tr>
<td>Ticlopidine (Ticlid)</td>
<td>Has been shown to be no better than aspirin in preventing clotting and may be considerably more toxic. Safer, more effective alternatives exist.</td>
<td>High</td>
</tr>
<tr>
<td>Ketorolac (Toradol)</td>
<td>Immediate and long-term use should be avoided in older persons, since a significant number have asymptomatic GI pathologic conditions.</td>
<td>High</td>
</tr>
<tr>
<td>Amphetamines and anorectic agents</td>
<td>These drugs have potential for causing dependence, hypertension, angina, and myocardial infarction.</td>
<td>High</td>
</tr>
<tr>
<td>Long-term use of full-dosage, longer half-life, non-COX-selective NSAIDs: naproxen (Naprosyn, Avapro, and Aleve), oxaprozin (Daypro), and piroxicam (Feldene)</td>
<td>Have the potential to produce GI bleeding, renal failure, high blood pressure, and heart failure.</td>
<td>High</td>
</tr>
<tr>
<td>Daily fluoxetine (Prozac)</td>
<td>Long half-life of drug and risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation. Safer alternatives exist.</td>
<td>High</td>
</tr>
<tr>
<td>Long-term use of stimulant laxatives: bisacodyl (Dulcolax), cascara sagrada, and Neoloid except in the presence of opiate analgesic use</td>
<td>May exacerbate bowel dysfunction.</td>
<td>High</td>
</tr>
<tr>
<td>Amiodarone (Cordarone)</td>
<td>Associated with QT interval problems and risk of provoking torsades de pointes. Lack of efficacy in older adults.</td>
<td>High</td>
</tr>
<tr>
<td>Orphenadrine (Norflex)</td>
<td>Causes more edema and anticholinergic adverse effects than safer alternatives.</td>
<td>High</td>
</tr>
<tr>
<td>Guanethidine (temelolin)</td>
<td>May cause orthostatic hypotension. Safer alternatives exist.</td>
<td>High</td>
</tr>
<tr>
<td>Guanadrel (Hycore)</td>
<td>May cause orthostatic hypotension.</td>
<td>High</td>
</tr>
<tr>
<td>Cyclosporide (Cyclospasmol)</td>
<td>Lack of efficacy.</td>
<td>Low</td>
</tr>
<tr>
<td>Isosorbine (Vasodilan)</td>
<td>Lack of efficacy.</td>
<td>Low</td>
</tr>
<tr>
<td>Nitrofurantoin (Macrodantin)</td>
<td>Potential for renal impairment. Safer alternatives available.</td>
<td>High</td>
</tr>
<tr>
<td>Dofetilide (Cardura)</td>
<td>Potential for hypotension, dry mouth, and urinary problems.</td>
<td>Low</td>
</tr>
<tr>
<td>Methyldopa (Androfil, Virilon, and Testrad)</td>
<td>Potential for prostatic hypertrophy and cardiac problems.</td>
<td>High</td>
</tr>
<tr>
<td>Thoridazine (Mellaril)</td>
<td>Greater potential for CNS and extrapyramidal adverse effects.</td>
<td>High</td>
</tr>
<tr>
<td>Metoprolol (Serentil)</td>
<td>CNS and extrapyramidal adverse effects.</td>
<td>High</td>
</tr>
<tr>
<td>Short acting nifedipine (Precardia and Acalia)</td>
<td>Potential for hypotension and constipation.</td>
<td>Low</td>
</tr>
<tr>
<td>Clonidine (Catapres)</td>
<td>Potential for orthostatic hypotension and CNS adverse effects.</td>
<td>Low</td>
</tr>
<tr>
<td>Mineral oil</td>
<td>Potential for aspiration and adverse effects. Safer alternatives available.</td>
<td>High</td>
</tr>
<tr>
<td>Cimetidine (Tagamet)</td>
<td>CNS adverse effects including constipation.</td>
<td>Low</td>
</tr>
<tr>
<td>Ethacrynic acid (Edecrin)</td>
<td>Potential for hypertension and fluid imbalances. Safer alternatives available.</td>
<td>Low</td>
</tr>
<tr>
<td>Desiccated thyroid</td>
<td>Concerns about cardiac effects. Safer alternatives available.</td>
<td>High</td>
</tr>
<tr>
<td>Amphetamines (excluding methylphenidate hydrochloride and anorexic)</td>
<td>CNS stimulant adverse effects.</td>
<td>High</td>
</tr>
<tr>
<td>Estrogens only (oral)</td>
<td>Evidence of the carcinogenic (breast and endometrial cancer) potential of these agents and lack of cardioprotective effect in older women.</td>
<td>Low</td>
</tr>
</tbody>
</table>

Abbreviations: CNS, central nervous system; COX, cycloxygenase; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion.


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Abstract

The **objective** of this literature review is to identify interventions effective in decreasing inappropriate prescribing and medication use in older adults. **Methods:** A literature review was performed using MEDLINE and PubMed to identify topics relating to the objective. **Results:** Older adults undergo changes with age that cause medications to work differently. Various prescribing criteria for older adults have been published and nearly 25% of ambulatory older adults were prescribed at least one inappropriate medication. Numerous prescribing and medication use interventions have been identified to reduce these preventable prescribing errors. **Conclusion:** The published prescribing criteria should be used as a general guideline for prescribing in older adults. Each older adult reacts to medications differently, so prescribers should use clinical judgment and the rule “go low and go slow” to avoid adverse effects. In addition, interventions should be used in combination to achieve appropriate prescribing and medication use in older adults.