## EVALUATING PATIENT MEDICATION AND COMPLEMENTARY THERAPIES DOCUMENTATION: COMPARATIVE ANALYSIS OF SOURCES, DISCREPANCIES AND THE POTENTIAL IMPACT OF ERRORS ON PATIENT CARE

by

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University of Pittsburgh, 2009

Complete knowledge of a patient's medications, including over-the-counter and alternative medicines, is essential to the healthcare professional in providing quality care. In addition to the multiple steps from prescribing, dispensing to administering of a drug medication, there are several factors that increase an individual's risk for an adverse event and approaches to reduce medication errors. The movement of healthcare systems to an electronic medical record provides the potential of building a better health care system. This retrospective study compares five sources of medication, medical record chart, specialist, electronic medical record, pharmacy, insurance provider and patient, to determine what is the most accurate source of documentation, and what factors leading to better knowledge and documentation of all of a patient's medications. This study also identifies additional risk factors, specifically drug affordability and the influence it has on a patient's behavior, and discusses some considerations for reducing medication errors. The prevention and reduction of adverse events is of public health significance as there is both a health and financial cost to treating these adverse events.

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### **1.0 INTRODUCTION**

When the Institute of Medicine (IOM) (IOM 1999) reported in 1999 that medical errors kill between 44,000 and 98,000 people in US hospitals per year, there was widespread concern and panic about patient-safety amongst healthcare professionals and the public. Even by utilizing the lower estimate of 44,000 deaths annually, deaths due to medical errors would rank as the eighth leading cause of death making it more prevalent than motor vehicle accidents (43,458) and breast cancer (42,297). Associated with medical errors is a monetary cost. The total annual cost of preventable adverse events (i.e. medical errors resulting in injury) is estimated between \$17 and \$29 billion annually. Over one half of these costs are due to direct health care costs, such as longer stay or treatment. While there has been conflicting opinions on whether these numbers in the IOM Report were exaggerated (McDonald, Weiner et al. 2000) or underestimated (Leape 2000), the report highlighted to the public and government the issue of medical errors on patient safety.

What are some of the underlying causes of medical errors? The National Ambulatory Care Service paints the picture of a growing reality, namely an aging population, multiple coexisting conditions (co-morbidity), increase in medicine therapy, and an increasing electronic medical record environment. In a national probability sample of non-federal office-based physicians in the United States, the National Ambulatory Medical Care Survey (Cherry, 2007) reported an estimated 963.6 million patient visits to physicians offices in 2005, which is an overall rate of 331.0 visits per 100 persons. In one-quarter of these office visits, electronic medical records (EMR) were used by physicians, and in 83.9% of the office visits, the claims were submitted electronically. There also has been a shift in the age of patients seen as the baby boomer generation ages. In 1995, the majority of the visits were by patients 25-44 years of age, while in 2005, the majority of visits were by 45-64 years of age. At least one chronic condition was reported in 52.7% of the patients with hypertension being the most prevalent (22.8%), followed by arthritis (14.3%), hyperlipidemia (13.5%), and diabetes (9.8%). Medication therapy accounted for 679.2 million (70.5%) of all office visits. In 2005, there were about 2.0 million drugs prescribed, in an overall rate of 210.7 drugs per 100 visits. The Kaiser Family Foundation reported for 2007, the sale of 3,457,595,838 prescription drugs in the United States totaling \$202,249,087,162. The retail prescriptions filled by mail order totaled \$53.11 billion or 20.5% of total prescriptions filled in 2007 (Kaiser Family Foundation 2008). This is close to a 100 fold higher than what was reported by the NDC Health (1991-1998) (NDC Health. 1991-1998), which estimated \$2.9 billion retail US prescriptions filled in 2000 which was up 62% from a decade earlier.

This increasing aging population with multiple illnesses (co-morbidity) requiring many medications (poly-pharmacy) increases the risk for medication errors. Kaufman et al. (2000) (Kaufman, Kelly et al. 2002) found that most of elderly patients (over 65 years) in an ambulatory population study took at least one prescription or nonprescription drug or a vitamin, mineral or herbal supplement weekly. Women's rates are higher with 94% who take at least one medication; 57% take five or more, and 12% take ten or more. In comparison, 91% of men use

at least one medication, 44% take five or greater, and 12% take ten or greater. Taking several medications with different regimens can be confusing, the elderly often have trouble understanding instructions (Patel, 2002), and even visiting nurses to the elderly find it difficult to reconcile multiple and conflicting medication orders (Strouse 2003). Complicating the situation further are patients buying prescription drugs on the internet (Anonymous. 2003), taking sample medications that may not be recorded in their chart (Hubbard, 2003) (Strouse, 2003) (Ashley, Kirk et al, 2002) and sharing of prescription medication (Daniel, Honein, et al. 2003). It has also been well known that there are several patients who are prescribed medications but never get them filled, discontinue or alter the prescribed medication regimen, take sample medications, or over the counter or herbal medicines without their physician's knowledge.

A physician's knowledge of which, how and when medications are taken are essential to the management of a patient's care. The recurring theme throughout the IOM report is that the majority of medical errors are due to basic flaws in the way health systems are organized and not solely on individual behavior. It is estimated that the combination of system flaws and human factors leading to adverse drug reactions are estimated to injure or kill more than 770,000 people in hospitals annually (Lesar, Lomaestro et al. 1997) which has been seen in multiple populations.

In looking at documented sentinel events submitted to the Joint Commission on Accreditation of Healthcare Organization (JCAHO), 'system flaws' have included drugs on a patient care unit that are toxic until diluted, illegible writing leading to misinterpretation of orders in medication records, and coordinating care amongst multiple physicians who may or may not have complete information on a patient. Recent approaches to lowering medical errors have included introducing hospital processes and procedures to reduce human errors, volunteer error reporting, to computer-based systems of prescribing, transcribing and dispensing. In 2003, the JCAHO issued "National Patient Safety Goals". Five of the six goals relate to medications: improve the accuracy of patient identification (requires two independent identifiers); improve the effectiveness of communication among caregivers ('read back' all verbal and telephone orders and use standardized abbreviations); improve the safety of using high-alert medications (remove concentrated electrolytes from patient care areas); improve the safety of infusion pumps (freeflow protection); and improve the effectiveness of clinical alarm systems (JCAHO 2003). The federal government is encouraging the implementation of systems such as the electronic medical record, to strengthen the process of detecting and preventing medication errors, especially adverse drug reactions (ADRs).

The idea behind this study originated through a series of observations from being part of a care team in an ophthalmology clinic looking at how the medication history is gathered and shared with the internal and wider health care team of the patients (i.e. the primary care physician, family members, etc.). There is a growing awareness of how alternative medications can interfere or enhance a prescription medication, and a movement of health care organizations towards an electronic medical record system with anticipation of creating a safer, health care system. The last compelling thought was in discussion with a colleague. The hallmark of treating patients is that physicians trust that patients get the prescriptions filled and take the medications accordingly. The question of the role of insurance companies came into place. Information goes into insurance companies about what has been filled with little to no feedback to the prescribing physicians. While it does not guarantee that the patient has taken the

medication, the resultant question became how does one create a safer, health care system? What types of information is helpful, timely and should be considered as part of the EMR system or any other system. To answer this question, one first needs to answer what is the best source of a patient's medication history.

### 1.1 PROBLEM STATEMENT

A large part of medication errors are due to the plethora and complexity of medications available, the multiple steps involved in prescribing a medication and the number of people involved. In the most simplistic case as illustrated in figure 1, after the physician determines the problem, prescribes the appropriate medication including dosage, the patient gets the prescription filled, the pharmacist transcribes and dispenses the medication, and the patient takes the medication as prescribed whether administered / assisted by a healthcare provider, family member / friend, or self.

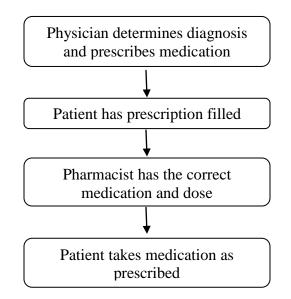


Figure 1: Medication Prescription Process

Within and between each of these steps are many opportunities for potential errors such as ordering (wrong dose, wrong choice of drug), transcribing (wrong frequency of drug administration, medication not transcribed, unclear handwriting, similar drug names being confused), dispensing (wrong drug, wrong dose, drug not available for dispensing), or administering (wrong dose of drug, over or under taking a medication, instructions on how to take the medicine unclear or not followed by patient), monitoring (not noting the effects of a given medication or allergies) and use (over or under taking of a medication).

The United States Pharmacopoeia (USP) (2002) reports that omission errors, incorrect doses, and administration of the wrong drug products had remained the same top three causes of medication errors in 1999 and 2000 as reported by health systems. Three percent of errors either harmed or killed patients. In direct observation of paper-based prescribing in medical/surgical ICU in a tertiary care medical center there were 185 incidents over 16.5 days. After removing the non-preventable and non-clinically significant observations, 110 of the remaining 132 (83%) led to potential ADR of which 22 (17%) led to actual, preventable ADR. Thus there was one error for every five doses of medication administered. All of the actual, preventable ADR occurred in the prescribing (77%) and administration (23%) stages. Errors included omission (23%), wrong dose (20%), wrong drug (16%), wrong administration technique (15%) and drug-drug interaction (10%). (Koop, Erstad et al. 2006). Other system errors were identified in a 2005 National Survey of the Work and Health of Nurses in Canada. A multivariate association was positively associated with working overtime, role overload, perceived staffing or resource inadequacy, low co-worker support, and low job security (Wilkins and Shields 2008).

In ten-year period looking at the types of ADRs among children in a retrospective chart review in a community-based, tertiary care, children's teaching hospital, Le et al. (Le, Nguyen et al. 2006) reported 1087 ADRs. The severity of most ADRs were low (rash, flushing, puruitus were the top three observations) occurring 89% predominantly in the general pediatric unit and NICU. The higher levels of severity (requiring treatment and in two cases resulted in death) occurred in 11% of reported cases that led to hospitalization or occurred during surgery and were noted among certain classes of drugs (anticonvulsants and anti-neoplastic agents). In the voluntary reporting system, pharmacists reported the most ADRs (89%), followed by nurses (10%) and then physicians (<1%). Of the 93% of ADRs documented, only 29% were noted in the patient's medical chart, 13% included follow-up education for the individuals involved, and 10% were updated in the allergy profile of the hospital computer system. (Le, Nguyen et al. 2006). In another study, a multidisciplinary panel of geriatric health care professionals aimed to reach consensus on a list of clinically important drug-disease interactions in older adults and to determine the prevalence of these interactions. Of the 28 individual drug-disease interactions involving 14 diseases or conditions, 2.5 (15.3%) of the 1340 veterans in the sample had  $\geq 1$ drug-disease interaction. The two most common drug-disease interactions were use of firstgeneration calcium channel blockers in patients with congestive heart failure and use of aspirin in patients with peptic ulcer disease (both, 3.7%) (Lindblad, Hanlon et al. 2006).

The JCAHO now requires accurate and complete medication reconciliation for all patients admitted to the hospital (JCAHO 2006). Specifically hospitals are expected to obtain a list of home medications from patients and compare it to their list of medications. Ideally, this should be compiled on admission or within the first 24 hours of admission. What has become challenging is the growing interest in complementary and alternative medicines (CAMs). Media hype and disappointment with current conventional medicines, has more patients turning to alternative treatments. As the human body is comprised of several interacting biological systems, a medication or CAM benefiting one disease may create potential problems in another part of the body. An example of dual conflicting effects in just the eye is the use of the herb Lily of the Valley. Lily of the Valley is used to treated unspecified conjunctivitis, however, has also been associated with disturbance of color perception (Fraunfelder 2004).

In a Canadian sample of 193 older adults with cognitive impairment, 15% used at least one herbal remedy and of these, 13.8% used two herbs and 44.8% used three or more herbs (Lee, Dergal et al. 2001). In a survey of herbal supplement use in a sample size of 271 individuals older than 50 years, mean use of prescription drugs was 2.26 and 5.91 for herbal and nutritional supplements, including 2.66 herbal extracts (Canter and Ernst 2004). These products were used to treat existing health problems (31% of users), prevent a particular disease (27%), promote general health (78%) and provide nutrients missing in their diet (52%) (Canter and Ernst 2004). Herbal products are also commonly used by patients with certain chronic medical conditions, including breast cancer (12%) (Burstein, Gelber et al. 1999), liver disease (21%) (Strader, Bacon et al. 2002), human immunodeficiency virus (22%) (Kassler, Blanc et al. 1991), asthma (24%) (Blanc, Trupin et al. 2001), and rheumatological disorders (26%) (Rao, Mihaliak et al. 1999).

In a 1990 survey of 1,539 adults, 33.8% of respondents used herbal medicines or nutritional supplements. By 1997, the number had increased to 42.1%, with most people paying the cost out-of-pocket (Eisenberg, Kessler et al. 1993; Eisenberg, Davis et al. 1998). The U.S. public spent an estimated \$36 billion to \$47 billion on alternative therapies in 1997. Of this

amount, between \$12 billion and \$20 billion was paid out-of-pocket for the services of professional alternative health care providers. These fees represented more than the public paid out-of-pocket for all hospitalizations in 1997 and about half of what was paid for all out-of-pocket physician services. An estimated \$5 billion of out-of-pocket is spent on herbal products (NCAM 2007).

Despite the growing interest in herbal medicines, it is estimated that only 23-40% of herb and nutritional supplement use by people greater than 65 years of age was known to their doctors (Eisenberg, Davis et al. 1998), (Cohen, Ek et al. 2002), (Canter and Ernst 2004). In a separate study, 64% of geriatric patients took CAM, but their use was documented in only 35% of medical charts, and 25% of people were taking herbal products with anticoagulant properties at the same time as prescribed anticoagulants (Cohen, Ek et al. 2002). Even if the patients informed their providers about their use of complementary and alternative medications, it is not clear that the information would be used effectively. A survey of 165 physicians at the State University of New York Health Service Center at Brooklyn found that most physicians lacked basic knowledge about CAMs and were reluctant to inquire about their properties (Silverstein and Spiegel 2001).

Many physicians do not ask further about CAMs because the mechanism, appropriate dosage amount and length of therapy for herbal medicines are unknown. Prescription drugs and overthe-counter, nonprescription drugs are monitored by the U.S. Food and Drug Administration (FDA) because they are sold for a specific indication and are marketed over state lines. By contrast, herbal medicines and nutritional supplements are not marketed to treat specific diseases, are exempt from interstate commerce law, and fall under the purview of the Dietary Supplement and Health Education Act of 1994. No efficacy or safety has to be proven to sell these agents (Fraunfelder 2004). The National Registry of Drug-Induced Ocular Side Effects lists the impact of herbal medicines. They have received 263 spontaneous reports, in addition to 60 case reports from the literature, citing canthaxanthine, chamomile, *Datura, Echinacea purpurea, Ginkgo biloba*, licorice, niacin and vitamin A are all associated with clinically significant ocular side effects (Fraunfelder 2004). Thus while the exact mechanism, appropriate dosage amount and length of herbal medicines is unknown, herbal medicines do affect the medicine therapies and increases a patient's risk for side effects making it difficult for a physician to determine the involvement and significance of CAM.

Checking for medication errors has typically fallen upon various members of the health care team most often the physician and nurse. While not typically considered part of the health care team, the role of the pharmacist to determine whether there may be potential adverse drug interactions when filling a prescription is becoming an increasing reality. A pharmacist in a behavioral health unit of a community hospital reviewed the patient's medications within 18 hours of admission after a technician. The mean number of medication discrepancies per patient was 2.9. Of these, 48% were related to an omitted or incorrect medication, 31% to an omitted or incorrect dose, and 13% to an omitted or incorrect frequency, 8% were miscellaneous (Lizer and Brackbill 2007). However, a pharmacist checking medication discrepancies assumes that the patient utilizes the same pharmacist or all of his/her medical information is located in a centralized patient-pharmacy database, and the herbal medicines are documented. This seldom is the case.

In these various pathways, there are multiple opportunities for medical errors whose affects can range from none, allergic reactions to life threatening. As it is a multiple process system, reducing medical errors becomes everyone's responsibility (Peth, 2003). This study focuses on a specific part of the prescription pathway that is the source of medication documentation and assumes that the participants were properly diagnosed and treated accordingly with best practice medicine. A physician with inaccurate information can have serious impact on the treatment of a patient, it may make the difference between prescribing a new medication, discontinuing or renewing a prior medication leading to a healthier or more sick patient. The physician must weigh the patient's health with the risks and benefits of the prescription. Thus when inaccurate or incomplete information is available, there is a potential risk for declining health status or adverse drug events, which is any injury resulting from a medical intervention related to a drug, usually undesirable. The adverse event can range from a rash, reduced effectiveness of a drug, to death.

### **1.2 PURPOSE OF THE STUDY**

In light of the movement towards more technological aided systems such as the electronic medical record and the computer physician order entry (CPOE), there are two main objectives to this study that focuses specifically on medication documentation. The first is a comparative analysis looking at the sources of medication documentation. The specific aims of the study are:

1. Determine whether medication documentation in a (a) chart; (b) computerized physician order entry system (CPOE – i.e. EasyScript) in an electronic medical record; (c)

pharmacy record; (d) insurance companies; (e) specialist and (f) as reported by the patient are comprehensive (i.e. does their medication list includes medications prescribed by all healthcare providers). Comparison of all the sources will allow for some analysis of both human and system errors, as well as outline paths of communication of information.

- 2. Determine the extent of awareness by the various physicians on which and on how medications are taken by a patient (medication discrepancy). This includes determining the extent to which medications are prescribed but not filled, administered differently than is prescribed, not taken on a consistent basis, taken in a self-medicated manner outside of the prescribed route or is self-medicating.
- Determine the potential impact of errors on disease management of a patient and clinical alerts (includes drug-drug interactions, drug allergies, dosage checks, duplicate therapies).

The second objective given the findings in the first objective is to identify the potential feasibility of establishing a collaboration of shared information between the academic medical institution utilizing a CPOE system, health plan and pharmacy to help improve patient care and thereby reduce medication errors. The benefits to the physician are readily obvious in providing better care by knowing what the individual is taking, and both the physician and pharmacy are then able to check for drug-drug- or drug-homeopathic interactions. Incorporating the use of insurance or health plan data, which contains all of the reimbursed medical interactions on a patient is extremely helpful to physicians, but as well serves to encourage and be able to market to individuals to stay within the medical, pharmacy system as they are able provide comprehensive care. Reducing potential adverse drug events helps all of the individuals

involved including avoidable sick time to the patient, physician time and medical expenses to the healthcare provider. This is the first study that looks at comparing so many different sources of medication with the hopes of shedding some light on what factors should be considered in order to provide healthcare providers and patients with the most accurate, up-to-date and readily accessible information.

## **1.3 DEFINITION OF TERMS**

**Medication or medicine** has a variety of definitions but generally is referred to as a drug or remedy.

**Polypharmacy** is the use of multiple medications and / or the administration of more medications than are clinical indicated, representing unnecessary drug use (Hajjar, Cafiero et al. 2007). Although, there is not a specific number, it commonly refers to patients taking four or more medications (Milton and Jackson 2007).

**Herbal medicines** are plants or plant extract for medicinal purposes. Herbs are generally defined as any form of a plant or plant product, including leaves, stems, flowers, roots and seeds. As they are a food source and herbal medicines are not regulated by the federal government like prescription medicine. Sometimes the scope of herbal medicine extends to include fungi and bee products, as well minerals, shells and certain animal parts.

**Conventional or contemporary medicine** is health science, biomedical research, and medical technology to diagnose and treat injury and disease typically through medication, surgery, or some other form of therapy. Conventional medicine is practiced by holders of M.D. (medical doctor) or D.O. (doctor of osteopathy) degrees and by their allied health professionals, such as physical therapists, psychologists, and registered nurses. (NCAM 2007)

Alternative medicine encompasses any healing practice that does not fall within the realm of conventional / contemporary medicine (i.e. is used in place of conventional medicine). Examples of alternative medicine include naturopathy, chiropractic, herbology, traditional Chinese medicine, Ayuveda, meditation, yoga, biofeedback, hypnosis, homeopathy, acupuncture and diet-based therapies.

**Complementary medicine** refers to use of alternative medicines together with conventional / contemporary medicine techniques. An example of complementary therapy is using a special diet to treat cancer instead of undergoing surgery, radiation or chemotherapy that has been recommended by a conventional doctor. This is often under the term of complementary and alternative medicine (CAM) (NCAM 2007).

**Medical Chart** is the confidential document that contains detailed and comprehensive information on the individual patient and their care experience.

**Co-morbidity** has been defined as (1) the concurrent presence of two or more chronic diseases or conditions; (2) (in people with disabilities) other medical conditions unrelated to the primary

disabling condition; and (3) the co-existence of other conditions with a defined index condition (Siebens 2007).

**Electronic Health Record (EHR)** is an individual patient's medical record in digital format. EHR coordinate the storage and retrieval of individual records. EHRs are usually accessed over a network, and may be made up of electronic medical records from multiple locations or sources.

**Electronic Medical Record (EMR)** is a patient's localized medical record in digital format. In health informatics, an EMR is considered by some to be one type of electronic health record, but in general usage of the terms EHR and EMR are used synonymously.

**Computerized Physician Order Entry (CPOE)** is the process of electronic entry of physicians' instructions for the treatment of patients under his or her care. These orders are communicated over a computer network to the medical staff (nurses, therapists or other physicians) or to the departments (pharmacy, laboratory or radiology) responsible for fulfilling the order (Farlex 2008).

**Medication reconciliation** is the process of comparing a patient's medication orders to all of the medications that the patient has been taking (JCAHO 2006).

**Medication errors** are defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use (NCC-MERP 2008).

Adverse event (AE) or drug event (ADE) or reaction (ADR) is any injury resulting from a medical intervention related to a drug, usually undesirable. Examples of such injuries include heart rhythm disturbances, diarrhea, fever, nausea and vomiting, renal failure, mental confusion, rash, low blood pressure, and bleeding (NCC-MERP 2008). An individual's response can vary from other individuals due to the person's disease state, age, weight, gender, ethnicity and general health. ADRs can also occur when commencing, decreasing/increasing dosages or ending a drug or medication regimen. ADRs can lead to non-adherence to taking a medication when there is a reaction. When the effect of a drug or medication is severe, the dosage may be adjusted or an additional medication may be added. Potential ADRs are defined as the potential to harm a patient (near-misses). ADRs can be further classified into intercepted (intercepted before it reaches a patient) and non-intercepted (reaches the patient but does not cause injury because the patients has sufficient physiological reserves).

#### 2.0 LITERATURE REVIEW

There are several factors that can increase a patient's risk for medical errors. While each alone is a factor, the combination of factors compounds the risk for adverse events and medical errors overall. These risk factors are in addition to the system errors mentioned earlier.

## 2.1 RISK FACTORS FOR ADVERSE DRUG REACTIONS

## 2.1.1 SIMILAR DRUG NAMES

Nearly 1,500 commonly used brand and generic drugs have similar names or look alike to other drugs that has confused patients. Together, these drug names contribute to more than 3,170 confusing drug name pairs (Pharmacopeia). These look and sound alike drugs are estimated to account for 25% of the medication errors that occur every year. For example,

- Clonidine (for high blood pressure) and Klonopin (for seizures)
- Celebrex (a painkiller) and Celexa (an antidepressant)
- Lamictal (for epilepsy) and Lamisil (an antifungal)
- Zyprexa (for schizophrenia) and Zyrtec (an antihistamine)

Many of the mix-ups involve a pharmacist having difficulty reading a physician's handwriting. However, even with computerized prescription systems, errors can occur when a physician could incorrectly click on the wrong item. For example, someone can miss clicking on 'Actos' versus 'Actonel'. Alternatively, a pharmacist could end up reaching for the wrong drug which was organized alphabetically but in the wrong order.

While the Food & Drug Administration (FDA) rejects about one-third of all proposed new drug names each year because they sound or look similar, there are too many drugs on the market to track them all. In a few cases, the mix-ups have been so frequent that the names of drugs have changed. For example after two deaths, the drug Reminyl prescribed for Alzheimer's was confused with the old diabetes drug Amaryl, and is now changed to Razadyne. Similarly, the cholesterol pill Omacor is now named Lovaza after being mixed up with the blood-clotting medication Amicar. The U.S. Pharmacopeia has recently created a USP's Drug Error Finder allowing a user to search more than 1,400 drugs involved in look-alike and/or sound-alike errors. They recommend that the indication for use be written beside the name of the medication.

## 2.1.2 HEALTH LITERACY

Health literacy is "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions" (Ratzan and Parker 2006). An individual's health literacy is important because what he/she understands helps shape his/her actions. It can mean the difference of taking a medication or not, or unknowingly altering the medication frequency or dose taken.

In a study evaluating knowledge of 172 patients newly prescribed medication after hospital discharge, between 4 and 18 days after discharge, patients were contacted via phone and asked

about the name, number, dosages, schedule, purpose, and adverse events of the new medication. Of the respondents, 86% were aware that they were prescribed a new medication, 64% could identify the name, 74% the number of new medications, 56% dosages, 68% schedule, and 64% purpose. Only 11% recalled being told the adverse events, and 22% could name at least 1 adverse event. Older patients were found to answer fewer questions correctly (Maniaci, Heckman et al. 2008).

#### 2.1.3 PHARMACOKINETIC AND PHARMACODYNAMIC CHANGES

The per capita consumption of drugs taken by older people is higher than the rest of the population. For example, in 2005, CAD \$24.8 billion was estimated to be spent in Canada on drugs of which 44% were prescribed to those aged 65 years and older (2006). In a study looking at the causes of ADRs, beta-blocker, diuretic, angiotensin-converting enzyme inhibitor, aspirin and non-steroidal anti-inflammatory drugs accounted for 82% of all ADRs. These events were more common with advanced age of patients, greater number of consultation problems and prescribed drug items (Tam, Kwok et al. 2008).

Therefore, in addition to the several types of interactions: drug—drug, drug—disease, drug—food, drug—alcohol, drug—herbal products, and drug—nutritional status, there are also age-related changes. As an individual ages there are changes in pharmacokinetics (what the body does to the drug), pharmacodynamics (what the drug does to the body), frailty, inter-individual variability (individual genetics, lifelong habits, and environment will result in heterogeneity between patients as they age), reduced homoeostatic mechanisms (cellular, organ, and systems reserves decrease with age), and psychosocial issues. These all need to be considered when drug

interactions are assessed and contributes to the unpredictability on how an individual will respond.

#### 2.1.4 COGNITIVE IMPAIRMENT OF OLDER POPULATIONS

Age-related changes in physical functional capacity, sensory acuity, and cognition are prevalent in older populations. It has been found that complexity of medication regimen alone does not necessarily lead to difficulties in medication management. The degree to which older adults possess and can apply psychomotor and cognitive abilities to the tasks required to administer medications as prescribed or directed also determines their capacity for medication management. In a retrospective study of 301 participants that were part of a self-medication program in a rehabilitation hospital, they measured the medication complexity index. The complexity index is the number of tablets taken per dose, the number of daily doses of medication taken each day, and additional directions that must be followed to manage medication regimens. As an example, one tablet three times a day = 3 versus One tablet three times a day with food is 3 + 3 = 6). The researchers found that the mean probability of making errors increased with Medication regimen complexity and MMSE (Mini-Mental State Exam) score. This was also found to be related to their functional ability to cook and MMSE score (Maddigan, Farris et al. 2003).

#### 2.1.5 PATIENT'S AND CAREGIVER'S KNOWLEDGE

Successful treatment of patients requires adherence to prescribed medications that have been found to be associated with the caregiver's involvement and patient's knowledge of drugs and drug treatment. The lack of adherence may lead to therapeutic failure with risks of relapse, progression of disease and prolonged illness and treatment. Ulfvarson et al. (Ulfvarson, Bardage et al. 2006) conducted structured interviews with 200 patients who had been recently treated in a medical ward. The mean age of patients was 79 years. The number of drugs reported in the medical chart ranges from 1 to 17 with the mean of 6.9, the number reported by patients was 7.3. When comparing the interview results with the information in the medical charts, 30% of the patients showed adherence. Patients who were non-adherence reported a higher consumption of drugs. There was no association between education level but implicate the quality of information influences adherence.

### 2.1.6 CO-MORBIDITY

Co-morbidity is defined as a chronic condition that coexists in an individual with another condition that is being described. For example, the presence of chronic heart failure such as arrhythmias in combination with conditions that predicate and contribute to the etiology such as hypertension, diabetes mellitus and hyperlipidaemia (Lang and Mancini 2006). Therefore, patients tend to take multiple medications for the various conditions. It is thus not surprising that co-morbidity has been associated with multiple medications and increased ADRs. It has also been associated with physical disability, higher health care use, poorer quality of life, and increased mortality (Boyd, Darer et al. 2005).

#### 2.1.7 **POLYPHARMACY**

The use of multiple medications (i.e. polypharmacy) in the elderly population is common, comprising 15% of the population. Twenty-three percent of women and 19% of men older than

65 years take at least five prescription drugs. Fifty-seven percent of women take more than five medications including over-the-counter drugs (Kaufman, Kelly et al. 2002). Polypharmacy can occur when multiple medications are being prescribed or when patients remain on the same treatment, sometimes unnecessarily.

All medications have the potential for adverse events, therefore, it is not surprising that the percentage of ADRs increases with the number of medications. In looking at emergency department visits, out of 205 consecutive visits, there were 226 potential ADRs. It was found that the probability of an ADR increases the risk from 13% for two drugs to 82% for over seven drugs. (Goldberg, Mabee et al. 1996) In a geriatric nursing home setting, after adjusting for the number of days of stay, it was found that for participants taking  $\geq$  9 different scheduled medications was at a 2.33 times higher than controls for experiencing an ADR (Nguyen, Fouts et al. 2006). In reviewing the literature in the countries of the United States, Canada, Australia, and Europe, polypharmacy was to be statistically significant predictor of hospitalization, nursing home placement, death, hypoglycemia, fractures, impaired mobility, pneumonia, and malnutrition.

Haijjer et al. reviewed twenty-one articles on polypharmacy in the elderly, and identified risk factors for polypharmacy from nine studies, which can be classified into three groups: demographic (increased age, white race and education), health status (poorer health, depression, hypertension, anemia, asthma, angina, diverticulosis, osteoarthritis, gout, diabetes mellitus, and use of  $\geq$  9 medications), and access to health care (number of health care visits, supplemental insurance, and multiple providers). They also reported in five studies, the number of

medications taken that were suboptimal or unnecessary for patients over 65 years ranging from 42% to 65%. These medications were classified into either a medication with no indication, lack of effectiveness, or therapeutic duplication (Hajjar, Cafiero et al. 2007). Similar results were found in a study of 128 veterans, 58.6% of patients had  $\geq 1$  unnecessary prescribed drug of which 41.4% was considered inappropriate due to lack of effectiveness. They identified risk factors for this association (P < 0.2) with unnecessary drug use: race (white), income (<\$30,000/year), number of prescription medications (mean 6.8, SD 2.8) and lack of belief in a 'powerful other' for their health locus of control. This last factor suggests that those patients who are less 'trusting' of the health care system are more likely to have unnecessary medication use (Rossi, Yong et al. 2007).

Seventy-five percent of elderly leave a doctor's visit with a new medication (Neary and White 2001). The etiology behind polypharmacy is as complex as the medications and treatment regimens. Ballentine has cited from the patient (hope for benefit, chemophilia, pressure from family, multiple chronic medical disorders, media influence, pharmaceutical industry influence), healthcare provider (following standards of care, disease parameter goals, research funding, perceived therapeutic benefits, pharmaceutical industry influence, cross-titration of lowering one drug while increasing another) and pharmaceutical industry (new drugs/improved technology, advertising", increased 'fast line' "direct to consumer: new drugs, investigator pressure/competition) are some of the multiple reasons contributing to this increase in prescribing of medications (Ballentine 2008). Additionally, as side effects of medications are not always immediate, shifting medications can make it difficult to directly pinpoint the cause.

However, in some conditions the use of multiple drugs is both beneficial and appropriate. For example, diabetes mellitus is often treated with multiple drugs at once. In tuberculosis, three or four drugs are often combined to prevent the emergence of resistant mycobacteria (Aronson 2006). It has thus been suggested that the terminology should be rational or obligatory polypharmacy to recognize legitimate prescribing versus indiscriminate polypharmacy for inappropriate prescribing (Routledge, O'Mahony et al. 2003). Possibly appropriate causes of polypharmacy include: multiple medical problems; and using further medication to treat ADRs. Usually or always inappropriate causes of polypharmacy are: multiple drug prescribers, no regular medication review, using further medication to treat ADRs, and prescribing of drugs that are not indicated (Milton and Jackson 2007).

Part of the challenge in rational polypharmacy is that it is best guided by validated evidence. In accordance with the ethics of clinical research, the participants must be competent to participate in a trial, thus subjects tend to be younger and healthier than the general elderly population. In the absence of high-quality evidence to guide prescribing, clinicians are forced to extrapolate. It then becomes a delicate balance between aggressively treating the patient and not harming the patient. As the population ages and concerns for safety increase, reducing polypharmacy in the elderly is one of the goals of Healthy People 2010.

To help assess polypharmacy, Bushardt et al. (Bushardt and Jones 2005) have developed nine key questions for the clinician to guide and help evaluate polypharmacy:

#### Table 1: Questions to Assist in Evaluating Polypharmacy

- 1. Is each medication necessary?
- 2. Is the drug contraindicated in the elderly?
- 3. Are there duplicate medications?
- 4. Is the patient taking the lowest effective dosage?
- 5. Is the medication intended to treat the side effect of another medication?
- 6. Can I simplify a drug regimen?
- 7. Are there potential drug interactions?
- 8. Is the patient adherent?
- 9. Is the patient taking an OTC medication, an herbal product, or another person's medication?

The challenge with these questions is that it takes time to obtain the most accurate information, to consider the situation and options, and to follow-up with the patient. Additionally, with so many other contributing factors such as pharmacokinetics, adherence, reliability of information, etc. that it can be challenging to determine which of the medications, if any, could be the source of the adverse event.

## 2.1.8 MULTIPLE SOURCES OF PHARMACEUTICALS

#### 2.1.8.1 Multiple Pharmacy Stores

Although, mentioned a few times in the literature as a potential risk factor, there is very little literature looking at the prevalence or impact of patients utilizing numerous pharmacies to concurrently fulfill medications. Choosing a pharmacy involves many factors: geographic proximity, familiarity, established relationships with the pharmacist/pharmacy, satisfaction with service and quality, low waiting times, time efficiency by being able to shop while prescription is being filled, lower costs/special deals, the insurance plan is accepted by pharmacy, or based on a

recommendation family/friend to name a few. Whether a patient ends up visiting multiple pharmacies by chance or choice, the ability of a pharmacist at one pharmacy to detect an adverse event with only a partial medication history increases the risk of an ADR occurring.

#### 2.1.8.2 Mail-Order Pharmacy

Mail-order sales have doubled from 1998 to 2001, from \$10.4 billion to \$20.7 billion, representing 12% of U.S. prescription drug sales (Foundation 2002). This growth is partly attributed to drugs that are supplied through distributors at prices are both reduced for the customer and the client, such as the employer. Thus, pharmacy benefit managers of companies are encouraging enrollees who take drugs regularly to order their prescriptions by mail.

The U.S. Department of Defense (DoD) converted to a mail order system in the early 1990s. Under the co-pay system a 90-day supply for most drugs was \$9 for branded products or \$3 for generics. The advantages for switching to a mail-order pharmacy include: (1) savings of 66% in filling of 90-day supply versus a 30 day supply in the retail network; (2) the government saves on each prescription by using federally-negotiated price discounts with the mail-order pharmacy; and (3) convenience of mail order for patients versus traveling to a pharmacy or military base. In 1999, sales through the mail order pharmacy order program was \$84 million and was expected to reach over \$1 billion in 2000 and a savings to the DoD of \$55 billion (Laurent 2000).

Ordering medications through the mail breaks the pharmacist-patient relationship as there is no longer a face to face interaction. Additionally, there are fewer insurance companies who accept claims through a mail order company causing individuals to pay out-of-pocket.

#### 2.1.9 SAMPLE MEDICATIONS

"Everybody likes something free, and free prescription drug samples are no exception. Patients love to receive them, and doctors feel good about handing them out" (Chimonas and Kassirer 2009). Drug samples are prescription medications packaged as one or more dosage units by a manufacturer or distributor. The drug samples are provided by a pharmaceutical company to a licensed practitioner free of charge, not to be sold but to promote the eventual sale of the drug. It may be a packet, card, blister pack, bottle, container, or other single package. Drug samples are vital for patients when a pharmacotherapeutic regimen is not well established, are poor, uninsured, underinsured, or in need of medications when pharmacies are closed. Drug samples are not to be used for long term or maintenance therapy as this bypasses the pharmacist and the typical safety checks.

In a survey of 131 physicians investigating what are their motivators for dispensing sample drug medications, physicians were presented with three different scenarios and asked to indicate their preferred drug choice, whether they would use a drug sample, and subsequently prescribe the sampled medication. In the first scenario, an insured woman with an uncomplicated lower urinary infection, 17% of respondents reported they would dispense a drug sample, of these respondents, 95% would dispense a drug sample that differed from their preferred drug choice. In the second scenario, 27% of respondents would dispense a drug sample to an uninsured man with hypertension, and 91% of these respondents reported they would dispense a drug sample instead of their preferred drug choice. In the third scenario, 82% of respondents reported they would dispense a drug sample to an uninsured woman with depression. Of these respondents, 49% indicated they

would dispense a drug different from the preferred drug choice. In all three scenarios, avoiding cost to the patient was the most consistent motivator (Chew, O'Young et al. 2000).

Chimonas and Kassirer (Chimonas and Kassirer 2009) highlighted negative consequences of getting something free when it comes to patient-health. The systems for distributing samples are insufficiently controlled, poorly documented, and stored improperly. The samples also have inadequate instructions for use, are poorly labeled or packaged, and aree often expired. A physician giving sample medications directly to the patient by-passes the pharmacist who is often involved in identifying potential harmful drug interactions, intercepting inadvertent medication errors and providing patient-friendly printout of instructions. If the distribution of drugs is inadequately documented in the patients' records, these patients would not be informed to discontinue the medication in the event of a product recall or emergence of new drug complications. Additionally, sample drugs are usually the newest agents on the market and not time-worn or well-tested drugs. An example is Vioxx which was voluntarily recalled in 2004 by Merck & Co., Inc. due to its dangerous and possibly deadly side effects and after the Food and Drug Administration issued a public health advisory. This arthritis drug has been linked to an increased risk of heart attacks, strokes, hypertension, and cardiovascular problems. Physicians would be unaware that they needed to follow-up on these patients if it was not documented in the patient's chart.

In looking at who receives the sample medications, in a U.S. nationally represented survey, only one-third of all sample recipients were of low income (defined as less than 200% of the poverty line). In contrast, those in the highest income category were most likely to have received

the free samples, and those who had continuous health insurance (Cutrona, Woolhandler et al. 2008). Many of the samples are appropriated by physicians for personal or family use or end up in an 'unknown destination" (Morelli and Koenignsberg 1992) (Westfall, McCabe et al. 1997). In one study, nearly half of the pharmaceutical representatives surveyed reported using samples themselves or giving them to their friends and relatives (Tong and Lien 1995). Additionally, the cost of drug samples raises the cost of health care as companies recover marketing costs through higher prices and increased sales volume. The use of samples also promotes the use of expensive products as these are the products patients are most likely to receive as samples.

#### 2.1.10 OVER-THE-COUNTER (OTC) PRODUCTS

Lam and Bradley looked at the prevalence of use and misuse of self-prescribed medications, as well as, individuals's opinions concerning nonprescription medications and dietary supplements in assisted living facilities. Among 29 women and 16 men with a mean ( $\pm$  SD) age of 84.8  $\pm$  6.9 years and a mean of 9.9  $\pm$  6.4 years of education, 84.4% were using self-prescribed OTC medications and dietary supplements at the time of this study. A mean of 3.4 products was used per participant. Nutritional supplements were most frequently used (32% of products), followed by gastrointestinal products (17%), pain relievers (16.3%), herbals (14.4%), topical products (12%), and cold/cough products (8.5%). Potential misuse was identified in 23 (51%) of the participants. Problems in the use of products included duplication (70%), potential drug/disease/food interactions (20.8%), and other inappropriate use (9.1%). The majority (76%) of the participants believed the products were helpful in maintaining health, 56% of them wanted more product information, 49% sought product information from family and friends which is more often than their physicians and nurses (40%) or pharmacists (11%) for advice (Lam and Bradley 2006).

Over-the-counter products can have varying effects on a patient. The most notable is the use of cough and cold medications that contain nasal decongestants, antihistamines, cough suppressants, and expectorants commonly used alone or in combination with other medication to temporarily relieve symptoms of upper respiratory tract infection in children less than 2 years. These coughs and cold medications have been associated with adverse events, including overdoses and deaths (CDC 2007).

### 2.1.11 HERBAL MEDICINES

Despite widespread use, the efficacy of many herbal medicines remains unproven or the evidence is weak (Ernst 2001). The decision to use or not use herbal medicine should ideally be based on a careful risk/benefit analysis. Herbal medicines present several types of risk to health, including intrinsic toxicity, adulteration with toxic substances, and negative herb-drug or herb-herb interactions. Additional specific risks for older people result from reduced clearance risks for older people result from reduced clearance rates of pharmacologically active compounds (Salmond 2002) and a general increase in susceptibility to toxic effects of drugs (Guyton 1991).

The potential for interactions is augmented because even standardized herbal extracts usually contain many rather than a single active ingredient (Guyton 1991) and use of multiple herbal medicines at the same time is common. In a sample size of 804 patients surveyed, 15% used herbal medicines. In 7% of the herb uses (12 cases) there were possible herb-drug reactions that

were classified as mild (no significant harm to patients) with the most common among diabetics taking nopal (prickly pear cactus) resulting in hypoglycemia (Bush, Rayburn et al. 2007). Many healthcare providers are not aware of CAM use by their patients. In one study 35% of patients discussed their use of CAM with their physicians. Most patients did not think that it was important for their physicians to know about it, and 20% did not think their doctor would understand (Eisenberg, Kessler et al. 201). This is further exacerbated by inadequate mechanisms to obtain/report ADRs associated with the use of herbal medicines and herb-drug interactions that would enable a physician to properly assess the use of CAMs.

In a survey of 271 individuals aged over 50 years in Britain, a mean of 2.26 prescription drugs and 5.91 herbal and nutritional supplements, including 2.66 herbal extracts were reported. Of the total number of 1218 herbal and nutritional supplements identified, 32.5% were reported to their doctors. The researchers found neither an obvious trend to either increase or decrease the use of herbal and nutritional supplements with age in either gender. The top seven single herbs that are reported used by patients are shown in the table below (Canter and Ernst 2004). While, the possible interactions are listed, it should be noted that the interactions are diverse and difficult to define and separate from other symptoms and conditions, i.e. increased effects of anticoagulants.

Herb	Reported Reasons for Use	Adverse Events Reported	<b>Possible Interactions</b>
Allium salivum	Heart function; general health; treat/prevent URTI; lower cholesterol; antiseptic /antibacterial; immune system; blood pressure; other	Dilute motion	Increased effects of anticoagulants, antiplatelet drugs; warfarin; reduces blood levels of anti-AIDS drug; inhibitory effect on cytochrome P450 isoenzymes; antihypertensive; lipid-lowering drugs

Table 2: Examples of the Suggested Use and Potential Effects of CAM

# Table 2 continued

Ginkgo biloba	Mental function; circulation; general health; peripheral vascular disease; tinnitus; migraine; other	Pain behind the eyes; bad taste; red and swollen fingers; headache; withdrawal headache and shakes; tingling feet; increased appetite	Increased effect of anticoagulants; increased risk of seizures with antiepileptic drugs and coma with trazodone; increased blood pressure with thiazide diuretics
Echinacea	Treat/prevent URTI; immune system; other	None	Increased effect of chemotherapy; decreased effect of drugs metabolized by cytochrome P450 isoenzymes; decreased effect of immunosuppressants
Oenothera biennis	Menopause; hair and skin; arthritis; breast pain; general health; other	Blood in urine; indigestion	Interaction with antipsychotics; risk of seizure with phenothiazines, other antiepileptic drugs and anaesthetics
Hypericum perforatum	Depression; anxiety; other	Increased sweating and aggravated menopausal flushes; headache; nocturnal erections and facial hair growth	Increased effects of digoxin; MAO inhibitors and serotonin uptake inhibitors; decreased effect of antiepileptic drugs and antidiabetics; increased effect of drugs causing photosensitivity; prolonged opioid-induced sleeping time; is a hepatic enzyme inducer; increases action of P- glycoprotein, thereby reducing plasma levels of drugs metabolized metabolised in the liver, including theophylline, ciclosporin, phenprocoucmon; warfarin, oral contraceptives; delirium with Vaeriana officinlis and loperamide
Ginseng	General health; energy; menopause; potency	None	Eleutherococcus senticosus may inhibit metabolism of hexobarbital; increase execretion of thiamine (vitamin B1); riboflavin (vitamin B2) and ascorbic acid (vitamin C); interact with cardiac, blood pressure medicines, antihyperglycaemics; elevate digoxin; increase effects of monomycin, kanamycin and insulin, Panax ginseng may interact with MAO inhibitors, stimulants and phenelzine; increase effect of antihyperglycaemics, increase INR with warfarin and manic symptoms with phenelzine
Aloe barbadensis	Digestion; general health; constipation; arthritis	Stomach pains	Long-term use may potentiate cardiac glycosides, corticosteroids or antiarrhythmic drugs (loss of potassium); reduce intestinal absorption of other drugs; increased action of antidiabetics

The Dietary Supplement Health and Education Act (DSHEA) of 1994 prohibits the FDA from the regulation of dietary supplements as food additives. Thus without official standards governing the production of alternative therapies in the United States, the potency and purity of these products produced by different companies are subject to substantial variation (Fraunfelder 2004). For example, ginseng (*Panax ginseng*) was evaluated by the American Botanical Council in 2001. They found that only 52% of products marketed as ginseng actually contained any of this botanical (Dharmanada 2002). Thus the difficulty in determining the extent of interactions is exacerbated by the lack of standards in the manufacturing of CAM products being sold presenting a risk factor for adverse events. In an effect to increase public safety, starting December, 2007 all adverse event reported to a manufacturer including herbal and nutritional products must be reported to the FDA within 15 days, thereby allowing the FDA to look at trends.

## 2.1.12 HEALTH INFORMATION BY OTHER SOURCES

Individuals are daily bombarded with messages about how a particular drug/product is beneficial to their health. This is most obviously seen through commercials, magazine advertisements or articles, the personal testimonies of friends and family members who can have similar findings but do not have the same underlying health status, and the growing access to information through the internet whether an advertisement, or an article written by a company or 'expert'. The amount of information given is often brief and to the point, with the list of risks either quickly announced as in a commercial, in small print as in most paper advertisements, or anecdotal as from friends and family members. Regardless, obtaining health information from other sources than one's physician is prevalent.

The direct-to-consumer marketing as in the commercials, advertisements and internet can not only interfere with the physician-patient relationship but puts the consumer in control of their own health. In a national survey looking at factors influencing consumers' opinions about the utility of direct-to-consumer, the researchers found that consumers of varying demographics value the information about both risks and benefits. Their perception of risk information is more important in shaping their opinions than learning about benefits, however, consumers believe that the quality of benefit information is better than that of risk information (Deshpande, Menon et al. 2004).

In the 2003 Health Information National Trends Survey of 6369 individuals, 63% of the US adult population surveyed reported going online for health information. While 62% of respondents expressing a lot of trust in physicians with 49.5% preferred going to the physician first for information, 48.6% actually reported going online first (Hesse, Nelson et al. 2005). The ease and availability of information on the internet also presents challenges to consumers with them having to sort through the enormous amounts of information, which at times can be conflicting. Therefore, health information over the internet can be considered as a third opinion. Searching the internet relies on the consumer's ability to determine what needs to be searched and how. But even with a good search strategy, the internet can contain inaccurate and misleading information. Molassiotis and Xu searched for information on herbs and cancer over the internet. Forty-three sites were identified by applying the criteria of DISCERN to judge the quality of health information. Most of the sites were rated as low quality on the accuracy of information, in revealing the sources of information, in biasness in their presentation of information or on the frequency of updates. It was found that commercial sites had the most

inaccurate or misleading information, emphasizing only the positive aspects of the use of herbs, with little or no evidence. Of the 43 sites, 7% of sites discouraged the use of conventional medicine. Additionally most of the websites had a school level of college reading level making it difficult for many individuals to understand the information presented (Molassiotis and Xu 2004).

Information gathered from other sources, whether commercials, advertisements, internet, friends or family members requires the individual to process and synthesize the information relative to his/her condition. The ability to do this is related to his/her level of health literacy. Can a patient differentiate between 'good' and 'bad' information, appropriately weigh the risks of one medication/CAM with the effects of another medication/CAM? For example, can an individual weigh which ADRs are not clinically significant such as in the combined use of angiotensin-converting enzyme inhibitor and a potassium-sparing diuretic. This combination is accepted and used with good results, although, occasionally predisposes a patient to developing life-threatening hyperkalemia. A patient upon reading could discontinue their medication without first consulting their physician. There is undoubtedly a variation in the health literacy of individuals, in their understanding of their own condition and the information being communicated, whether to discuss this with their physicians, or to try it on their own.

#### 2.1.13 CHANGING MEDICATION SCHEDULES

In a case study of 76 year old patient receiving warfarin (coumadin) therapy on an outpatient basis due to deep vein thrombosis, the patient's condition warranted a dosage change. It was changed from 2 MG/day to 4mg of warfarin for 6 days/week and 2mg of warfarin one day/week.

The change in dosage was noted in the outpatient EMR chart notes but the initial dosage of "WARFARIN (COUMADIN) NA 2MG TAB TAKE AS DIRECTED BY COUMADIN CLINIC BY MOUTH EVERY DAY TO PREVENT BLOOD CLOTS" was left unchanged on the patient's medication list. The prior medication was copied and pasted with the instructions 'take as directed'. The change was noted in the EMR chart notes, but left unchanged in the patient's medication list. Before the exact information was obtained, the patient had three hospitalizations. What is the reason for this discrepancy? In looking at the patient's interests of costs the physician did a work-around to reduce burden on the patient. A change in prescription would have monetary costs for the patient. The result is that this leads to confusing information and relies upon individuals to remember the correct prescription. The CPOE is often written imprecisely by the anticoagulation clinic to accommodate the frequent dosing changes from month to month. Whenever a dosage is changed it results in a new co-payment. This workaround has created a problem of inaccurate information only if the patient knows and can verbalize the correct dosing regimen, the clinic note is available and is read, and this 'work around' is anticipated by all those who use the system (Caudill-Slosberg and Weeks 2005).

## 2.1.14 IDENTIFYING AN ADVERSE EVENT

With the many possible drug interactions – i.e. drug-drug, drug-disease, drug-food, drug-herbal and drug- nutritional – combined with management of co-morbidities and polypharmacy, it is difficult for anyone to tease out the agent which is causing the adverse event, which may even occur several days/weeks after a drug is discontinued. In the following table Mallet et al. (Mallet, Spinewine et al. 2007) has recommended the following questions to help clinicians detect drug interactions.

- 1. Identification of the nature of the interaction.
  - a. Is there a potential interaction between a drug and another drug, disease, food, nutrition, or a combination of any of these factors?
- 2. Understanding the mode of action of the interaction.
  - a. Can the pharmacokinetic interaction be explained in terms of absorption, distribution, metabolism, or elimination of the drug?
  - b. Is the interaction pharmacodynamic?
  - c. What is the time course of the interaction? Several factors will affect the time course of the interaction, such as the mechanism of the interaction, the pharmacokinetics of the object drug, the nature of the interacting drug (inhibitor, inductor, substrate), the sequence of prescription, and the baseline concentration of the target drug.
  - d. Is this interaction well documented in published work, or are there strong suspicions (theoretical or clinical) to expect that an adverse drug interaction might take place?
  - e. Would the potential interaction appear when a drug is added or discontinued?
- 3. Identification of potential or real clinical outcomes for the patient.
  - a. What are the short and long-term clinical outcomes for the patient?
  - b. Is the patient having new problems (e.g. fallings and gait difficulties, bleeding, blood pressure changes, confusion) that can be explained by a drug interaction?
  - c. Does the patient have risk factors that might increase the likelihood of an adverse outcome (e.g. with regard to comorbidities, other drugs taken, dose and duration of treatment, pharmcogenetics)?
- 4. Monitoring and follow-up for potential drug interactions
  - a. Is an appropriate monitoring plan in place e.g. INR, serum drug concentration, electrolytes, blood pressure, glucose concentration? Who is responsible for follow-up to promote continuity of care? Does this plan account for the estimated time course of the interaction?
  - b. Are caregivers vigilant to monitor for the appearance of new symptoms after any changes to drug treatment?
  - c. Has the drug interaction been documented in the patient's medical record?

Many of these questions can be difficult or time consuming to answer. The mode of action of the interaction may require repeat visits through monitoring and additional testing to discern. Thus due to the multiple factors involved, it is very difficult to pin point the exact causation of the interaction. Even when the causation is known, there may be limited alternative drugs available to treat the condition. Table 3 looks at the drug interaction, but fails to take into account the additional factor of human error or involvement, such as a patient altering or the pharmacist dispensing the incorrect dose, both of which may be unknown to the healthcare provider without a detailed interview of the patient.

There are numerous possibilities for the root cause of an ADR that makes identifying an ADR so difficult and likely underreported. Several investigators, including researchers at the FDA have developed logical evaluation procedures or algorithms to evaluate the probability of an ADR. Algorithms such as the widely accepted Naranjo algorithm all have the aim of helping the clinicians investigate whether that particular drug is known to cause such a reaction, rule out alternative explanations, and establish a temporal link between the onset of the reaction and drug administration (Kelly 2008). A large part of the challenge is the lack of any mechanism to obtain information about the prevalence of an ADR to confirm the observation. There is not a consistent place or requirement to report ADRs for marketed drugs as the question becomes who is responsible for verifying these events and the association to a drug? The other hindrance to reporting an ADR is that it takes time to identify and monitor the contributing factors.

## 2.2 CAUSE AND EFFECT DIAGRAM

The Cause and Effect Diagram, also known as the 'fishbone' or 'Ishikawa' after its creator Kaoru Ishikawa, is used to systematically list all of the different causes, potential or real, that result in a single effect or output. Applying the cause and effect diagram to the prescription process, illustrates causes that could be attributed to an adverse event. This graphical representation illustrates the relationship between a given outcome, ADR, and the factors that influence the outcome. It helps to graphically present and identify areas where there may be problems.

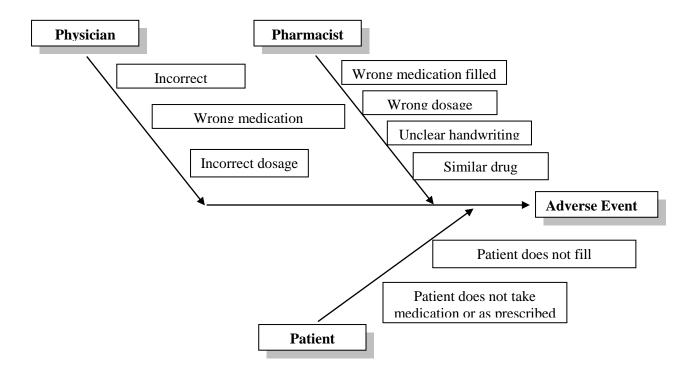


Figure 2: Cause and Effect Model for Adverse Event

The cause and effect diagram applied to the prescription process revises the medication process in Figure 1 by adding in the above risk factors for an ADR. By diagramming the possible steps and causes, one can identify possible root causes and the basic reasons for a specific effect, sort out and relate interactions among factors, and analyze existing problems so that corrective action can be taken.

# 2.3 APPROACHES TO REDUCING MEDICATION ERRORS

## 2.3.1 MEDICATION SHEET / LIST

The medication list in a patient's chart quickly conveys all medications the patient is currently taking, all past medications and the exact combinations of medications being taken at the time of each patient visit. It commonly lists allergies, medication (brand & generic), dosage (strength and frequency) and date reviewed (Rooney 2003). All if not most of the information is obtained by a healthcare professional through the patient/care provider and updated on subsequent visits. Herbal medicines (Cockayne, Duguid et al. 2005) and OTC are infrequently gathered and documented.

Advantage	Disadvantage
1. Efficient charting	1. Located in only one place
2. Safer refills	2. Subject to handwriting errors.
3. Communication with other physicians	
4. Facilitates information recall	
5. Documents allergies	

Table 4: Advantages and Disadvantages to Medication sheet /list

### 2.3.2 PRE-PRINTED ORDER SHEETS

Pre-printed order sheets have been introduced to reduce writing and transcription errors. The forms have pre-printed standardized information such as the name of the drug with the remaining patient-specific information to be entered in by the healthcare provider. In a pediatric emergency

department out of 2058 visits reviewed, 411 (52.2%) orders were on regular form (blank), and 376 (47.8%) were given a new form requesting specific fields – date, time, dose, patient weight, dose, frequency, route. The drug errors were noted 68 (16.6%) and 37 (9.8%), respectively. Thus the use of a form requesting specific information decreased errors by two-fold.

### 2.3.3 MEDICATION RECONCILIATION

### **2.3.3.1 Reconciliation by Patients**

Another approach is requesting that the patient keep an updated list. Varkley et al. (Varkley, Cunningham et al. 2007) conducted a study comparing medication histories documented in the EMR versus an intervention. In the intervention, patients were sent a reminder letter to bring their medication bottles or an updated list. The patients were then asked to verify and correct the information in the printout from the EMR. The nurse or pharmacist then updates the EMR list and generates a new medication list. Through this intervention, the researchers observed statistical significant showing a 88.9% to 66% reduction in prescription errors. The majority of discrepancies noted were minor.

#### **2.3.3.2** Reconciliation by a pharmacist

In a literature review examining (1) studies documenting the interventions made by pharmacists and their role in inpatients (2) articles presenting the outcomes of a satellite pharmacy and (3) articles examining pharmacist involvement in pediatric outpatient clinics, the researchers concluded that the pharmacist review of medication charts is very important in identifying medication errors (Sanghera, Chan et al. 2006). In one study, a pharmacist working an emergency department prospectively obtained the medical histories from the patients. There was a noted increased compliance to the hospital's medication reconciliation policy for admitted patients, and the medication histories had fewer errors (Hayes, Donovan et al. 2007). In a separate study, pharmacists also improved the care (Kabouli, Hoth et al. 2006) in an emergency department. The study showed a rate of errors 16.09 per 100 medication orders with the control group, compared with 5.38 per 100 orders in the intervention group (Brown, Barnes et al. 2008). In a randomized controlled trial, telephone counseling and continuous reinforcement by a pharmacist was associated with a 41% reduction in the risk of death, and an increase in compliance (Wu, Leung et al. 2006)

### 2.3.3.3 Healthcare team

In a prospective study in an ambulatory internal medicine clinic, the completeness of medication documentation in the electronic medical record was analyzed. The intervention involved standardizing the entire visit process from scheduling the appointment to signing of the final clinical note by the physician. Each member of the healthcare checked the accuracy of the documented medication list. Immediately after the intervention, a second data collection was done to assess the effectiveness of the intervention. Completeness of the individual medication increased from 9.7% to 70.7% (p<0.001). However, completeness of the entire medication lists only improved from 7.7% to 18.5%. This was mainly due to the lack of route (85.5%) and frequency (22.3%) for individual medications listed. In addition, documentation of over-the-counter and 'as needed' medication was often incomplete. The incorrectness in the medication list was mainly due to misreporting of medications by patients or failure of clinicians to update the medication list when changes were made (Nassaralla, Naessens et al. 2006).

In using the exact same intervention separated by one year, clinical pharmacists performed drug therapy reviews, educated physicians and patients about drug safety and polypharmacy, and determined corrective actions to reduce polypharmacy. Patients who were prescribed five or more different drugs concurrently for long-term use (>199 days) in the six months before the search through claims data were considered at a high risk of harm from polypharmacy. Pharmacy claims were further evaluated to identify patients with the following combinations: two or more narcotics; two or more benzodiazepines; the combination of a nitrate plus sildenafil, and in patients with glycoslyated hemoglobin values above 8.5%; or three or more oral antidiabetic drugs. Information on prescription cost/member/month, number of prescriptions/member/month, and rates of polypharmacy events/1000 members were measured before and after each of the two interventions. In the first and second interventions, 6693 and 6039 patients, respectively, were identified. After the first intervention, the overall rates of polypharmacy events decreased from 29.01 to 9.43/1000 patients (67.5% reduction). The number of prescriptions/member/month decreased from 4.6 to 2.2 (52.2% reduction), prescription cost/member/month decreased from \$222 to \$113 (49.1% reduction), and overall institutional drug cost was reduced by \$4.8 million. Six months after the second intervention, the overall rate of polypharmacy events was reduced from 27.99 to 17.07/1000 (39% reduction), the number of prescriptions/member/month decreased from 4.5 to 4.0 (11.1% reduction), and prescription cost/member/month declined from \$264 to \$239 (9.5% reduction). Overall institution drug costs were reduced by \$1.3 million. Therefore, by providing clinical information and decision support there were reductions in both polypharmacy and cost.

### 2.3.4 COMPUTERIZED PHYSICIAN ORDER ENTRY (CPOE)

CPOE is reported to: decrease delay in order completion; reduce errors related to handwriting or transcription; allow order entry at point-of-care or off-site; provide error-checking for duplicate or incorrect doses or tests; and simplify inventory and posting of charges (Farlex 2008). It is also reported to saves hundreds of billions of dollars in annual costs, it can offset shortages in nursing supply and is strongly advocated by researchers, clinicians, pharmacists, business councils, the Institute of Medicine, state legislatures, health care agencies and the lay public. The use of a CPOE implies that medication prescriptions will be written in one location, and all the information about the patient's medicine will be accessible by everyone involved in the patient's healthcare.

Studies have found that CPOE improves time in delivery and accuracy of medications by standardized scripting and computer generated prescriptions, thus eliminating confusing written physician's notes (Anonymous. 2003). Bates et al. (1998) in a controlled trial found that CPOE can reduce serious medication orders by 55%. Evans et al. (1998) found that a clinical decision support system can reduce the errors even further. Tierney et al. (1993) in a randomized controlled trial, order entry reduced 12.7% in total charges and 0.9 day decrease in length of stay. Features of CPOE often include use of a medication list (Payne, Nichol et al. 2002), computer alerts notifying when there is a potential drug-drug interaction (Payne, Nichol et al. 2002), pharmacy information system (Payne, Nichol et al. 2002), and ability to override the system (Carpenter and Gorman 2002).

The use of a CPOE in a pediatric clinic reduced the number of non-intercepted serous medication errors by 7%. The researchers also identified several human-machine interface problems, particularly surrounding selection and dosing of pediatric mediations (Walsh, Landrigan et al. 2008). Jacobs et al. found similar findings (Jacobs 2007). In comparing a pediatric ward that implemented a CPOE with a ward that did not, there was a 40% decline in errors in the ward with the CPOE (Potts, Barr et al. 2004). There is also a growing pressure to use a computer prescription system. For example in 2008, Massachusetts' largest health insurer, Blue Cross Blue Shield, will require doctors to use computer prescription systems by 2011 if they want to qualify for bonus payments.

Advantages	Disadvantages
1. discrete orders	1. requires redesigning of
2. capability of drug-drug interaction	workflows and analysis of
3. quality assurance	information
4. free of handwriting identification problems	2. ongoing training of staff
5. faster to reach the pharmacy	3. discrete orders replaced free text
6. less subject to error associated with similar drug	4. expensive to implement and
names	maintain
7. easily linked to identify the prescribing physician	a. initial purchase or licensing of
8. able to link to ADR reporting systems	systems
9. available and appropriate for training and education	b. hardware and other
10. claimed to generate significant economic savings	infrastructure requirements
11. with online prompts, CPOE systems can	c. the savings are not seen as a line
a. link to algorithms to emphasize cost-effective	item on budgets that can be used
medications	elsewhere

 Table 5: Advantages and Disadvantages to CPOE System

#### Table 5 continued

b. reduce underprescribing and overprescribing	5. b. hiring additional staff (eg IT)
c. reduce incorrect drug choices	6. cost of implementing systems
12. increase access to the medical record	7. integration of systems with
13. efficiency gains – lab, pharmacy	existing systems
14. decrease in billing errors and improved cash flow	8. lost productivity while
15. reduction in costs for paper storage	becoming familiar with the
16. reduction in prescription drug costs	system
17. improved ability to produce patient education	9. upgrade of systems / equipment
materials and medication lists	
18. improved ability to access guidelines and standards	
for good prescribing	
19. reduction in ADE	
20. reduction in medical costs associated with ADE	
21. improvements to patient health related QOL	
22. improved ability to conduct research to further	
patient care.	

In the National Health Care Survey (NHCS) conducted by the Centers for Disease Control (CDC) surveying a variety of health care settings, during 2001-03, electronic medical records were used in physician offices (17%), hospital emergency (31%) and outpatient departments (29%). In physician offices, information technology was more frequently used for billing patients (73%) than for maintaining medical records electronically (17%) or ordering prescriptions electronically (8%). Additionally, automated drug dispensing systems were available in hospital emergency departments (40%) more frequently than in outpatient departments (Burt and Hing 2005). The survey however, did not indicate how many of these EMR systems are connected with other offices. Similarly several years later, in a survey of 3,350 office-based physician practices nationwide only 12.4% or physicians use comprehensive

EMR systems in 2006, which was not significantly up from 9.3% in 2005. The CDC defined comprehensive EMR systems as those with computerized orders for prescriptions and tests and has the ability to report test results and clinical notes. They have found that doctors do not always use all EMR features available in their systems. The CDC found that about 2.3% of physicians turn off some available features, which most likely were to result in improved management and quality of care. Of the physician reporting using the full EMR, only 63.7% use guideline-base intervention or screening test reminders, 52.9% use CPOE, and 46.5% computerized test order entry (Manos 2008). However, only 30% of hospitals use CPOE (Goldrick and ALARIS. 2003) partly due to the expense in setting up a system and the lack of interest amongst physicians to use the system.

Despite all of the successes reported by EMRs, 30% of EMR implementation attempts have failed over the past few years, due to a variety of reasons (poor project management, technical challenges, and a failure to create a compelling business model for the participants (Castro 2007). Thus not only is cost a consideration, but also presentation and implementation of the EMR are keys to success. Some of the criticisms against CPOE are that the information can be misleading and inaccurate. Use of an antiquated software and poor system integration whereby viewing one patient can be up to 20 screens is a poorly designed system and interface. One study found that 22 potential risks relate more to poor training (Keillor and Morgenstern 2005; Levick and Lukens 2005). To assist in training of the EMR fixed orders facilitated resident training but requires less critical thinking (Hegedus 2005). Many CPOE implementations involve agreeing on change on work patterns and thought processes of clinicians, rather than

focusing on the organization of work and continually analyzing causes of errors, reassessing and refining the system (Bierstock, Kanig et al. 2005).

In a different pediatric clinic, several factors were found to lead to the increased mortality rate at Children's Hospital of Pittsburgh's Pediatric ICU when a CPOE was introduced. The factors included – prescriber and staff inexperience caused slower entry of orders at first, use more staff time, and is slower than person-to-person communication in an emergency situation. Physician to nurse communication could worsen if each group works alone at their workstations. Additionally, automation creates a false sense of security, a misconception that when technology suggests a course of action, errors are avoided (Han, Carcillo et al. 2005). In other settings, shortcut or default selections can override non-standard medication regimens for elderly or underweight patients resulting in toxic doses. Frequent alerts and warnings could interrupt work flow, causing these messages to be ignored or overridden. Additionally, CPOE and automated drug dispensing were identified as the cause of error by 84% of over 500 health care facilities participating in a surveillance system by the United States Pharmacopoeia (Santell 2004).

In a qualitative and quantitative study of 261 house staff interacting with a CPOE system at a tertiary teaching hospital, the researchers found that a widely used CPOE system facilitated 22 types of medication error risks. Examples of facilitated medication error risks included CPOE displays that prevent a coherent view of the patient's medications, pharmacy inventory displays mistaken for dosage guidelines, antibiotic renewal notices placed on paper charts rather than in the CPOE system, separation of functions that facilitate double dosing and incompatible orders, and inflexible ordering formats generating wrong orders. These were classified as:

- Information errors: fragmentation and system integration failure
  - Assumed dose information based on pharmacy warehousing and purchasing and not clinical guidelines – ie. Guideline is 20-30 mg, but pharmacy stocks 10 mg, so 10 mg is displayed.
  - Medication discontinuation failure ordering new or modifying existing is a separate process than discontinuing or cancelling. Without discontinuing the dose, physicians can increase or decrease the amount (i.e. giving a double dose, every 6 hours and every 8 hours).
  - Procedure-linked medication discontinuation faults medication linked to procedures or tests, if the procedure or test is cancelled, the medication is not.
  - Immediate orders and give-as needed medication discontinuation faults NOW (immediate) and PRN (give as needed) orders may not enter the usual medication schedule and are seldom discussed at handoffs.
  - Antibiotic renewal failure. To maximize appropriated antibiotic prescribing, house staff is required to obtain approval by infectious disease fellows or pharmacists. Lack of coordination can produce gaps. Typically before the third day, the house staff request continuation or modification and use a sticker on the chart. However, when house staff order medications, they primarily use electronic charts, thus missing the warning stickers. It then becomes confusing to discern whether the antibiotic was discontinued or missed.
  - Diluent options are a new CPOE feature on some systems. House staff is to specify diluents, but many house staff were unaware of impermissible combinations.
     Pharmacists catch many of these but it is time-consuming and not ensured.

- Allergy information delay. CPOE provides feedback on drug allergies, after the medications are ordered.
- Conflicting or duplicative mediations does not display information available on other hospital systems
- Human-machine interface flaws: machine rules that do not correspond to work organization or usual behaviors
  - Patient selection patient's names do not appear on all screens requiring the user to view multiple screens
  - Wrong medication selection up to 20 screen may be needed to see all of the patient's medications
  - Unclear log on/log off can result in either unintended patients receiving medication or patients not receiving intended medication.
  - Failure to approve medications after surgery when patients undergo surgery, the CPOE cancels their previous medications. Surgeons must re-enter CPOE or reactivate previously ordered medications.
  - Post-surgery 'suspended' medications patients needed to be logged out of postanesthesia care before CPOE will process medication orders.
  - Loss of data, time, and focus when CPOE is nonfunctional periodic maintenance of crashes. The CPOE manager estimated 2 or 3 weekly crashes of at least 15 minutes are common.
  - Sending medications to wrong rooms when the computer system has shut down if the computer system is down when the patient is moved, the drug can be sent to the wrong room

- Late-in-day orders lost for 24 hours orders requested for 7 am or tomorrow, if an intern enters in orders, and it is after midnight, the orders may come in the following day.
- Process of charting electronically leads to inaccurate and delayed medication administration – nurses charting of medications contemporaneously, requires stop administering the drug, logging in to the computer, finding patient, individually entering medication time. Up to 60% of nurses report that they do not enter medications in contemporaneously.

The researchers (Koppel, Metlay et al. 2005) thus recommend emphasizing workflow, aggressive examination and resolution of technology problems, and diligent investigation of error causes that will support resolution.

In a pre- and post-CPOE implementation study, 135 errors prior and 164 post were noted. The reported error rate per patient pre-CPOE was 5% and per prescribed dose 0.12%. For six months immediately after CPOE implementation, error rate was 10.75% and 0.25%. Seventy-one percent (117/164) of errors were considered CPOE-related. The majority (79%) did not reach the patient, 21% reached the patient with 1 reporting in harm to the patient. Within the medication administration cycle – there were more transcribing errors (not entered by pharmacy, wrong dose, wrong medication, wrong patient into the pharmacy system) and fewer dispensing and administration errors (unauthorized dose, omissions). In the prescribing process – inappropriate medication, duplicative orders, wrong patient, wrong dose were noted. Some of the contributing causes were – (a) non-compliance to policy and procedure (40%) – e.g. a previous order may not have been discontinued when a new dose change was entered, resulting in two active orders for the same medication with different dosages. (b) computer entry errors

(25%) – wrong patient. (c) initial load errors (19%) – entered as 'scheduled' versus "PRN". (d). computer design issues (10%) – two printouts for the same medication, thought duplicate but in the system stated one for today and one for tomorrow – as the date was not on the printout. (Bradley, Steltenkamp et al. 2006)

In a separate study, nurses were asked to highlight concerns with a CPOE. They noted that there is decreased access to nursing narratives - the nursing notes are embedded in huge volumes of electronic notes, nursing notes are either shift summaries of templates which are hard to read and may have as many of six pages with up to 100% of the fields empty. Additionally, while numerical data is transcribed, written text is often bedside nursing narratives which remain handwritten and are not included in the EMR. In the study, the nursing notes were found to have unique information linked to the ADR. There was also a lack of decision support for medication administration (physicians entered 78% of all medication orders directly). The rest of the medications were entered by pharmacists or nurses via verbal or protocol orders. Drug-drug, drug-age, drug-lab alerts were triggered at the time the order was entered. With multiple individuals involved in order entry, the nurses must frequently check the system for new orders entered. The nurses review the orders and sign electronically that they have seen the order. However, as there is no decision support offered to nurses at the time of verification nor do they have access to the responses of the provider to the alerts given at the time of ordering, they are unaware of any drug-drug interaction alerts. The system incorporated bar-code administration, but there were no drug-lab alerts due to lack of an interface. The system also failed to code nursing data that often included bedside notes, decision support regarding questions of dosage, indications or expected side effects. (Weir, Hoffman et al. 2005).

Studies on CPOE systems are difficult to replicate and compare due to the various types of CPOE systems that are being used. Several CPOE systems are either bought as a package (Beyea, Hicks, et al., 2003) or are developed in house (Peth. 2003) (Schneider, 2002). Additionally, it is difficult to compare the local environment in which the CPOE system operates. While many of the studies can be unique to the system and the healthcare environment, they outline factors that should be taken into consideration in the development and implementation of an EMR system.

## 2.3.5 CLINICAL DECISION SUPPORT SYSTEM

An integrated system includes CPOE, pharmacy and laboratory information systems, and an, electronic drug dispensing system. A clinical decision support system assists healthcare professionals by combining a knowledge database with set available data to generate patient-specific advice. Through the use of a clinical decision support system most prescribing errors decreased in the selected categories studied, drug-allergy detection, excessive dosing, incomplete or unclear orders. Seventy-three administration related errors were intercepted through bar-code scanning for every 100,000 doses charted (primarily wrong time, dosing earlier than scheduled). (Mahoney, Berard-Collins et al. 2007).

Several CPOE systems use automated drug alerts during order entry to reduce ADRs. In one study, out of 108 alerts, 0.9% were significant crucial alerts and 16% were significant drug interaction alerts. Of the alerts, 61% involved duplication of medication or medication class. The rest involved topical medications, inhalers or vaccines. The healthcare providers classified 1 out of 9 automated alerts useful. There was variability in the relevance of alerts, suggesting a

smarter system for critical alerts and the option to tailor the alerts to providers (Spina, Glassman et al. 2005).

In a retrospective study examining collected medication and laboratory data from a 140-bed community hospital over a period of six months, the researchers applied the rules from a computerized knowledge base. The aim was to determine if the resulting alerts might have allowed a clinician to prevent or lessen harm related to medication toxicity. There were 8829 activations of the rule set, generating a total of 3547 alerts. In total, 528 were high or critical, 664 were medium, and 2355 were low priority alerts. The researchers reviewed 56 charts that were of high priority alerts, five were found to be non-preventable and two were preventable. Thus, by proportion it is estimated that by applying the rules from a computerized knowledge base, one would be able to identify 94 non-preventable and 37 preventable ADEs. (Seger, Jha et al. 2007).

### 2.3.6 PERSONAL DIGITAL ASSISTANT

In contrast to a paper chart system that is moveable anywhere needed, an EMR system requires use of a computer linked to a central server. Thus, a study was conducted to determine whether a point-of-care personal digital assistant based patient record and charting system could reduce the number of resident progress-note documentation discrepancies in a neonatal intensive care unit. There were significantly fewer documentation discrepancies of patient weights in notes written by using the PDA system. There were no significant changes in the number of notes with documentation of medications or vascular-lines (Carroll, Tarczy-Hornoch et al. 2004). This suggests that the portability of a PDA at the point of care, can reduce some of the criticisms highlighted with EMRs as noted in the prior section.

#### 2.3.7 MEDICATION SAFETY VIA THE INTERNET

In an effort to improve patient-physician communication, adult patients were enrolled into a patient internet portal at three primary care offices. For patients receiving a new prescription or a changed prescription, a secure electronic message was sent to patients ten days after their appointment. Patients were asked if they filled the prescription or experienced any medication-related problems. Their response was forwarded to their primary care physician. Out of 1821 patients, 267 charts were randomly reviewed for three months following the first electronic message. Of the sent messages to patients, 79% were opened and 12% were responded to, of which 77% responded within 1 day. Patients identified problems with filling their prescriptions (48%), problems with drug effectiveness (12%), and medication symptoms (10%). Clinicians responded to only 68% of patients' messages of which 93% were answered within 1 week. Clinicians often supplied or requested information (19%), or made multiple recommendations (15%). During this time, patients experienced 21 ADEs of which 17 were reported electronically (Weingart, Hamrick et al. 2008), thus this may be an effective method of reporting given the information is reviewed and recorded and in a timely manner.

Advantage		Disadvantage
1. Communication tool betw	reen the	1. Requires that the patient be somewhat
<ul><li>physician and the patient</li><li>2. Can help triage questions.</li></ul>		knowledgeable in ADRs and their health care
		2. Requires that the patient be comfortable with email technology.

Table 6: Advantages and Disadvantages to Medication Safety via the Internet

The above interventions demonstrate a reduction in adverse events and illustrate the numerous approaches taken in preventing, identifying and alerting healthcare providers of an ADR. The choice of intervention is highly reliant on the problems, resources, and local environment.

# 2.4 SOURCES OF MEDICATION DOCUMENTATION

Medication can be documented in several sources. The table below shows some of the most common sources and where one would expect to find out what medications a patient is taking. It should also be noted that apart from the patient, each source has an element of time. For instance, the source is considered to be accurate when the information is gathered, reviewed and updated. If one of the sources is not updated, than this becomes less accurate and thus reliable information. The check marks represent what information is expected to be located in which source.

	Sources of Medication Documentation						
Medication	Patient	EMR	Chart	Specialist	Pharmacist	Insurance Company	
Name	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	
Dose	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	
Frequency	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	
Route	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$		$\checkmark$	
Cost	$\checkmark$				$\checkmark$	$\checkmark$	
Sample	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$			
Over-the-Counter	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$			
Alternative	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$			

 Table 7: Comparison of documentation sources for expected medication information

## 2.4.1 MEDICAL RECORD CHART

The paper chart is the oldest and most common method of documenting a patient's history with a healthcare provider. It serves as both the medical and legal record of a patient's clinical status, care, history and healthcare involvement. The detailed information is intended to provide a patient's clinical condition by detailing diagnoses, treatments, tests, responses to treatment, as well as any other factors that may affect the clinical state of a patient. The advantages and disadvantages of the medical record chart are outlined in Table 8.

	Advantages	Disadvantages
1.	Easy to use – no specialized training	1. Handwriting can be illegible
	needed	2. Portable - Easy to misplace
2.	Portable – can be moved anywhere	3. Long-term patients can have multiple
3.	Can handle multiple forms of	charts which can be bulking and heavy
	communication (i.e. letters, faxes, etc.)	4. Low security / privacy
4.	No technological equipment needed (i.e.	5. Chart can only be in one location at a time
	computers, etc.)	6. If chart is not available for filing, it may not
5.	Require large amounts of storage space	contain the most recent information
6.	Requires dedicated staff for continuous	7. Sequential information can be difficult to
	filing	synthesize in looking through several pages
7.	Low cost to implement	and sections

#### Table 8: Advantages and Disadvantages of the Medical Record Chart

Although, it is the least secure form, using the patient record does not require specialized implementation or equipment other than an office organization system. One of the biggest challenges in keeping the medical chart with current information is having it accessible when new information becomes available. Every time new information becomes available whether through a phone call with a patient, lab results, or correspondence from a physician if the chart is not present this increases the risk for missed documentation. Some pieces of information are added into the chart at a later time and some never at all.

Jampel et al. (Jampel, Parekh et al. 2005) looked at documentation of glaucoma and glaucoma medications by primary care physicians. Glaucoma medications have potential side effects such as low blood pressure, reduced pulse rate, fatigue, and shortness of breath, as well as, can interact with other medications including for high blood pressure, colds and breathing

difficulties, diabetes, mental depression, mental problems and psychotic disturbances and heart rhythm control. It was found that out of 100 patients, 55% of medical records of the primary physicians mentioned eyedrops. Of the charts, 31% mentioned glaucoma but no eyedrops, 8% glaucoma plus eyedrops, 7% mentioned specific eyedrops but no glaucoma and 40% mentioned both glaucoma and specific eyedrops.

#### 2.4.2 ELECTRONIC MEDICAL RECORD

EMR aims to facilitate communication between the patient-provider in several aspects: 1. process of care by mediation discussion, 2. names of medications and list of medications and 3. identification of medication themes (dosage information and graphs representing previous and current therapies) through the ability to look at the whole prescription profile (Arar, Wen et al. 2005).

Advantages	Disadvantages	
1. Higher level privacy and security	1. difficulty in adding older records to the	
2. Less amount of space and time required	system	
for transporting than paper records	2. synchronization of records utilizing	
3. Remote access	different systems	
4. Structure forms improve readability	3. hardware limitations – workstations,	
5. improved billing accuracy	laptops	
<ol> <li>reduction in duplication of services</li> <li>facilitation of clinical trials</li> </ol>	<ol> <li>cost advantages and disadvantages – cost to the organization, benefit to the patient</li> </ol>	

Table 9: Advantages and Disadva	antages of the Electronic Medical Record
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#### **Table 9 continued**

8. aids in standardization	5. start-up costs and software maintenance
	costs
	6. temporary workers require training
	7. inertia – most organizations resist change
	8. liability barriers – failure or damages
	caused during installation or utilization
	9. ownership of electronic records – who
	responsibility to maintain (company or
	hospital)
	10. un-alterability of records, spurious records
	and digital signatures – simple mistakes
	create spurious documents
	11. customization – cost

Wagner and Hogan measured the accuracy of medication records stored in the electronic medical record of an outpatient geriatric center. The authors analyzed accuracy from the perspective of a clinician using the data and the perspective of a computer-based medical decision-support system. During a scheduled office visit, the clinician determined from available sources whether the patient, vials, any caregivers, and the medical chart. In 83% of medication records the compound, the dose, and schedule of a current medication were correctly represented; 91% represented correctly the compound, and the number of current medications were missing per patient was 0.37. The principal cause of errors was the patient (36.1% of errors), who misreported a medication at a previous visit or changed (stopped, started, or dose-adjusted) a medication between visits. The second most frequent cause of errors was failure to capture changes to mediation made by outside clinicians, accounting for 25.9% of errors.

Transcription errors were a relatively uncommon cause (8.2% of errors). When the accuracy of records was analyzed from the perspective of a clinical decision system, 90% were correct for compound identity and 1.38 medications were missing or not coded per patient. The cause of the additional errors of omission was a free-text 'comments' field. These are unreadable by current clinical decision support applications, but used by clinicians in 18% of records to record the identity of the medication (Wagner and Hogan 1996).

#### 2.4.3 PHARMACY

The pharmacist receives the prescription and dispenses the medication. Thus, the pharmacist has direct information on the name, dose, frequency and route of what was prescribed to the patient. They also have information on what, how much, and when a refill was made. Almost all of the pharmacies have a database that contains the specific prescription information filled by the patient at that pharmacy. As the pharmacist is one step removed from the physician who prescribes the medication and is able to see the medications that other healthcare providers have prescribed, they are often thought to be able to provide the global picture and identify potential ADRs. Many pharmacists are also able to take the time to explain the use and mechanism of a drug to a patient. Being able to thoroughly check ADRs, assumes that a patient sees the same pharmacist for all of their medications. However, several patients for various reasons, e.g. to save costs, time, have their prescriptions filled at different pharmacists are unaware of CAM, OTC, and sample medications that are taken by the patient unless they are told by the patient.

### 2.4.4 INSURANCE PROVIDER

The insurance provider is a possible source of medication documentation as regardless of how many pharmacies the patient visits, all of the information is forwarded to the insurance provider. Thus from a global perspective, the insurance provider can view trends in prescribing, what and how often the medication is being filled and can potentially highlight any potential adverse events or changes in medications dispensed. This information collected from the insurance provider can also provide indicators of compliance. For example, how often the prescription is filled can help determine the frequency of the medication and whether it is taken. The limitations of the insurance provider as a source of documentation are: OTC and CAM are not processed through the insurance company, and many patients in order to save money are increasingly paying out of the pocket thus by passing the insurance company.

#### 2.4.5 PATIENT

The patient is often thought to be the ultimate source for medication documentation as they are the ones who know what, how much and how often a medication is taken, as well as, whether there are other medications/CAM being taken. This assumes that the patient understands and is able to recall (whether verbally or written down) the dose, frequency and route, as well as, correctly follows the instructions that are provided, e.g. when to take the medication, what foods to avoid, what are indications of an ADR, etc. The patient then becomes an active participant in helping the provider understand the most accurate picture including reporting of CAMs, OTCs and alterations to drug therapy.

# 2.5 COMPARATIVE SOURCES OF DOCUMENTATION STUDIES

There is varied literature looking specifically at comparing one source of documentation versus another source. Most of the literature in this area focuses on the implementation of an EMR and the benefits, challenges, and effects upon adverse event detection. The research however, does not compare the information against multiple sources. Thus this study is the first to look at multiple sources of documentation for medication accuracy.

Review Type	Number of cases	Results	Authors
Retrospective	90 electronic and 90 paper chart	EHR were 40% more complete than paper chart; retrieval of information was faster by EHR	Tsai and Bond (Tsai and Bond 2008)
Prospective	500 patients	100% in pharmacy record 66% in hospital file 76% structured drug review	Glintborg et al (Glintborg, Poulsen et al. 2007)
Prospective	326 charts	53.7% undocumented prescription medication, 51.2% non prescription medication or natural products were missing in charts.	Mersfelder and Bickel. ((Mersfelder and Bickel 2008)
Prospective	620 patients	41.7% drug discontinuation orders and 58.3% changes in drug doses were identified by chart review versus electronic prescribing system. Changes were most often due to ineffective treatment (30.8%) and ADRs (21.9%)	Eguale et al. (Eguale, Tamblyn et al. 2008)

 Table 10:
 Summary of Prior Research on Comparative Medication Documentation

# Table 10 continued

Retrospective	84 patients using a Patient Gateway to update medications in the EMR versus 79 patient who were not	54% Patient Gateway users were slightly reported higher correct than non-users (61%).	Staroselsky et al. (Staroselsky, Volk et al. 2008)
Prospective	85 patients through phone interview	233 discrepancies between patient and EMR. Most common discrepancy medication no longer being used by patient (70.4%), followed by omission from the EMR of a medication being taken by a patient (15.5%). 79.8% were system errors and 20.2% were patient errors. Most common patient-generated omission was multivitamin (27.7%), most common system omission was an expired drug (48.4%).	Orrico (Orrico 2008)

#### **3.0 BACKGROUND OF THE STUDY**

#### **3.1 THE CITY OF PITTSBURGH**

The city of Pittsburgh has a large, diverse population that is comparable to other cities. Pittsburgh is the second largest city in the U.S. state of Pennsylvania with a population of 312,819 at the time of this study.

### 3.2 UNIVERSITY HOSPITAL SYSTEM

The University of Pittsburgh Medical Center Health System (UPMC-HS) is comprised of twenty hospitals and a network of satellite clinics and services. About 4 million people are seen through the UPMC-HS every year within the Western Pennsylvania area. At the time of this study, UPMC-HS was in the process of implementing a system-wide CPOE system called PowerOffice Chart (PCO), which was custom built for UPMC-HS. The computer physician order entry system part of PCO is called EasyScript. The advantages of evaluating medication documentation in this system is that it allows for comparison of pre- and post- PCO implementation by comparing clinics that are currently participating in the system to those who are awaiting to 'go live'. UPMC-HS has built their own pharmacy database within the system, has a pharmacy on the main campus with online ordering and healthcare plan to serve its constituents. With multiple satellite clinics around the city, the patient base reflects the diverse

population seen in the city. UPMC offers a health insurance plan and an array of commercial, Medicare and Medicaid products.

### 3.3 PRIVATE PHYSICIAN PRACTICE

The practice of Solano and Kokales was chosen as it was one of the first clinics to implement the PCO system and use EasyScript. At the time of this study, only 50% of the physicians were actively using the EasyScript system, thus the practice operated in a dual environment of paper and electronic medical records. This was an ideal environment as many of the first challenges in dealing with an EMR system were being identified and worked through.

## **3.4 MEDICARE – PART D**

This study was presented to individuals at the same time Medicare – Part D was being introduced across the nation. Medicare – Part D is a federal prescription drug coverage that covers both brand-name and generic prescription drugs at participating pharmacies. It was enacted as part of the Medicare Prescription Drug Improvement and Modernization Act (2003) that went into effect on January 1, 2006. The aim of the program is to provide protection for people who have very high drug costs or unanticipated drug bills in the future and is open to all individuals with Medicare. The drug coverage has several plans that the individual can participate in with a monthly premium, which varies by plan and yearly deductible. The plan chosen determines how the cost of the prescription, including a co-payment or co-insurance.

### 4.0 METHODOLOGY

This is a retrospective, descriptive, cross-sectional study in a general internal medicine outpatient clinic (Solano & Kokales Internal Medicine Associates-UPMC) that is part of UPMC. This clinic has been utilizing a CPOE system (PowerChart Office – PCO) for two years. This was an ideal clinic as the physicians were familiar with the program and are utilizing it on a continual basis. This study started recruiting participants in November, 2005.

# 4.1 HUMAN SUBJECTS

Eligibility criteria for the study includes being over the age of 40 years, having been diagnosed with arthritis, diabetes or hypertension, and has either Highmark Blue Cross Blue Shield or UPMC as his/her insurance provider. The racial, gender and ethnic characteristics of the proposed subject population reflects the demographics of Pittsburgh and the surrounding area and/or the patient population of the University of Pittsburgh Medical Center. There were no exclusion criteria based on race, ethnicity, gender or HIV status. Children were not enrolled into the study. Women who are pregnant were not excluded from the study. University of Pittsburgh Institutional Review Board approval was obtained prior to the initiation of the study.

## 4.2 RECRUITMENT PROCEDURES

The clinic staff identified return patients diagnosed with arthritis, hypertension or diabetes that have been seen for at least the last year, who have an appointment scheduled over the next month and have UPMC Healthplan or Highmark Blue Cross Blue Shield as their provider. Arthritis, hypertension, or diabetes can be concomitant with other conditions. To be in compliance with HIPAA regulations, one month in advance, clinic staff of the participating practice mailed letters on practice letterhead from the respective physician with a matching coded, postage-paid postcard to potential participants who have either the diagnostic code of hypertension or diabetes (see invitation letter). The postcard asked if the individual was interested in being contacted by the research group (yes or no), requested his/her phone number, best time to call, and comments. By coding the postcard, the returned postcards were matched to the patients without having them to put their name on the postcard where others can see it thus preserving confidentiality.

Only those potential participants who have indicated on the postcard that they were willing to be contacted by the research group were contacted. Prior to the upcoming medical appointment, the researcher contacted them to explain the study and ask them some screening questions (see screening script). A waiver for screening over the phone prior to obtaining informed consent was requested as this research study present no more than minimal risk of harm to the subjects and involves no procedures for which written consent normally required outside of the research context.

Once the individual is determined to be eligible, the researcher asked each participant a series of open-ended questions. The participant was mailed two copies of the consent form (one to sign, date and return, and one for his/her records), a form to list their medications including name, dose, frequency as prescribed and as taken, and for what indication was recorded from the participant, and authorization for release of records from his/her primary care physician, insurance company and all of the pharmacies that the individual has visited in the last six months. The researcher coordinated the requests for copies from each of the medication documentation sources and conducted a chart review of the medication documented. The source, dates of entry, name of the medication, dose and frequency were recorded.

### 4.3 **RISK/BENEFIT RATIO**

Breach of confidentiality was possible as a result of participating in this study. There were no other risks associated with this study as it gathered retrospective data and did not involve any intervention.

All study information was located in a password secure database on a password secure server accessible only to the research team. Paper information were kept in a locked drawer behind locked doors in the researcher's office. Once the information was gathered from all the potential sources, the participant's identifiers and their information was coded with a number and identifiers stripped. This allowed for analysis in a masked fashion.

# 4.4 COSTS AND PAYMENTS

There were no costs or payments given to participants in this study.

# 4.5 CHANGES TO STUDY DESIGN

After meeting with the first few participants, the methodology was reassessed and it was determined that the method of gathering medication information would be changed. The two changes were:

1 In the original design of the study, prior to the appointment, the researcher would contact the prospective participant to explain the study and request him/her to bring in all of his/her prescribed and alternative medications to the appointment. At the appointment, the researcher would review and ask him/her to sign the consent form, a records release form from the practice, as well as, from the insurance company, specialists, pharmacies that the participant has utilized in the last six months.

Very few brought in all of his/her medications, had the original containers with the name and dose of the medication (i.e. were transferred to pillboxes), brought in his/her vitamins/alternative medicines, and were unaware of the names and addresses of the pharmacies. Space constraint was also an issue to identify a room to speak privately with the participants versus in the general waiting room. In all of the cases, the researcher requested permission to speak with the participant later to gather the information. It was decided then that the same information was able to be gained from the participant through a phone call and via the mail. This method was also preferred to avoid any potential participant biases or extraneous entries by the physicians or clinic staff as they were unaware of who agreed to participate. Collection of information outside of the medical appointment setting allowed for a separation from his/her physician and the researcher.

2. In the original design, the researcher was going to also request copies of the participant's medical record from the specialists that the participant has seen in the last six months.

Many of the specialists declined forwarding copies of the chart and instead the letters from the specialists in the chart were used as source documentation. This change allowed examining what information is communicated between health care providers. This became part of the research question indicating what of the prescribed medications is being communicated to the primary care physician.

### 4.6 INSTRUMENTATION

A list of medications including name, dose and frequency that were filled during an eight month period were requested from all of the reported documentation sources (EMR, chart, pharmacist(s), specialists, insurance provider, and participant). The eight month period takes into account what medications that were prescribed before the initiation of the study. These were documented in a spreadsheet and examined for what information was and was not shared in common with the other documentation sources.

The study also had a qualitative component where participants were asked:

- 1. Does someone attend your doctor's appointments with you or assists you with your medications?
- 2. Are the instructions from your physician or pharmacist clear and easy to understand?

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- 3. Can you tell me what CAM/OTC or sample medications you have taken in the last six months?
- 4. How do you pay for your medications co-pay or out-of-the-pocket?

# 4.7 STUDY VARIABLES

The table below outlines the outcome variables that were collected as part of the study.

Quantitative Variables	Qualitative Variables
Age	Indicators of Independence
Sex	• appointment accompanients
Insurance Provider	• instructions from
Number of conditions	physician/pharmacist
Number of medications	• assistance with medications
Number of CAMs	Prescription Coverage
Number of adverse events - major, moderate and minor	• method of payment
Number of sources of medication	Sample Medications
Percentage of medications/CAM in common with the 'gold	
standard'	

#### **Table 11: Study Variables**

# 4.8 DATA ANALYSIS

The medication, CAM and OTC data collected from the paper chart, CPOE, specialist, insurance company, pharmacy, and patient were combined to form the 'gold standard' to which the various sources were compared for differences. These discrepancies were then categorized. Data was

compiled and categorized according to error type: difference in name of medication, dose and frequency. These drugs and CAMs/OTCs were then entered into a pharmaceutical database, Drugs Interaction Checker, to determine drug-drug interactions. The Drugs Interaction Checker accessed via Drugs.com is a free internet service provider by Cerner Multum, Inc (Multum). The drug interactions database provides a list of reactions that may occur when different drugs are taken at the same time. While there are many internet drug interaction checkers, this one was used as it represents what is accessible to the general public, that includes over-the-counter medication and the most common alternative medicines. Several of the other internet accessible databases did not include in OTC or CAM.

Data analysis involved descriptive statistics by comparing the correctness, which is the proportion of recorded observations for completeness, listed as part of the 'gold standard',versus incompleteness, which is the proportion of absent observations for each of the various sources. Additionally, a logistic regression analysis using the software program MedCalc was done to determine which variables are correlated with a higher percentage of medications/CAM in common with the 'gold standard' and factors that create a higher risk for adverse events.

The collected data open-ended questions were examined within the context of the participant and overall to determine whether there were common themes emerging.

#### 5.0 **RESULTS**

## 5.1 **RESPONSE RATE**

A total of 110 were invited to participate in the study of which 54 (49%) individuals agreed to participate in the study. Of the total number of individuals, four were omitted due to insufficient data for a triangulation approach needed to establish the "gold standard' of the medication/herbal medicines. Several other individuals had expressed interest either through responding 'yes' on the postcard or by calling the researcher. However, these individuals later declined participation once they realized that this study was unrelated to the Medicare – Part D drug coverage plan which was also being introduced at the same time, or misunderstood the goals of the study and stated that they already had prescription drug coverage. Many who did participate in the study were interested as they realized that medication documentation was a problem or alternatively, were encouraged by family members in the medical profession to participate.

## 5.2 CHALLENGES TO THE STUDY

There were two challenges to the original methodology that resulted in the study design being changed. One of the goals was to obtain all of the medication sources including the specialists for comparison of what information is documented in establishing the 'gold standard'. This proved to be very difficult as many of the specialists had the information interspersed throughout

the patient chart and thus had difficulty producing copies of the records. Thus the design of the study was changed to what is being reported by the specialists to the primary care physician as recorded in the patient chart. In communication with one of the primary care physician as there are now so many drugs for various ailments, he relies on the specialists to prescribe the appropriate care. Across all of the 50 participants, there were a total of 8 patient letters from specialists that mentions medications. One individual had two different specialist letters in the chart. While this number seems very low, it is difficult to ascertain the significance of this number as it was neither asked of participants how many specialists were seen in the last six months, nor was it recorded how many specialists, only two provided the name of the drug and dosage. In the other six cases, only the name of the drug was mentioned. In one letter, the physician wrote 'standard glaucoma medications'.

The second challenge was encountered in the first two participants who when asked to bring in the bottles of all medications and CAM, including vitamins and herbs, brought in either a list of medications or a pre-filled daily pill box. This was changed to speaking with individuals over the phone and asking them to read the bottles. The majority stated that they do not report to their physician the vitamins and herbs that they take as they did not feel this was necessary information. One individual recognizing the potential effects had reported what she had been taken, but noticed that the physician did not write it down. Even when the researcher asked for all CAM taken, some of CAMs (particularly a company-specific formulation or a combination of CAMs) could not be located in Drugs.com to determine whether there was a potential drug-drug interaction. Thus while it is understood that CAM and lesser extent OTC can vary by strength in a formulation, a generic classification closest to the item was selected in the Drug Interaction Checker.

In obtaining medication documentation from the insurance company and pharmacies, each source was asked to provide the name, dose and frequency of each medication recorded for an individual over the last six months. What was received from all of the insurance companies was the name of the drug (brand or generic) and how much was paid. The information from the pharmacies was not much clearer in that the drug name and dose was given, but typically not how often it is to be taken. In these reports, the number of refills and cost by the participants were included. While it can be said that the drug information is in the computer system of these organizations, it is of concern that the requested information could not be readily produced.

The EMR system contained information about the drug name (brand and generic), dose, frequency, and the physician whom prescribed the medication. In several instances, it also included CAMs. It did not however, include the medications prescribed by the specialists, sample medications, nor could it be ascertained whether the prescription was filled and taken. The chart similar to the pharmacies contained the name of the medication and the dose, but not the frequency nor CAMs. Using the table 7 presented earlier, the resultant sources of information from the study are presented below. The check mark denotes information that is expected and present in a source, and the 'x' marks what is expected but not observed in the source documentation.

	Sources of Medication Documentation								
Medication	Patient	EMR	Chart	Specialist	Pharmacist	Insurance Company			
Name	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$			
Dose	$\checkmark$		$\checkmark$	rarely	$\checkmark$	$\checkmark$			
Frequency	$\checkmark$	$\checkmark$	$\checkmark$	Х	Х	Х			
Route	$\checkmark$	rarely	rarely	$\checkmark$	rarely	$\checkmark$			
Cost	$\checkmark$				$\checkmark$	$\checkmark$			
Sample	$\checkmark$	Х	Х	Х					
Over-the-Counter	$\checkmark$	Х	X	X					
Alternative	$\checkmark$	Х	X	X					

 Table 12: Revised location of medication documentation by source

X = not present, Y = present

# 5.3 DESCRIPTIVE STATISTICS

## 5.3.1 PARTICIPANT DEMOGRAPHICS

The resultant 19 (38%) male and 31 (62%) female participants were analyzed in this study. The age range of the participants was 42 to 91 with a median of 66 years. The average number of conditions reported by the participant and/or recorded in the paper medical chart ranged from 1 to 12 with a median of 3.5 and an average of 4.1. Nearly equivalent numbers of participants, 22 (44%) and 28 (56%), had UPMC HealthPlan or Highmark Blue Cross/Blue Shield coverage,

respectively. Inclusive in these numbers is one individual whom had both plans. A total of 690 medications and herbs were reported by all of the participants, with a range of 3 to 38, median of 14 and mean of 13.8.

#### 5.3.2 DATA COLLECTION

For each participant, Appendix C tabulates the range of missing values, number of conditions reported/recorded, number of over-the-counter and herbal medicines, and the number of sample medications. A Venn diagram illustrates how many of the reported/recorded medication/CAM are in common or different amongst the various sources (i.e. electronic medical record, participant, paper chart, specialist letter within the chart, insurance company and pharmacies). Also included are the types of drug-drug interaction errors when drugs are taken in combination and the level of significance (major, moderate or minor) as identified through Drugs.com. This research did not include drug-food interactions that are known to occur that affect the bioavailability of a compound, absorption, and/or have an additive or diminished effect on a drug.

As an example of the tabulated data, Subject #10 has 3 sources of medication documentation (EMR, Participant, and the Pharmacy). Of the observed 14 in total medications/CAMs, 5 were shared in common amongst the 3 sources and 1 was shared between the EMR and the participant but not with the pharmacy. Additionally, there were medications/CAMs not found in the other sources of 2 and 5 not listed in the EMR or participant, respectively. Of the 5 listed only by the participant, 3 of them were CAMs, Oscal, Centrum Silver, and Aspirin, that were not documented in either the EMR or the pharmacy as these are available over-the-counter.

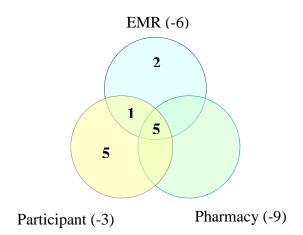


Figure 3: Venn Diagram Showing Documentation Sources with Gold Standard

In this participant, a total of 8 moderate and 3 minor risk potential drug-drug interactions were identified. Management guidelines for these drug-drug interactions included: monitoring for signs of muscle pain, tenderness or weakness; altered blood pressure control (noted 3 times); effective calcium channel blocker therapy; diminished or inadequate analgesic and anti-inflammatory effects; altered renal function; recommendations for adjusting dosing and amount; and reported observations however, the clinical significance is unknown. Of these 11 identified potential drug-drug interactions in this participant, 6 moderate and 2 minor involved over-the-counter medications/CAMs that were self-prescribed by the participant and were not documented either by the physician or the pharmacy.

All of the continuous variables were determined to have a normal distribution.

#### **5.3.2.1 NUMBER OF CONDITIONS**

In total, 206 conditions were reported by all participants. The range was from 1 to 12 conditions per participant with a mean of 4.12 and a median of 3.5. While 3 participants had only one condition, the remaining 47 had equal or greater than two conditions. Thus 94% of participants had co-morbidity that require co-management of more than one condition and subsequently presents a greater risk for polypharmacy.

### 5.3.2.2 TOTAL NUMBER OF OVER-THE-COUNTER/CAM

Of the 50 participants, 38 (76%) reported taking Over-the-Counter (OTC)/CAM which sums in total 107. The range of number of OTC/CAM per participants was from 1 to 10, with a mean of 2.82 and a median of 3. The large majority of OTC/CAM were classified as CAM – such as vitamins, minerals, herbs; and were lesser classified as over-the-counter medication – such as ibuprofen that were taken on a regular basis. With the exception of a suggestion from a physician in two cases (4%) to take either a multivitamin or calcium supplement, all of the other observations of CAM were self-prescribed.

### **5.3.2.3 SOURCES OF MEDICATION/CAM**

The overall number of medication sources for each participant ranged from 3 to 9 with a mean of 4.48 and a median of 4. To establish the gold standard, the name of the medication/herbal medicine alone was used to compare the sources as this was the only most consistent information available across all of the documentation sources.

## **5.3.2.4 DRUG-DRUG INTERACTIONS**

In looking at all of the participants, 637 drug-drug interactions were identified in 50 individuals, 39 (26%) individuals had a major, 48 (96%) moderate and 32 (64%) minor risks. Of the 637 drug-drug interactions, 74 (12%) involved a CAM which includes vitamins and supplements. Nearly all of the CAMs were self-prescribed. The number of drug-drug interactions in the participants ranged from 0 to 101 with a mean of 12.74 and a median of 8. There were in total 637 potential drug-drug interactions of which 39 were major, 490 were moderate and 114 were minor. The management of the drug-drug interactions can be classified into three groups: major (i.e. extreme caution in co-administration, dosing interval recommendation); moderate (i.e. monitor of clinical and laboratory work - serum potassium levels, blood glucose, etc. and monitor for symptoms of disease - CNS and respiratory depression, hypotension, hematological complications, etc.); and minor (i.e. clinical significance unknown).

Many of the major interactions were cautioning against concomitant medications of the same class. For example in the potential drug-drug interaction between Trazodone and Cymbalta, the use of agents with serotonergic activity such as serotonin inhibitors, monamine oxidase inhibitors, tricyclic depressants, 5-HT 1 receptor agonists ergot alkaloids, lithium, St. John's wart, phenylpiperidine opiods, dextromethorphan, and 5-hydroxytryptophan any of which may potentiate the risk of serotonin syndrome. Thus, caution is advised to consider whether the potential benefit of the medication treatment outweighs the risk of concomitant use of multiple serotonergic agents (Multum). It is possible that these medications were not administered concomitantly rather that they were prescribed sequentially to determine which medication would be appropriate for the individual. Recalling that the medication documentation source is

the most accurate when the information is gathered, reviewed and updated, it is possible that the medication discrepancy represents information at different points in time. However, this temporality also creates uncertainty in the validity and timeliness of the information documented.

## 5.4 DATA ANALYSIS

## 5.4.1 MEDICATION DOCUMENTATION SOURCES VERSUS GOLD STANDARD

To determine the percentage of the documented medications from the various sources that were shared with the 'gold standard', the total number of reported medication/CAM for each source was divided by the 'gold standard'. The assumption was that all of the listed medications/CAM carry equal value to the participant's health and are important for the healthcare providers to be aware. Thus, it was assumed that it was equally important to know whether the participant has been taking a hypertension medication, as it was to know whether an over-the-counter or CAM was being taken. It is however, recognized that clinically some medications to control disease are more significant if it was missed or not taken versus having missed taking a multivitamin. For the purpose of this study, all medications/CAMs are considered equally important to the participant's health. Thus, continuing with the above example, the percentage each source shares with the 'gold standard' is 57% (8/14) in the EMR, 79% (12/14) in the patient, and 36% (5/14) in the pharmacist.

For each of the subjects, the source of medication documentation that was shared the most in common with the 'gold standard' was determined to be the best source of medication documentation. The highest percentage was plotted against the source for each participantThe

various best sources for the participants are plotted on the figure below. If there were more than one documentation source that shared the highest number of medications/herbal medicines in common with the gold standard, they both were plotted in the respective category. This was done as either source can serve as an accurate indication of what the patient is or is to be taking.

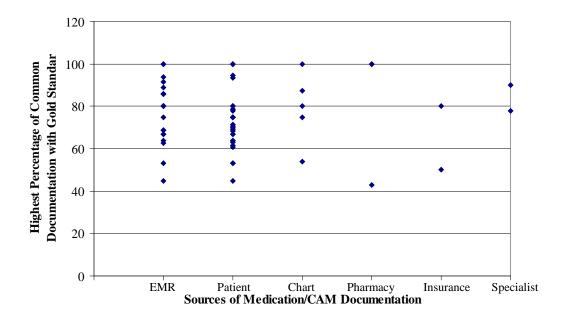


Figure 4: Graph of Highest Percentage in Common with Gold Standard by Source

As shown in the figure above, both the EMR and the patient were the most frequently observed to have medications/herbal medicines in common with the 'gold standard' as compared to the other documentation sources. The EMR and patient had 21 and 28 observations, respectively. With a similar frequency and the exact same range of observations in common with the gold standard (43% to 100%), it is difficult to visually detect a difference between the EMR and patient source of documentation. Thus to distinguish between the two documentation sources, a correlation between the EMR and 'gold standard' and the patient and 'gold standard' was done using Pearson correlation coefficient. All of the participants were included in the calculation to represent the best source of documentation overall if one had a choice. The results

are shown in the table and scatter diagrams below. The patient source had a sample size of 47 due to lack of data for 3 individuals.

Variables	Sample Size	Correlation	Significance	95% Confidence	
v arrables	Sample Size	coefficient r	level	interval for r	
EMR, Gold Standard	50	0.5585	P<0.0001	0.3318 to 0.7243	
Patient, Gold Standard	47	0.8174	P<0.0001	0.6929 to 0.8946	

Table 13: Correlation between the EMR and the Patient with the Gold Standard

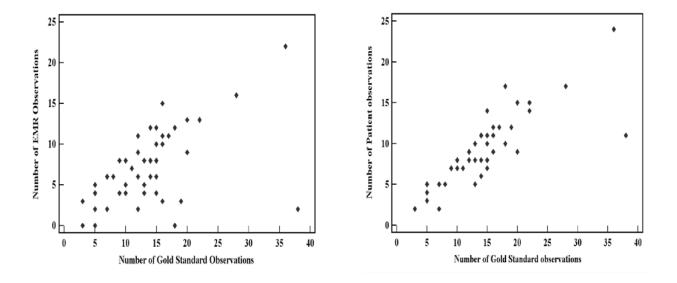


Figure 5: Graph of Correlation of EMR and Patient, and Gold Standard

Based on the frequency data, the scatter diagrams and correlation coefficients for both the patient and the EMR have a positive correlation as expected. Both with a p < 0.0001, the correlation coefficient of 0.8174 versus 0.5585 is slightly higher and with a smaller confidence interval in the patient versus EMR source and noted by a smaller spread on the graph. The number of patient observations and number of Gold Standard observations are more closely related thus suggesting that the patient is a best source of medication/CAM documentation.

#### 5.4.1.1 Highest Shared Medication/CAM with Gold Standard

Amongst participants, the lower limit percentage range of shared documented medications/CAM from the various documentation sources with the gold standard was 0% to 60%, with a mean and median of 27%. The upper limit percentage range of shared documented medications/CAM from the various documentation sources was 42.9% to 100%, with a mean of 76.1% and a median of 75%. The upper limit percentage for each participant is diagrammed in the cumulative frequency graph below. This is the highest observed percentage of medications/CAM shared with the 'gold standard' for each participant regardless of the source. As shown in figure 6, the results have a significant range and follow a normal distribution.

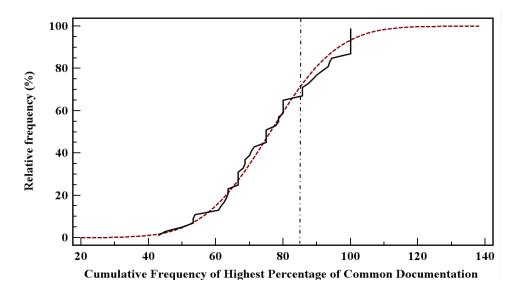


Figure 6: Graph of Cumulative Frequency of Highest Percentage in Participants

Hypothetically, if having greater than 80% of an individual's medications/CAM documented is considered a good estimate to appropriately manage an individual's care, then 20 individuals would fall into this category. This group was called the more accurate group. Thus, for the

remaining 30 individuals, regardless of the source, the healthcare provider would be challenged to determine what the participant is or has been taking. The later group was referred to as the less accurate group.

#### 5.4.1.2 Characteristics of the Highest Shared Medication/CAM with Gold Standard

Are there characteristics within the more accurate group, the subset of 20 individuals which have 80% or greater in common with the gold standard regardless of source, that results in more reliable information? Results of the statistical analysis of the two groups are shown in the two tables below. In the first table, the ratio of males and females, and the ages of the participants between the two groups were very similar.

More Accurate			Less Accurate			
Females	Males	Ratio	Females	Males	Ratio	
13	7	1.65	18	12	1.6	
Age Range	Mean	Median	Age Range	Mean	Median	
40-80	59.5	60	40-90	62.67	60	

Table 14: Sex Ratio and Percentage in Common with Gold Standard

The graphs below compare the source of documentation between the more accurate against the less accurate. If there were two sources indicating the highest in common with the gold standard, both sources were indicated. For the more accurate group, the most commonly reported source was the EMR, followed by the patient and the chart. In contrast in the less accurate group, the most commonly reported source was the patient, followed by the EMR and the chart.

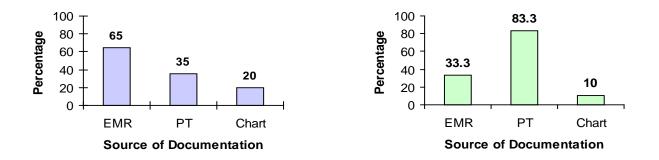


Figure 7: Documentation Source of the More (L) versus Less (R) Accurate Groups

In comparing the two groups, using the Pearson correlation coefficient between the source and the total number of medications (gold standard), the results are indicated in the table below.

	More A	ccurate	Less Accurate			
	r	Р	r	Р		
EMR	0.5371	0.0146	0.7692	< 0.0001		
PT	0.4931	0.0272	0.8205	< 0.0001		

Table 15: Pearson Coefficient of Two Source with the Gold Standard

These results indicate that in the more accurate group, both the EMR and Patient source was closely correlated with the EMR being more highly correlated. In the less accurate group, the difference between the EMR and patient source were both statistically significant with a P <0.0001. The correlation between the patient versus EMR and the total number of medications was slightly greater with the patient versus EMR group. Thus for the more accurate group, the EMR was more closely related to the gold standard, whereas in the less accurate group the patient source was more closely related to the gold standard.

Logistical regression analysis was performed comparing the two populations in the table below. Three variables were found to be statistically significant at p < 0.001 - the total number of medications, number of drug-drug interactions, and number of moderate drug-drug interactions. There was no difference in age, number of conditions, number of sample medications, number of CAMs/OTC, and Health Plan between the two groups.

	More Accurate				Less Accurate						
	No.	Range	Mean	Median	No.	Range	Mean	Median	t-test	DF	Significance level
No. conditions	20	2-10	3.9	3.0	30	1-12	4.27	4.0	0.36	48	0.7211
No. Sample Medications	2	1	1	1	4	1	1	1	-	-	-
No. of CAMs/OTC	10	1-5	1.9	1	28	1-10	3.14	3	1.96	36	0.0574
Total Meds	20	3-18	9.2	8.5	30	7-38	16.83	15	4.31	48	0.0001
No. Drug- drug interactions	20	0-20	6.85	4.5	30	1-101	16.67	11.5	2.22	48	0.0311
Minor	9	1-6	1.78	1	23	1-24	4.26	3	1.46	30	0.1542
Moderate	18	1-17	6.28	4.5	30	1-63	12.57	8.5	2.02	46	0.0494
Major	3	1-5	2.67	2	10	1-14	3.1	1.5	-0.17	11	0.8668

 Table 16:
 Comparison of More and Less Accurate Groups

The variable with the lowest p-value (0.0001) was the total number of medications. In looking at the difference between the two groups, the less accurate group had not only a large mean number of total medications (16.83 versus 9.2) that were taken, but also the range number

of medications taken was greater (7 to 38 versus 3 to 18). Similarly for drug-drug interactions, the mean number (16.67 versus 6.85) was greater in the less accurate group and the range was wider (1 to 101 versus 0 to 20). Of the drug-drug interactions including drug/OTC/CAM, the number of moderate drug-drug interactions was the most significant. In the less accurate group, the mean number of moderate drug-drug interactions was 12.57 versus 6.28 in the more accurate group. While the number of CAMs/OTCs between the two groups was not significant, a higher percentage of individuals took CAMs/OTCs in the less accurate group (93.3%) versus (50%) in the more accurate group.

### 5.5 QUALITATIVE QUESTIONS

A series of open-ended questions were asked to gather information on how participants managed their medications.

### 5.5.1 INDICATORS OF INDEPENDENCE

Three questions were asked of individuals to assess the level of independence and cognitive ability.

#### 5.5.1.1 Accompaniment to Doctor's Appointment

The first question was whether someone accompanies them to the appointment. Eight individuals (16%) had someone accompany him/her to the doctor's appointment. This was a family member with the most often being a spouse. They report having a family member/spouse

accompany him/her to the appointment was optional except in one case where the daughter attends all of the appointment with her father.

#### 5.5.1.2 Assistance with Medications

The second question was whether they needed assistance with their medications. All of the participants said that they could manage getting and sorting out their own medications. One participant commented that he let his wife do it for him so that she would have something to do. The final question was whether the instructions from the physician or pharmacist were clear. All of the participants reported that the instructions from their physician/pharmacist were clear and all reported that they seek clarification from their physician and not of their pharmacist. Additionally, all but one of the participants were able to correctly identify which drug was presented for which condition. The one female individual who could not correctly identify her drugs relied upon the comprehensive AIDS clinic that managed all of her care including having all of her prescriptions filled at a specific pharmacy.

### 5.5.1.3 Prescription Coverage and Method of Payment

In the third question, participants were asked about the extent of their prescription coverage and how were medications purchased. Forty-two individuals (84%) had a co-pay, where most individuals did not report difficulties with their co-pay. However, one individual reported that in the prior year three months into the coverage, the individual had already reached the maximum coverage and thus the remaining costs had to be paid by the participant. Two individuals reported that they had a 'poor deductible' in that the participant had to pay out of pocket \$2500, and the other \$4000 per year in medication costs before coverage started. Thus, the individuals had to pay first a significant amount before the coverage began.

The most surprising data were from the eight individuals (20%) who paid out of pocket. The main reasons given were difficulties in not being covered last year; no prescription coverage; and the insurance company pays only 20%. Two of the eight individuals reported using \$10 coupons that were received in the mail upon switching pharmacies. One individual reported traveling half an hour to a different pharmacy location part of the same chain in order to receive the discount. In the past, this individual had reported to having her prescription filled at 5 different pharmacies. The difference in price of paying out-of-pocket was found by one individual to be \$7.50 at a warehouse club store versus \$10.00 through the insurance company. Many times this was not 'advertised' rather the pharmacist informed them of the difference. In a third individual, a friend had received a bag of a sample medication through her son who is a physician. She has since then been taken off this medication and had given it to the participant who takes the exact same medication. The participant then refills his medication bottle with the sample medication. Another individual reported 'altering' the frequency of taking the medication as this would lengthen the number of pills. These later four participants mentioned this in confidence and asked that it not be reported to their physician.

### **5.5.1.4 Sample Medications**

The participants were then asked if they had taken any sample medications or medications prescribed to someone else. No one reported taking someone else's medication. A total of 6 (12%) sample medications were reported when asked to report what medications they were taking. Many of these individuals did not consider being given a sample from their doctor for a new prescription or for seasonal medications such as allergies taking a sample medication. One individual reported that even though the medication is not new, he still asks at every appointment

for sample medications to help cover costs. He also reports that his wife disproves of his asking due to embarrassment.

#### 5.5.1.5 Other Comments

Two individuals reported that they were discontinuing a medication after completion of the filled prescription. One participant had discontinued the medication due to side effects and the other participant had already thrown the medication away. They were going to inform their physician at the next appointment.

As part of their health plan, several individuals reported obtaining their medications through the hospital pharmacy, but were required to obtain their injectable medications through mailorder. One individual commented on ordering his medications online through a pharmacy in Canada to save costs. In this later case, the individual paid for the medication out-of-pocket.

At the time of the study, none of the pharmacies that are part of a grocery store or drug store chain shared the same database. Each store had its own database and thus could not detect if a patient had previously visited the chain of stores at a different location. Consequently this diminished the pharmacist's ability to detect drug-drug interactions.

Overall, there were two frequent comments arising from the qualitative questions: (1.) Drug affordability and strategies on reducing costs; and (2.) vitamins and herbs are not medications and thus are not important to be told to their physician.

#### 6.0 DiSCUSSION

Of the 50 participants, the average profile of a participant had 4.12 conditions and 76% of the participants took on average 2.82 over-the-counter medications or CAMs. The mean number of drug-drug interactions per participant was 12.74 with the majority presenting moderate risks to the participant. Recommendations for monitoring include clinical and laboratory work, and symptoms to look out for. The risks noted in drug-drug interaction database are based on reported cases and animals studies (minor risks) and provide guidance to the physicians. The interplay of the drug and the individual, changing of medications and delayed effects of medications is a complex environment that makes it difficult to identify an ADR and attribute it specifically to one medication. However, whether the risks were minor, moderate or major, as the pharmacodynamics and pharmacokinetics of each individual is so unique, the aim is to reduce the number of potential drug-drug interactions.

Obtaining accurate information about the medication and CAM that a patient is taking is complex due to the number of risk factors that are involved. Of the fourteen risk factors for medication errors listed in Section 2.0, ten of the risk factors were identified in this study. These include patient's and caregiver's knowledge, co-morbidity, polypharmacy, multiple sources of pharmaceuticals, sample medications,, over-the-counter products, herbal medicines, health information over the internet, changing medication schedules, and identifying an adverse event. The other risk factors of similar drug names, health literacy, pharmacokinetic and pharmacodynamic changes, and cognitive impairment of older populations may not have been identified as these were not targeted in this study. Each of these risk factors can lead to an ADR, and there is a high probability that several risk factors are inter-playing at the same time.

#### 6.1.1 AIM 1: BEST SOURCE OF MEDICATION DOCUMENTATION

This study had three aims. The first aim was to determine whether medication documentation in a (a) chart; (b) computerized physician order entry system (CPOE – i.e. EasyScript); (c) pharmacy record; (d) insurance company; (e) specialist, and (f) as reported by the patient are comprehensive (i.e. does their medication list includes medications prescribed by all healthcare providers). On average, a participant had 4.48 sources of medication. Of the six sources of documentation examined in across all of the participants (EMR, patient, chart, pharmacy, insurance provider, and specialist), both the patient and the EMR had a similar frequency and the exact same range of observations, and were found to be statistically significant as the best source of documentation. However, the patient source had a higher correlation coefficient and a smaller confidence interval with the gold standard in comparison to the EMR with the gold standard. Therefore, this suggests while both the EMR and patient are good sources of documentation, the patient source is a better source than the EMR.

In an effort to identify one referral source for a physician that would result in the highest percentage of medication/CAM of a source shared with the gold standard, a secondary analysis was done. The population was separated into two groups: individuals whose highest source is 80% or higher consistent with the gold standard versus individuals whose highest reported

source was less than 80%. Individuals with the highest source of 80% or higher consisted of 20 individuals, resulting in the second group with 30 individuals. This first group was called the more accurate group and the second group was referred to the less accurate group.

In comparing the characteristics between the more accurate and less accurate groups, the highest reported source documentation for these two groups differed. In the more accurate group it was the EMR in 65% of the individuals, versus in the less accurate group, the patient was reported to be the highest source in 83.3% of the individuals that were in common with the gold standard. While the Pearson correlation coefficient comparing the EMR and patient sources with the two groups were almost the same in the more accurate group, the EMR was slightly higher. In the less accurate group, the resultant Pearson correlation coefficient was statistically significant for both the EMR and patient sources with the patient being slightly higher.

To answer what would account for the different sources in the two populations, the question 'What are the characteristics of each of the groups that would result in one group being more accurate than the other?' was addressed. There was no difference in age, sex, insurance providers or number of sample medications. There was however, statistical significant difference between the number of total medications reported, and the number of potential drug-drug interactions specifically the number of moderate risk drug-drug interactions. While the number of individuals taking CAMs/OTC was higher in the less accurate group than in the more accurate group, the number of CAMs/OTC was not statistically different.

This suggests that factors contributing to the less accurate group are more individuals taking CAMs/OTC, which also contributes to a higher number of total medications and in turn a higher risk for moderate drug-drug interactions. Since CAMs/OTC are not consistently recorded in any of the sources, the physician is likely unaware of the CAMS/OTC as well as, potential drug-drug interactions to be able to monitor the patient appropriately. This then accounts for why the patient as a source has a higher correlation with the gold standard.

#### 6.1.2 AIM 2: EXTENT OF AWARENESS OF A PATIENT'S MEDICATIONS

The second aim of the study is related to the first to determine the extent of awareness by the various physicians on which and how medications are taken by a patient (medication discrepancy). This includes determining the extent to which medications are prescribed but not filled, administered differently than is prescribed, not taken on a consistent basis, or taken in a self-medicating manner outside of the prescribed route.

None of the sources of medications consistently listed the name, dose, route, or frequency of the medication to allow for an accurate comparison. This includes letters from other physicians who are participating in the care of the patient. The information provided in the letter sometimes included the name of the drug and less frequently the dose and frequency. There is also a potential delay for the primary care physician to receive the letter due to time required for transcription, receipt, and filing, thus the information may not be in real time. Letters from specialists are typically filled separately from the patient visits and thus are not readily available with the other list of medications often listed either in the front of the chart or with the patient visit. This can be further complicated when the clinic utilizes an EMR system. The letter is either scanned into the system and thus becomes one of the many screens to search or is filed separately from the EMR system. Given the EMR and patient had a higher correlation with the gold standard,, a feedback mechanism from the insurance provider, the pharmacist, or specialist would not necessarily increase gathering of complete information. The expectation of an EMR system amongst family physicians and specialists who are using the same EMR to record drug information is that this information could be shared more easily.

Additional factors identified through the qualitative questions are that CAMs/OTCs taken by a patient are not consistently reported by the patient nor recorded in either the EMR or paper chart, and the patient does not always report that they have discontinued a medication or taken someone else's medication. Sample medications were often given by the physician or requested by the patient for medications that were on a trial basis to determine the efficacy, or were for seasonal ailments. These were also not consistently noted in the patient's chart or the electronic medical record. Additionally, participants reported requesting samples for a drug that was costly. These requests were sporadically filled and even less noted in the patient's record. In one case, a participant was taking sample medications that were received through a family member of a friend who had access to the medication. This later case and all undocumented sample medications possesses an increased risk to the patient as any drug recalls will not be able to be traced to the patient. Thus the medication discrepancy between the physician and patient can have considerable gaps.

### 6.1.3 AIM 3: POTENTIAL DRUG-DRUG INTERACTIONS

The third aim of the study was to determine the potential impact of errors on disease management of a patient and clinical alerts (includes drug-drug interactions, drug allergies, dosage checks, duplicate therapies). A total of 637 drug-drug, drug-CAM/OTC interactions were identified in 50 individuals. Using the web-accessible Drug Interaction Checker, 26% of individuals had a major, 96% moderate and 64% minor risk potential of having a drug-drug or drug-CAM/OTC interaction. Recommendations for major risks included cautioning co-administration and self administration prior to consulting a healthcare provider (CAMs), moderate risks included monitoring for signs of additive/diminished drug effects, toxicity and signs of organ dysfunction, and minor risks were reported when the clinical significance was unknown due to a lack of studies/reports or based on animal studies.

It is unknown in the process where identifying the potential drug-drug interactions is to occur. Theoretically, the primary care physician managing the patient's overall care receives the letters from the specialists and is able to identify potential drug-drug interactions. However, this study found that not all of the specialist's letters contained the patient's medications, and if the medication was listed, it rarely contained the dose and frequency. All of the specialists letters were filed in the patient chart and were not integrated into the patient's EMR unless the healthcare provider documented it into the EMR. One physician reported that they could not be aware of all the different types of medications and relied upon the specialists to inform them. Only on a few occasions were OTC/CAMs recorded on the patient record and even less frequent in the EMR system. There are several reasons why the OTC/CAM is not documented: (1). it is not often reported by the patient, (2). there is no mechanism for recording it in the EMR, (3)

there is no standardization for CAMs and thus there is wide variation in formularies, and (4) even if it was documented it is unclear what could be the potential effects. Thus, the potential for drug-drug interactions exist, however, the exact mechanism or recommendations for monitoring are unclear.

The second logical point in the process for checking drug-drug interactions is at the pharmacy as the pharmacists have the knowledge and information on prior filled medications to check and explain drug-drug interactions. There are several challenges to this that have been observed in this study: (1). People visit different pharmacies including online pharmacies for a variety of reasons (convenience, as required by the healthcare plan, cost). Even with an integrated pharmacy system, as patients have been shown to choose different pharmacy chains it is difficult for a pharmacist to accurately perform a drug-drug interaction check. (2). Pharmacies do not keep track of CAM/OTCs. (3). All of the participants reported asking their physician and not pharmacist for information.

The third logical point in the process for checking drug-drug interactions is that the health insurance provider processes the claims regardless of which pharmacy a patient visits. Insurance companies have information on the name, dose and frequency of a medication. By using the dose and amount supplied, the insurance company can also project when a refill is needed. If the patient is not refilling a prescription according to the estimated completion date, this may then suggest non-compliance or altering of the medication schedule thus providing a feedback mechanism to the physician. However, as the insurance company knows only of prescriptions that have been filled, they are unaware if the patient decides not to fill a medication. The insurance company is also unaware of OTC/CAM and sample medication that a patient may be taking. This study also reported due to drug affordability and limited allowances, many individuals are choosing to pay out-of-pocket thus avoiding the insurance company. Several grocery stores such as Walmart, Sam's Club, Giant Eagle, are offering reduced set prices on generic and OTC drugs that are paid out-of-pocket once again bypassing the insurance companies.

#### 6.1.4 OTHER FINDING

#### **6.1.4.1 Extent of Drug Affordability**

Patients who do not take their medications as prescribed are often considered non-compliant by the health care community. Addressing the underlying assumption of non-compliance, different strategies have been developed including pill reminders, physicians counseling patients on the importance of regularly taking medications, pharmacies sending refill notices to patients following the medication frequency schedule. Non-compliance was not the focus of this study and many individuals reported knowing what the drug name, dose, frequency and indication were, but due to cost developed their own strategies for affordability.

Several of the participants mentioned visiting different pharmacies to take advantage of discounts when a prescription is transferred. At the time of this study, none of the pharmacy chains including grocery stores had an integrated pharmacy record system. Thus a pharmacy in another neighborhood could not detect that a patient visited the pharmacy chain before. This was discussed earlier in that it limits the ability of a pharmacy to perform drug-drug interactions. One patient even reported driving two neighborhoods over to avoid detection and to take

advantage of the coupon received in transferring her prescription. In all of the cases where this was reported, the participants did not wish to tell their physician as they were embarrassed that they could not afford the medication.

In this study of fifty participants, out of the fourteen risk factors, 10 (71%) of these risk factors were observed patient's and caregiver's knowledge, co-morbidity, polypharmacy, multiple sources of pharmaceuticals, sample medication, over the counter products, herbal medicines, health information by other sources, changing medication schedules, and identifying an adverse event. One of the possible reasons that the other risk factors were not noted was that there were not questions designed to obtain this information. However, an additional risk factor was identified in this study, drug affordability. It is therefore, quite amazing given all the identified risk factors that more major adverse event, there are perhaps more ADRs that are not detected.

Any of the actions of not reporting regular taking of OTC/CAM, switching pharmacies, discontinuing or altering the dose or frequency of a medication without consulting the physician, and taking sample medications results in the patient being the most accurate source of medication documentation. By doing these things, the patient takes responsibility into their own hands for the management of their health to monitor the symptoms and to take the appropriate action.

### 6.1.5 SECOND OBJECTIVE OF THE STUDY

The second objective of the study given the findings in the first objective is to identify the potential feasibility of establishing a collaboration of shared information between the academic medical institution utilizing a CPOE system, health plan and pharmacy to help improve patient care and thereby reduce medication errors. The benefits to the physician are readily obvious in providing better care by knowing what the individual is taking, and both the physician and pharmacy are then able to check for drug-drug- or drug-homeopathic interactions. Incorporating the use of insurance or health plan data, which contains all of the reimbursed medical interactions on a patient is extremely helpful to physicians, but as well serves to encourage and be able to market to individuals to stay within the medical, pharmacy system as they are able provide comprehensive care.

Reducing potential adverse drug events helps all the players involved including avoidable sick time to the patient, physician time and medical expenses to the healthcare provider. It has already been discussed that information from insurance companies and pharmacies while helpful adds a lesser extent to the completeness of the medication documentation. Given the findings of the study, there are perhaps other strategies that should be considered. This study hopes to shed some light on what factors should be considered in order to provide healthcare providers and patients with the most accurate, up-to-date and readily accessible information that will be addressed in the next section.

#### 7.0 INTERPRETATION

A medication error is defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, or patient. Such events may be related to professional practice, health care products, procedures and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding, dispensing; distribution; administration; education; monitoring; and use. The medication error process can be related to the Swiss cheese model developed by James Reason in 1990. In the Swiss cheese model, each step in the medication pathway is like multiple slices of Swiss cheese, stacked together, side-by-side. Reason hypothesized that most accidents or in this case, medical errors, can be traced to one of more of four levels of failure: organizational influence, unsafe supervision, preconditions for unsafe acts, and the unsafe acts themselves.

As shown in the figure below, in the Swiss cheese model, each slice of cheese represents an organization's defenses or barriers against failure (Gregory and Kaprielian 2005). While each hole in the cheese slices represent individual weaknesses in separate parts of the system, and are continually varying in size and position in all slices. Each slice of cheese is an opportunity to stop an error and when there are smaller and fewer number of the holes, there is a lesser risk for an error. In the second figure, when there is an alignment of holes, the system as a whole

produces failures permitting (in Reason's words) "a trajectory of accident opportunity". Thus all of the defenses are absent allowing an error to occur.

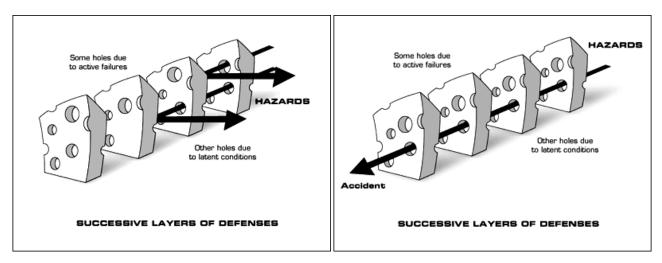


Figure 8: Reason's Swiss Cheese Model

Horn and Hansten (Horn and Hansten 2004) applied the Reason's Swiss Cheese Model to drug therapy errors. They comment in tracing back an adverse event, it is always where someone – e.g. the prescriber, pharmacist, nurse of patient – could have taken action to prevent it.

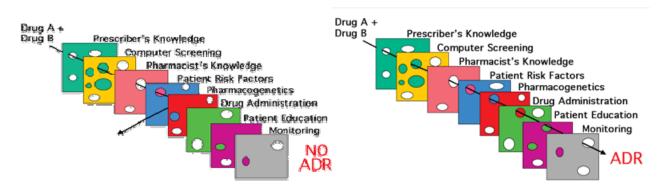


Figure 9: Swiss Cheese Model Applied to an ADR

Similar to Reason's model the slices represent the defenses against adverse outcomes from a drug interactions, however, unlike Reason's Swiss Cheese Model the holes are dynamic, opening, closing and changing location as the individual defenses change over time. In the figure above, the initiating event is Drug A and Drug B. When one of the defenses, such as a pharmacist checking for possible drug interactions between drugs, a trajectory of a hazard arrow or ADR can occur. Alternatively, when a patient visits more than one pharmacy, takes CAMs without their physician's knowledge, a patient maybe be creating or enlarging more holes thus leading to a trajectory of accident opportunity. There are active defenses, i.e. when someone intervenes, and latent defense, i.e. a patient's pharmacogenetics renders him/her resistant to the ADR, or the dose or duration of the drug is insufficient to produce an ADR. Additionally, even when all the holes line up there are some ADRs where the outcome is not clinically significant such as the example given earlier about the combined use of angiotensin-converting enzyme inhibitor and a potassium-sparing diuretic. This combination is used with good results, although, occasionally predisposes a patient to developing life-threatening hyperkalemia.

What is missing from this model and the surprising finding of this study is the influence of drug affordability on patient's behavior by not reporting OTC/CAM to their physicians. In this study, patients were taking sample medications, switching pharmacies, and altering dose/frequency with the underlying rationale to reduce costs. This becomes not a non-compliance issue to taking medication, rather survival of the patients in affording healthcare and maintaining/achieving better health status. Individuals are actively taking responsibility for their healthcare in their own hands by their own actions, thus intentionally or unintentionally individuals are shifting the health locus of control to themselves (internal versus to powerful others or chance) and enlarging the holes in the Swiss Cheese Model. These observations are

contrary to the IOM's report on medical errors being largely basic flaws in the way health systems are organized as the report fails to take into account human behavior for survival.

Drug affordability may be defined as the absence of economic barriers to a good or service. The two frequently used measures are: a consumer's ability to pay and his or her physical access to a good or service. The popular magazine Consumer Reports conducted a study and found that 29% of people who had health insurance were 'underinsured' with coverage so poor that they postponed medical care because of costs (Consumer Reports, 2007). While most health insurance programs are designed to subsidize costs based on income, it cannot measure or address the consumer's unwillingness to pay in light of other expenditures. As costs have increased this has forced some individuals to pay by credit cards in order to maintain or achieve a better health status. Other individuals have resorted to altering their own medication therapy (i.e. changing dosing from twice a day to once a day) to lengthen the drug supply. Cost barriers often lead to not filling a prescription or skipping or splitting doses owing to cost.

There is very little research literature on this topic, but to help individuals manage the cost of prescription medication, in a recent article published in the popular magazine Smart Money, the author lists four ways to cut drug costs.

#### **Table 17: Recommendations for Saving Prescription Costs**

- 1. Take advantage of store promotions four supermarket chains offer for free generic antibiotic giveaways to shoppers with club cards.
- 2. Go for generics recommends readers to ask their physician for a generic equivalent or for a comparable drug.

#### Table 17 continued

- 3. Shop around compare drug prices at various pharmacies and ask for price matching to another pharmacy which is often not advertised. The author cautions that if different prescriptions are filled at different pharmacies that they tell the pharmacist of all the medications to avoid any possible adverse events.
- 4. Split pills some pills are available at twice the dose and at the same price as lower doses.

They also suggest that the reader ask their physician if they can take the medicine every other day or once a day instead of three times a day (Spina, Glassman et al. 2005). While many of the five recommendations may help save money for the consumer, these suggestions actually increase an individual's risk for ADRs and encourage self-management outside of the care of a healthcare provider. For example, obtaining and taking antibiotics on their own; buying in bulking means less visits and monitoring by a physician; shopping around reduces the ability of one pharmacy to accurately detect potential drug-drug interactions; and splitting pills could alter the dose taken are all personal behaviors.

In looking at the influence of drug affordability on a drug purchase, Ranji, Wyn et al. looked at a sample size of 1177 women ages 18-64 who use greater than 1 prescription drug on a regular basis. Of non-elderly women, 54% reported that they were taking a prescription medication on a regular basis and 32% reported  $\geq$ 1 affordability barrier in the prior year and either forgo or delay a prescription and/or reduce facing a cost barrier, regardless of income level. Uninsured women had the highest odds of facing a cost barrier, regardless of income level. Low-income, uninsured women were nearly seven times as likely to face a cost barrier to prescription drugs, compared with higher income women with insurance. Even uninsured women with incomes  $\geq$ 200 % of the federal poverty level had 5 times the odds of facing a prescription medicine cost

barrier, and low-income, insured women experienced two times the odds of a prescription medicine cost barrier, compared with their higher income, insured counterparts. Lack of health insurance coverage was significantly associated with experiencing cost barriers, regardless of income level, underscoring the critical role that insurance coverage plays in protecting women from out-of-pocket costs and for accessing prescription medicines. Limiting out-of-pocket spending was found to be important for low-income women who have insurance, because even minimal costs can act as barriers for this group (Ranji, Wyn et al. 2007).

Of 1606 elderly patients sampled, half of whom had exceeded their drug benefits from the previous year, and all had total drug expenditure in their cap level. Two-thirds reported difficulty paying for medications, and 25% decreased medication use because of cost. Most wanted providers to ask about medication affordability (81%), consider cost (86%), offer choices (70%) and to persuade them or decide for them which medication to use (88%), but few said providers asked about affordability (17%), usually or always discussed prices (19%) or offered choices (45%), although nearly all said providers chose their medications (93%). Sixty-two percent had asked providers for help with drug costs, although, 34% used less medications because of cost or had difficulty paying for medications had not asked for help (Tseng, Dudley et al. 2007).

As the economy has moved from a manufacturing-based to a service economy, health insurance coverage has become less stable as the service sector has less access to health insurance. With rising health insurance premiums, many small employers can no longer afford to offer health benefits which results in employees contributing a larger share to their coverage. According to the US Census Bureau, nearly 46 million Americans or 18% of the population under 65 years were without health insurance in 2007 (DeNavas-Watt, Proctor et al. 2008). Similarly, the Agency for Healthcare Research and Quality, using the Medical Expenditure Panel Survey (MEPS) estimated that 54 million Americans (27%) under the age of 65 are uninsured. With the change in economy, most laid-off workers lost their health insurance with their incomes and private healthcare coverage is becoming too costly to afford. This in turn will increase the number of individuals seeking Medicaid and State Children's Health Insurance Programs thus driving up state expenses as revenues are declining (Chu and Rhoades 2008). The Urban Institute estimates that nearly 65.7 million Americans may be unemployed by 2019 posing an enormous cost to the Medicaid and states programs (Holahan, Garrett et al. 2009).

McKinsey Consulting estimates that Americans spend \$294 billion on out-of-pocket medical costs annually including doctors' office co-payments to surgeries and prescription medications. Of this about 25% (\$74 billion) of the annual expenses is being charged to regular standard credit cards. Unlike optional purchases, medical expenses are often unavoidable thus making it a appealing for lenders to create special financing. Viewing a growing industry, GE Money and Citibank both have special credit cards that can only be used for elective medical procedures, such as LASIK vision correction, liposuction, and cosmetic dentistry, which are generally paid out of the pocket. GE Money's CareCredit card limits their 7 million users to a network of doctors, and there are plans for MasterCard Worldwide and OptiumHealth to issue a debit card that draws funds from existing healthcare spending and flexible spending accounts. While making it easier for consumers to pay and hospitals to collect, one missed pay can raise interest rates to 27% (Kavilanz 2009). Thus what is a good strategy to build a layer of defense to increase detection and prevention, and reduce the number of ADR?

The cause and effect model presented earlier in this study needs modification. It accounts for system factors, but not personal behaviors that are fluid and dynamic. Thus the framework for this study must be revisited to incorporate the findings from this study. In the diagram on the following page, the prior identified risk factors are the double lined box in pink and the hatched lines and shaded in blue are the additional risk factors identified in this study. Many of the potential causes (inputs) are patient-related thus, emphasis should be placed on the patient's role in the medication process.

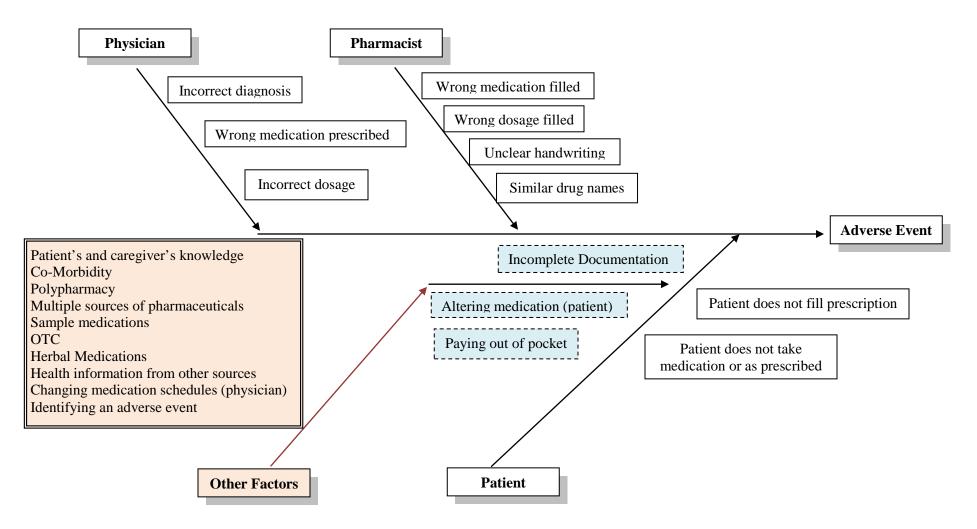


Figure 10: Revised Cause and Effect Model for the Medication Process

#### 7.1.1 CONSIDERATIONS FOR DEVELOPING A STRATEGY

The approach to reduce the possibility of ADRs is a multi-step process. As discussed, there have been several systems approaches (use of a medication sheet / list, medication reconciliation by patients / health care provider, pre-printed order sheets, computerized physician order entry, clinical decision support system, personal digital assistant medication safety via the internet, a common EMR system). Because one cannot seal off all the holes in the defense system, strategies must involve a systematic approach to strengthen all of the defenses.

#### 7.1.1.1 Healthcare Professional and Patient Awareness

Reducing the number of ADRs involves developing awareness of everyone in the medication process, including physicians, nurses, pharmacists, patients and their families. This can involve reminding the healthcare team to collect and the patient to report the medication history including name, dose, frequency, and indication in a culture that minimizes blame and maximizes communication. Tools to gather the information can include a medication list for patient's to complete, a readily access method for healthcare professionals to gather and record the information and a mechanism for a healthcare professional to review the medication history and determine whether there are any potential drug-drug interactions.

The Institute for Healthcare Improvement (IHI) in December 2006 launched the 5 Million Lives Campaign aiming at reducing harm from high-alert medications. The campaign focuses on four categories of drugs – anticoagulants, narcotics and opiates, insulin and sedatives, as they are more likely to be associated with harm. The IHI has developed several tools for medication reconciliation and suggestions for healthcare organizations to implement. Thus a feasible strategy for medication reconciliation and review of indiscriminate polypharmacy is to target the higher risk groups. These would include: patients over 40 years, having co-morbidity of greater than 3 concurrent conditions, polypharmacy of greater than 6 medications and on medications for longer than 6 months. Thus, one could identify higher risk individuals by weighting the risk factors similar to the Medication regimen complexity as described by Maddigan et al. discussed earlier. Thus individuals would be scored 1 (over the age of 40 years) + 1 (more than 3 conditions) + 1 (greater than 6 medications) + 1 (on medication for longer than 6 months) + 1 (takes herbal medicines) + 1 (involves either an anticoagulant, narcotic and opiate, insulin and sedative) = 6. Individuals over the score of 4 would be flagged for medication reconciliation and review.

### 7.1.1.2 Central Database Accessible to Healthcare Providers

The second objective of this study was to determine the feasibility of establishing a collaboration of shared information. The benefit of shared information is that collectively it gathers information from multiple sources and is thus not dependent upon the communication between the physicians, nor upon the understanding and recall of the patient. It also is a mechanism to detect polypharmacy and unnecessary drug use. The best system is one that captures all of the information (name, dose, frequency, route, and indication of the medication) and not just pieces. It has worked for the Alberta Government who invested billions of dollars into creating Alberta Netcare EHR which captures all testing, prescribed dispensed drugs, known allergies and intolerances, thus providing up to date, accurate medical information to authorized health professionals. It also has incorporated decision support tools such as drug-to-drug and drug-to-allergy interaction alerts to avoid prescriptions that conflict. It now contains over 90% of all

prescription activity on patients across Alberta. The main reason for the success is in contrast to the United States, Alberta has a one payor system.

#### 7.1.1.3 Drug Plan for Patients

For various reasons, individuals may be unable to pay whether for a temporary period or over a time span. Individuals should not be forced to weigh their health status against their basic food and shelter costs, nor should they go into debt with credit cards paying for medication. This can include fixed pricing so individuals are not forced to search out opportunities to save money. While the focus is on reducing costs, New York State designed and developed an integrated workers' compensation/health plan prescription drug program that also captures drug information. The ONECARD RX indicates to the pharmacy that the visit is part of the client's insurance prescription drug plan network and the prescription is filled at no cost. The ONECARD RX is accepted where the program has negotiated generic substitution, reduced administrative fee and negotiated pricing. Obtaining a prescription at no cost is an incentive for the clients, it reduces the overall cost for the plan and controls where the clients go to get the prescriptions filled. Similarly, pharmacies are offering clients different incentives to encourage clients to have prescriptions filled at only their pharmacy chain. These include cheaper generics, pill packaging broken into days of the week, and drug-drug interaction checks. These are examples of individual efforts and collaboratively working together to capture drug information is one step in the multi-step process. This can be a challenge due to the number of stakeholders involved each with different interests and systems, but is a method of not only controlling costs but where a patient obtains their medications for better record keeping. It would be also informative to find out whether the effect of Medicare- Part D that was being introduced when this study was being conducted has any effect on patient behavior.

#### 7.1.1.4 Increasing Access for Patients to Medications

Even though affordability is a barrier, some healthcare plans do not allow a patient access to medications. In some cases, patients can only obtain a 30-day supply for routine medications where a 90-day supply would be more affordable. There was some rational to the article in the magazine Smart Money. Additionally, some brand medication is more effective to patients who are only able to purchase the generics. One of the eligibility criteria for this study was having an insurance provider. It would be interesting to see the perspectives of individuals who do not have health insurance and what their attitudes and approaches are to medication therapy.

#### 7.1.1.5 Mechanism to Identify, Report, Assess, and Feedback of Drug-Drug Interactions

A mechanism for identifying, reporting, assessing at a global level to better define higher risk ADRs, and feeding back to healthcare professionals drug-drug and drug-OTC/CAM interactions is key for detecting and preventing real ADR. Pharmacists were found the most often to voluntarily report ADRs and have been shown to be very beneficial when they are part of the healthcare team. They are knowledgeable in prescription drugs, OTC and many CAM available in their store that they would be able to filter out some of the confusing, non-essential alerts. However, as pharmacies extend longer hours resulting in multiple pharmacists, ordering through the internet, etc, the one-on-one relationship with a pharmacist is becoming lost. There is also the reality of whom does the pharmacist have responsibility to report the ADR to – a central database, but also to the physician? And is the pharmacist or another healthcare specialist the best able to navigate through all of this information?

#### 7.1.1.6 Patient's Behavior

The patient has a variety of rationale for not reporting OTC/CAM; altering the frequency and/or dose of a medication; non-compliance; taking sample medications without their physician's knowledge; visiting multiple pharmacies which all makes determining drug-drug interactions extremely difficult. As long as there is a cost to healthcare and barriers to cost, patients will always be seeking and developing different strategies to make healthcare more affordable. A key strategy would be to educate patients on what types of information to provide to their physicians. This includes a written list of all the medications from other physicians including name, dose, frequency, route and indication; what is a side effect and who and when it needs to be reported to; and what to do if they decide to discontinue a medication. It has been shown that patients seek information first online and receive a lot of information through direct-to-consumer advertising. Information through these vehicles can help steer patients towards reliable individuals, who can help them discern the information. One challenge is that this study showed that patients are reluctant due to embarrassment of informing their physicians about their strategies to reduce costs. Therefore, further research needs to be done on understanding the barriers and perspectives of the patients.

### 7.1.1.7 Use of an ADR Helpline

The resultant multi-prong approach is centralizing information with mechanisms for detecting and reporting ADRs relayed through a qualified healthcare provider that respects the variety of patient's behaviors and multiple stakeholders. Until a collaborative agreement can be made amongst the stakeholders (physicians, insurance companies, pharmacies, patient), one approach that does not interfere with the physician-patient relationship of the patient who is too embarrassed to inform the physician is a third party such as the state health department which has no stated interest. A healthcare provider such as a nurse who understands the various conditions, medications, patient behaviors can weed out the unnecessary information and triage the questions so that a patient can more appropriately inform a physician, or a patient can report all the medications and find out if there are drug-drug interactions. A drug information telephone line can be established that would also help individuals with health literacy, understand side effects, the role of informing their physicians of medications or even help build the medication list for the patient to share with healthcare providers with a list of potential drug-drug interactions with evidence based guidance for a physician to consider in terms of monitoring. The cost would be for the health department and the savings across the health system.

#### 8.0 CONCLUSION

Patient safety needs to be a state of mind and not a technology. As human error can never be taken from the equation, more research needs to be done to further understand the barriers and challenges so that a better solution can be developed that would reduce ADRs. While the suggestions for building a better defense system against ADRs does not address all the gaps or holes in the Swiss cheese, it has highlighted more clearly some of the holes and the importance of not only system changes but also patient behavior. A secondary study would be worthwhile to explore the implementation of using the public health department as a resource for patients in drug information, as well as, further studies into understanding the role of drug affordability and the health locus of control with the aim of building the best system. As aging population associated with co-morbidity and polypharmacy expands, coupled with the economic challenges with the changes in the economy, the results and questions raised during this study are important to consider as the problem will likely grow with time.

### **APPENDIX** A

### INVITATION LETTER TO PARTICIPANTS ON PRACTICE LETTERHEAD

#### Dear (Patient):

Solano & Kokales Internal Medicine Associates – UPMC is participating in a research study looking at the documentation of medication in a patient's chart, computer record (where applicable), insurance company, pharmacies, and as reported by the patient. The purpose of this study is to examine the various sources of medication documentation and compare them for accuracy and completeness.

We invite you to participate in a study looking at Evaluating Patient Medication and Complementary Therapies being conducted through the Department of Behavioral and Community Health Science at the Graduate School of Public Health at the University of Pittsburgh.

We are inviting:

- Individuals over the age of 40
- Who have been diagnosed either with arthritis, diabetes or hypertension
- Have either UPMC Healthplan or all Highmark Blue Cross Blue Shield products to include by not limited to the following ClassicBlue, COMPLETE-care, Security 65, Signature-65, SelectBlue POS, KeystoneBlue HMO, SecurityBlue, DirectBlue, PPOBlue, Medigap, Preferred Blue, Freedom Blue, Community Blue, Keystone HMO, and Direct Pay Keystone as your insurance provider

Participation involves:

- Answering a few questions about your medical history and medications taken over the last six months
- Authorizing the release of medication records from your physicians, insurance plans and pharmacies
- This study requires a one-time visit <u>only</u>

You are under no obligation to participate in this study as it is voluntary. I will continue to be responsible for your ongoing medical care, regardless of your decision. The study does not alter the management of your condition and your records have not and will not be released to the research group without your consent. We can gather all the necessary information at your next appointment and over the phone. There is no required ongoing follow-up or evaluation for the study. There is also no cost to participate.

If you are interested in finding out more about the study, please return the enclosed preaddressed postage-paid postcard and a member of the research team will contact you within a few weeks. If you have any questions about this study, please do not hesitate to Ms. Tammy Mah at 412-647-8235. She would be delighted to discuss the study with you. Thank you and we look forward to hearing from you.

### Sincerely,

Patient's attending physician

#### **APPENDIX B**

### SCREENING SCRIPT

Thank you for inquiring to find out more our research study. My name is \_\_\_\_\_\_, and I am a research coordinator at the University of Pittsburgh. The purpose of this research study is to compare the accuracy of documentation of medication in various sources including the patient's medical chart, PowerChart Office / EasyScript (a computerized medical chart system in some offices at the University of Pittsburgh Medical Center), pharmacies utilized by the patient and as recorded by his/her insurance provider. This is accomplished by asking the patient to report as well as, the researchers examining the various sources of medication documentation on the dosage, frequency and route of all medications that is either physician prescribed, self-prescribed, herbal and vitamin supplements, and medication samples.

Participation involves answering questions about your medical and medication history, authorizing the release of your health records from all of your physicians who you have seen for the past six months or more, any pharmacies where you have your prescriptions filled, and from your health insurance company. Do you think you might be interested in participating in this study?

**[If No]:** Thank you very much for allowing me to speak with you today. Please feel free to contact us if you have any future questions or if you decide you might be interested in the future.

**[If Yes]:** But before enrolling people in this study, we need to determine if they are eligible. I would like to ask you a few questions regarding your age and medical history. You don't have to answer these questions if you don't want to. Our eligibility status with respect to the study may change as more information is gathered regarding your medical history. You also need to understand that all information that I receive from you by phone, including your name and any other identifying information will be kept strictly confidential in our locked offices. The purpose of these questions is to determine whether you are eligible for our study. Your participation is voluntary; you do not have to complete these questions.

Screening Script (cont.)

1.	Do I have your permission to ask you these questions?	Yes	No
2.	Are you over the age of 40 years?	Yes	No
3.	Have you been diagnosed with hypertension, arthritis,		
	or diabetes?	Yes	No
4.	Do you have either Highmark Blue Cross Blue Shield		
	or UPMC Healthplan as your insurance provider?	Yes	No

Coordinator \_\_\_\_\_ Date \_\_\_\_\_

### **APPENDIX C**

### **PARTICIPANT PROFILES**

In the tables and diagrams below are the profiles for each of the participants. The table includes information on the participant's demographic information (sex, age), number of medical conditions at the time of participation, range of missing medications / herbs / alternatives medicines identified from the various sources (EMR, participant's medical chart (paper), participant, pharmacist(s), insurance company, specialist(s) letter(s) found in the participant's medical chart as available. Also included in the number of medications / herbs / over-the-counter medicines as reported by the participant and how many sample medications are taken.

The Venn diagram is a pictorial representation of how many of the sources share the same information from a drug list, this looks only at the occurrence of a medication / herbal medicine. The center where all the circles intersect is considered the 'gold standard' which is all of the reported medications / herbals combined. Indicated in brackets beside each of the sources is the number of medications / herbals that are missing. i.e. -5 states that five medications were not listed as compared to the gold standard.

The types of errors are indicated in the table beside the figure with associated risks.

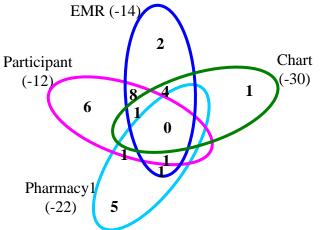
				_					
Sex	Age	No. of	Total No. of		nge of Missin		No. of Self	No. (	of Sample
Ber	Age	Conditions	Meds/CAMs	Meds/C	CAMs from So	ources	Prescribed		Meds
Μ	87	7	9		2-5		1		0
	EMR (-5)								
Errors									
					Туре	Event			Risk
Partic	cipant /			hart	Dose	Missing		-	
	2)			-5)	Frequency	Missin	g		-
(	_/		3	-3)	Drug-Drug	Furose	mide-Lisinop	ril	Moderate
			$f \setminus f$		Drug-Drug	Verapa	mil-Centrum	Silver	Moderate
		2			Drug-Drug	Aspirin-Lisinopril			Moderate
					Drug-Drug	Verapamil-Aspirin		Moderate	
2					Drug-Drug	Ig Verapamil-Lipitor			Moderate
		Specialist (-2)			Drug-Drug	g Verapamil-Lisinopril Mir			Minor
Man	ageme	-			Drug-Drug	Furose	mide-Aspirin		Minor

agem nt:

- Monitor blood pressure (2), diuresis, electrolytes, renal function; calcium channel blocker therapy
- Monitor for signs of prolonged bleeding and reduced antihypertensive effect; \_
- Clinical significance is unknown. \_

Participant #4

Sex	Age	No. of	Total No. of	Range of Missing	No. of Self	No. of Sample
DUA	nge	Conditions	Meds/CAMs	Meds/CAMs from Sources	Prescribed	Meds
Μ	57	12	36	12-30	1	0

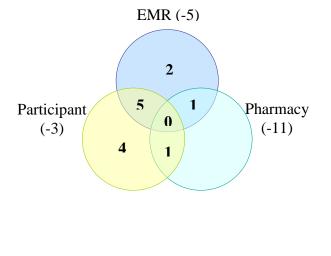


Errors	Errors					
Туре	Event	Risk				
Dose	Missing	-				
Frequency	Missing	-				
Drug-Drug	Motrin-Medrol Dosepak	Moderate				
Drug-Drug	Zithromax-Lovastatin	Moderate				
Drug-Drug	Zithromax-Seroquel	Moderate				
Drug-Drug	Lovastatin-Prevacid	Moderate				
Drug-Drug	Neurontin-Remeron	Moderate				
Drug-Drug	Neurontin-Seroquel	Moderate				
Drug-Drug	Remeron-Seroquel	Moderate				

Management:

Monitor for signs of GI ulceration and bleeding; muscle pain, tenderness or weakness (2); torsade de pointes; CNS and respiratory depression (2)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
Μ	68	2	13	3-11	3	0



Errors		
Туре	Event	Risk
Dose	Missing	_
Frequency	Missing	-
Drug-Drug	Aspirin-Micronase	Moderate
Drug-Drug	Lisinopril-Glucophage	Moderate
Drug-Drug	HCTZ-Glucophage	Moderate
Drug-Drug	HCTZ-Lisinopril	Moderate
Drug-Drug	Micornase-Lisinopril	Moderate
Drug-Drug	Aspirin-Lisinopril	Moderate
Drug-Drug	Micronase-Testim	Moderate
Drug-Drug	Aspirin-Vitamin E	Moderate
Drug-Drug	Micronase-HCTZ	Moderate
Drug-Drug	Aspirin-Avalide	Moderate
Drug-Drug	Doxycycline-HCTZ	Minor

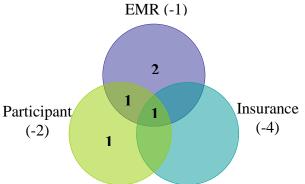
Management:

- Monitor for signs of hypoglycemia (4);
- Monitor blood glucose (1); blood pressure; renal function (2)
- Caution against self-medication without first consulting a healthcare provider

-

Participant #3

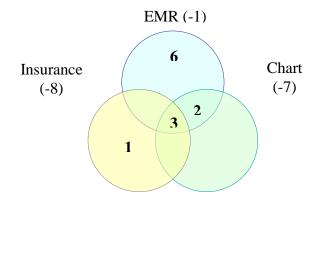
Sex	Δαο	No. of	Total No. of	Range of Missing	No. of Self	No. of Sample
Sex	Age	Conditions	Meds/CAMs	Meds/CAMs from Sources	Prescribed	Meds
Μ	67	2	5	1-4	1	0



Errors		
Туре	Event	Risk
Dose	80 mg (pt) vs 180 mg (EMR)	-
Frequency	Missing	-
Drug-Drug	Cipro-Aspirin	Moderate
Drug-Drug	Cipro-Mefloquine	Moderate
Drug-Drug	Cipro-Centrum Silver	Moderate

- Monitor for signs of CNS stimulation; arrhythmia
- Dosing interval recommendations

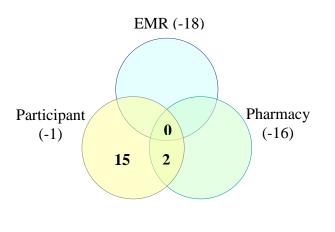
Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	77	5	12	1-8	0	0



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Diltiazem-Clorazepate	Moderate
Drug-Drug	Diclofenac-Celexa	Moderate
Drug-Drug	Clorazepate-Celexa	Moderate
Drug-Drug	Diltiazem-Celexa	Moderate
Drug-Drug	Diclofenac-Diovan	Moderate
Drug-Drug	Diclofenac-Fosamax	Moderate
Drug-Drug	Calcium + D-Fosamax	Moderate
Drug-Drug	Lotrisone-Advair Diskus	Moderate
Drug-Drug	Diltiazem-Lotrisone	Moderate
Drug-Drug	Dilitazem-Diclofenac	Moderate
Drug-Drug	Diltiazem-Calcium + D	Moderate
Drug-Drug	Lotrisone-Celexa	Moderate
Drug-Drug	Clorazepate-Calcium + D	Minor

- Dosage adjustment, dosing interval recommendations
- Monitor for signs of hematologic bleeding; excessive or prolonged CNS and respiratory depression; serotonergic activity; gastric ulcers; systemic glucocorticoid effects; excessive calcium channel blocker effects (2)
- Monitor blood pressure (2)
- Clinical significance unknown

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	63	2	18	1-18	3	1

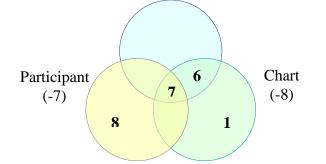


Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Atenolol-Elavil	Moderate
Drug-Drug	Atenolol-Endocet	Moderate
Drug-Drug	Elavil-Endocet	Moderate
Drug-Drug	Atenolol-Calcium + D	Moderate
Drug-Drug	Elavil-Hydrocodone	Moderate
Drug-Drug	Calcium + D-Iron	Moderate
Drug-Drug	Zinc-Iron	Minor

- Monitor for signs of hypotension (2); excessive or prolonged CNS and respiratory depression (2)
- Dosing interval recommendation (3)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	66	4	22	7-9	5	0

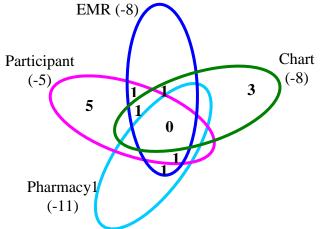
EMR (-9)



Errors				
Туре	Event	Risk		
Dose	Missing	-		
Frequency	Missing	-		
Drug-Drug	Bupropion-Reglan	Major		
Drug-Drug	Diovan HCT-Celebrex	Moderate		
Drug-Drug	Diovan HCT-Metformin	Moderate		
Drug-Drug	Metoprolol-Diovan HCT	Moderate		
Drug-Drug	Aspirin-Diovan HCT	Moderate		
Drug-Drug	Bupropion-Valsartan	Moderate		
Drug-Drug	Metoprolol-Celebrex	Moderate		
Drug-Drug	Aspirin-Celebrex	Moderate		
Drug-Drug	Gemfibrozil-Celebrex	Moderate		
Drug-Drug	Diovan HCT-Celebrex	Moderate		
Drug-Drug	Toprol-XL-Metformin	Moderate		
Drug-Drug	Toprol-XL-Viactiv Calcium	Moderate		
Drug-Drug	Diovan HCT-Bisacodyl	Moderate		
Drug-Drug	Toprol-XL-Bupropion	Moderate		
Drug-Drug	Toprol-XL-Diovan HCT	Moderate		
Drug-Drug	<b>Bupropion-Diovan HCT</b>	Moderate		
Drug-Drug	Toprol-XL-Restoril	Moderate		
Drug-Drug	Bupropion-Restoril	Moderate		
Drug-Drug	Diovan HCT-Restoril	Minor		
Drug-Drug	Reglan-Restoril	Minor		
Drug-Drug	Aspirin-Prilosec	Minor		

- Extreme caution when co-administration can reduce the seizure threshold
- Monitor blood pressure (3); renal function
- Concomitant administration not recommended (4)
- Monitor for signs of GI ulceration and bleeding; celecoxib toxicity; hypoglycemia; excessive CNS and respiratory depression
- Dosing interval recommendations
- Caution self-medication prior to consulting healthcare provider
- Clinical significance unknown (3)

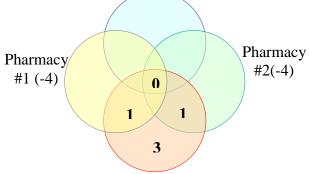
S	Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
	F	80	5	13	5-11	4	1



Errors					
Туре	Event	Risk			
Dose	Missing	-			
Frequency	Missing	-			
Drug-Drug	Ibuprofen-Aspirin	Major			
Drug-Drug	Aspirin-Calcium carbonate	Moderate			
Drug-Drug	Calcium carbonate-alendronate	Moderate			
Drug-Drug	Levothyroxine-Calcium carbonate	Moderate			
Drug-Drug	Ibuprofen-Alendronate	Moderate			
Drug-Drug	Aspirin-Omeprazole	Moderate			

- Monitor for signs of GI ulceration and bleeding, toxicity
- Dosing interval recommendations (2)
- Clinical significance unknown

Sex	Ago	No. of	Total No. of	Range of Missing	No. of Self	No. of Sample
ЗСХ	Age	Conditions	Meds/CAMs	Meds/CAMs from Sources	Prescribed	Meds
М	81	2	5	3-9	5	0
	EMR (-5) Errors					



Errors					
	Туре	Event	Risk		
	Dose	Missing	-		
y	Frequency	Missing	-		
	Drug-Drug	Atenolol-Hyzaar	Major		
	Drug-Drug	Atenolol-Centrum Silver	Moderate		

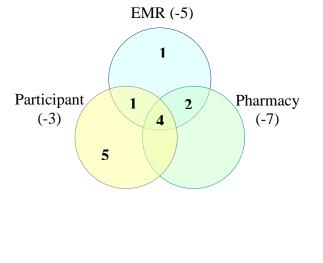
Participant (-0)

- Monitor serum potassium levels; blood pressure, blood glucose
- Dosing interval recommendation

Sex	Age	No. of Total No. of Conditions Mode/CAMe			Range of Missing Meds/CAMs from Sources		No. of Self		f Sample
-		Conditions	Meds/CAMs	Meds/	CAMs from So	urces	Prescribed	N	leds
Μ	81	2	14		3-8		3		0
	EMR (-6)								
					Errors				
					Туре	Event			Risk
	,	2			Dose	Missi	ng		-
Partici	nant		Dharmaa	7	Frequency	Missi	ng		-
(-2)	• /	1	1 Pharmacy 1 (-9) Drug-Drug Niacin-Zocor				Moderate		
(2)	/	5	(-9)		Drug-Drug	Aspir	in-Felodipine	Moderate	
	6				Drug-Drug	Calci	um-Fosamax		Moderate
			Drug-Drug			Felodipine-Calcium		Moderate	
		$\mathbf{X}$			Drug-Drug	Aspir	in-Calcium		Moderate
					Drug-Drug	Nitro	glycerin-Tem	Moderate	
					Drug-Drug	Felod	ipine-Nitrogl	ycerin	Moderate
					Drug-Drug	Aspir	in-Diovan		Moderate
					Drug-Drug	Tema	zepam-Calci	um	Minor
					Drug-Drug	Aspir	in-Nitroglyce	erin	Minor
					Drug-Drug	Aspir	in-Niacin		Minor

- Monitor for signs of muscle pain, tenderness or weakness; altered blood pressure control (3); effective calcium channel blocker therapy; diminished or inadequate analgesic and anti-inflammatory effects; altered renal function
- Dosing interval (2) and amount adjustments recommended
- Clinical significance unknown

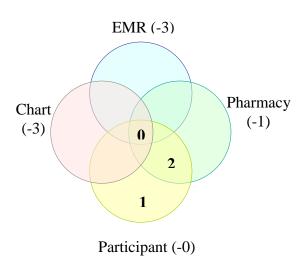
Corr	1 00	No. of	Total No. of	Range of Missing	No. of Self	No. of Sample
Sex	Age	Conditions	Meds/CAMs	Meds/CAMs from Sources	Prescribed	Meds
М	91	2	13	3-7	3	0
•		•			•	



Errors					
Туре	Event	Risk			
Dose	Missing	-			
Frequency	Missing	-			
Drug-Drug	Diltiazem-Aspirin	Moderate			
Drug-Drug	Lasix-Celexa	Moderate			
Drug-Drug	Diltiazem-Celexa	Moderate			
Drug-Drug	Calcium carbonate-Ferrous Gluconate	Moderate			
Drug-Drug	Diltiazem-Centrum Silver	Moderate			
Drug-Drug	Diltiazem-Proscar	Moderate			
Drug-Drug	Aspirin-Calcium carbonate	Moderate			
Drug-Drug	Diltiazem-Calcium carbonate	Moderate			
Drug-Drug	Aspirin-Celexa	Moderate			
Drug-Drug	Ranitidine-Calcium Carbonate	Minor			
Drug-Drug	Lasix-Aspirin	Minor			

- Monitor for signs of prolonged bleeding time and antihypertensive effect; hypotension; excessive serotonergic activity; altered calcium channel blocker therapy (2); diminished or inadequate analgesic and anti-inflammatory effects; hematologic complications
- Dosing interval (2) and amount adjustments recommended
- Clinical significance unknown

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
М	63	2	3	0-3	1	0

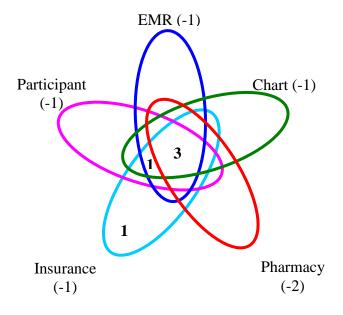


Errors						
Туре	Event	Risk				
Dose	Missing	-				
Frequency	Missing	-				
Drug-Drug	Propanolol-Acetaminophen	Minor				

Management:

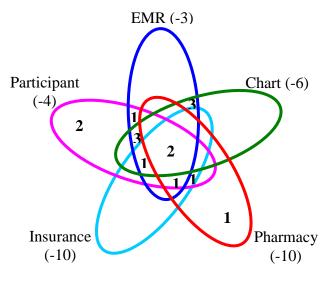
- Clinical significance unknown

Sex	Age	No. of	Total No. of	Range of Missing	No. of Self	No. of Sample
DUX	Age	Conditions	Meds/CAMs	Meds/CAMs from Sources	Prescribed	Meds
М	72	4	5	2	0	0



Errors					
Туре	Event	Risk			
Dose	Missing	-			
Frequency	Missing	-			
Drug-Drug	No interactions				

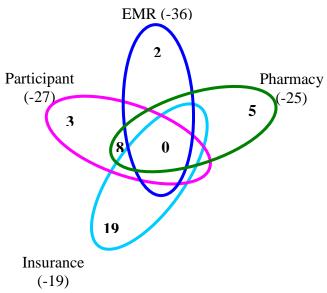
Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds	
М	83	6	15	2-9	1	0	



Errors					
Туре	Event	Risk			
Dose	Missing	-			
Frequency	Missing	-			
Drug-Drug	Fursemide-Metoprolol	Moderate			
Drug-Drug	Aspirin-Diclofenac	Moderate			
Drug-Drug	Metroprolol-Diclofenac	Moderate			
Drug-Drug	Furosemide-Diclofenac	Moderate			
Drug-Drug	K-Dur 10-Lisinopril	Moderate			
Drug-Drug	Aspirin-Lisinopril	Moderate			
Drug-Drug	Lorazepam-Lisinopril	Moderate			
Drug-Drug	Furosemide-Lisinopril	Moderate			
Drug-Drug	Furosemide-Lorazepam	Moderate			
Drug-Drug	Lisinopril-Diclofenac	Moderate			
Drug-Drug	K-Dur 10-Cyanocobalamin	Minor			
Drug-Drug	Metoprolol-Levothyroxine	Minor			
Drug-Drug	Metoprolol-Aspirin	Minor			
Drug-Drug	Levothyroxine-Zocor	Minor			
Drug-Drug	Furosemide-Aspirin	Minor			
Drug-Drug	Metoprolol-Lorazepam	Minor			

- Monitor serum potassium levels; blood pressure (5); blood glucose; renal function (4); electrolytes
- Monitor for signs of GI ulceration and bleeding; hypotension; diuresis; hypotension
- Clinical significance is unknown (6)

Sex	Age	Age No. of Total No. of Conditions Meds/CAMs		Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds	
F	52	10	38	19-36	2	0	



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency		-
Drug-Drug	Prilosec-Atazanavir	Major
Drug-Drug	Zoloft-Mirtazapine	Major
Drug-Drug	Mirtazapine-Citalopram	Major
Drug-Drug	Atropine-Potassium Chloride	Major
Drug-Drug	Imitrex-Citalopram	Major
Drug-Drug	Atenolol-Reyataz	Major
		Major
Drug-Drug	Inderal-Reyataz	Major
Drug-Drug	Colchicine-Reyataz	Major
	Digitek-Reyataz	Major
<u> </u>	Zoloft-Imitrex	Major
Drug-Drug	Lipitor-Reyataz	Major
1rug-Drug	Colchicine-Kaletra	Major
Drug-Drug	Prevacid-Reyataz	Major
Drug-Drug	Prevacid-Lipior	Moderate
Drug-Drug	Inderal-Diovan	Moderate
Drug-Drug	Prednisone-Diovan	Moderate
Drug-Drug	Combivir-Lipitor	Moderate
Drug-Drug	Zithromax-Lipitor	Moderate
Drug-Drug	Potassium Chloride-Diovan	Moderate
Drug-Drug	Hydromorphone-Diovan	Moderate
Drug-Drug	Digitek-Lipitor	Moderate
Drug-Drug		Moderate
	Atenolol-Diovan	Moderate
Drug-Drug	Temazepam-Mirtazepine	Moderate
Drug-Drug	Warfarin-Kaletra	Moderate
Drug-Drug	Inderal-Kaletra	Moderate
Drug-Drug	Digitek-Kaletra	Moderate
Drug-Drug	Metoclopramide-Kaletra	Moderate
Drug-Drug	Prednisone-Kaletra	Moderate
Drug-Drug	Zoloft-Kaletra	Moderate
Drug-Drug	Glimepiride-Kaletra	Moderate
Drug-Drug	Kaletra-Mirtazapine	Moderate
Drug-Drug	Atenolol-Mirtazapine	Moderate

# Participant #15 (cont.)

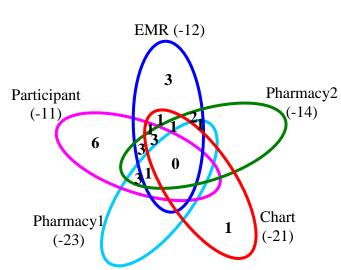
Errors Type	Event	Risk
7.4	Inderal-Mirtazapine	Moderate
<u> </u>	Bumetanide-Mirtazapine	Moderate
	Hydromorphone-Mirtazapine	
	Metoclopramide-Mirtazapine	
<u> </u>	Bumetanide-Actonel	Moderate
Drug-Drug	Tums-Actonel	Moderate
	Zoloft-Lantus	Moderate
	Kaletra-Lantus	Moderate
<u> </u>		Moderate
	Citalopram-Lantus	Moderate
	Prednisone-Kaletra	
	Glimepiride-Kaletra	Moderate
	Lantus-Kaletra	Moderat
	Warfarin-Reyataz	Moderat
	Lantus-Reyataz	Moderat
	Prednisone-Reyataz	Moderat
	Tums-Reyataz	Moderat
	Glimepiride-Reyataz	Moderat
	Kaletra-Reyataz	Moderat
	Prednisone-Lantus	Moderat
	Bumetanide-Lantus	Moderate
Drug-Drug	Inderal-Lantus	Moderat
Drug-Drug	Atenolol-Citalopram	Moderat
Drug-Drug	Warfarin-Citalopram	Moderat
Drug-Drug	Inderal-Citalopram	Moderat
Drug-Drug	Bumetanide-Citalopram	Moderat
Drug-Drug	Hydromorphone-Citalopram	Moderat
Drug-Drug	Metoclopramide-Citalopram	Moderat
	Prilosec-Citalopram	Moderat
	Temazepam-Citalopram	Moderat
	Zoloft-Citalopram	Moderat
<u> </u>	Glimepiride-Citalopram	Moderat
	Kaletra-Citalopram	Moderat
	Atenolol-Lantus	Moderat
	Mirtazapine-Reyataz	Moderat
	Zoloft-Glimepiride	Moderat
	Atropine-Pyridostigmine	Moderat
	Atenolol-Prednisone	Moderat
	Warfarin-Prednisone	Moderat
	Inderal-Prednisone	Moderat

### Participant #15 (cont.)

Errors Type	Event	Risk
	Atenolol-Tums	Moderate
	Inderal-Tums	Moderate
	Atropine-Tums	Moderate
	Atenolol-Zoloft	Moderate
	Kaletra-Reyataz	Minor
	Warfarin-Bumetanide	Minor
	Warfarin-APAP	Minor
	Inderal-APAP	Minor
	Combivir-APAP	Minor
	APAP-Atropine	Minor
	Prilosec-Glimepiride	Minor
	Prevacid-Kaletra	Minor
	Amoxicillin-Zithromax	Minor
Drug-Drug	Combivir-Kaletra	Minor
	Digitek-Prevacid	Minor
Drug-Drug	Digitek-Tums	Minor
Drug-Drug	Prednisone-Tums	Minor
	Temazepam-Tums	Minor
Drug-Drug	Warfarin-Vitamin C	Minor
Drug-Drug	Inderal-Vitamin C	Minor
Drug-Drug	Warfarin-Lipitor	Minor
	Metamucil-Glimepiride	Minor
Drug-Drug	Digitek-Prilosec	Minor
Drug-Drug	Warfarin-Inderal	Minor
Drug-Drug	Potassium Chloride-Lantus	Minor
	Digitek-Metoclopramide	Minor
Drug-Drug	Metamucil-Lantus	Minor
Drug-Drug	Atropine-Digitek	Minor

- Concomitant medication not recommended (16)
- Monitor for signs of serotonin syndrome (4); GI injury; unexplained muscle pain, tenderness, or weakness (6); musculoskeletal toxicity (1); hypotension (13); excessive or prolonged CNS and respiratory depression (14); hydrocorticism; hypoglycemia (18); hypocalcemia (2); signs of bleeding (11); adrenal function; cardiac function; excessive serotonergic activity (3); cholinergic crisis; altered prokinetic efficacy
- Monitor serum colchicine levels (2); blood pressure (5); electrolyte level (5); body weight (4); serum potassium; serum digitoxin levels (5); serum digitalis levels (2); serum sodium
- Dosing interval recommendation (8)
- Clinical significance unknown (21)

S	Sex 4		No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds	
	F	61	4	28	11-23	5	0	



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Motrin-Aspirin	Major
Drug-Drug	Percocet 10/325-Lomotil	Moderate
Drug-Drug	Percocet 10/325-Imodium	Moderate
Drug-Drug	Synthroid-NovoLog	Moderate
Drug-Drug	Synthroid-Humulin R	Moderate
Drug-Drug	Synthroid-Glucophage	Moderate
Drug-Drug	Synthroid-Calcium	Moderate
Drug-Drug	Lomotil-Loperamide	Moderate
Drug-Drug	Lomotil-Calcium	Moderate
Drug-Drug	Lomotil-Percocet 10/325	Moderate
Drug-Drug	Percocet 10/325-Effexor XR	Moderate
Drug-Drug	Percocet 10/325-Neurontin	Moderate
Drug-Drug	Novolin L-Avandia	Moderate
Drug-Drug	Humulin R-Avandia	Moderate
Drug-Drug	Glucophage-NovoLog	Moderate
Drug-Drug	Glucophage-Novolin L	Moderate
Drug-Drug	Glucophage-Humulin R	Moderate
Drug-Drug	Avandia-NovoLog	Moderate
Drug-Drug	Effexor XR-Neurontin	Moderate
Drug-Drug	Lotrisone-Avandia	Moderate
Drug-Drug	Lotrisone-Flonase	Moderate
Drug-Drug	Calcium-Fosamax	Moderate
Drug-Drug	Aspirin-NovoLog	Moderate
Drug-Drug	Aspirin-Novolin L	Moderate
Drug-Drug	Motrin-Fosamax	Moderate
Drug-Drug	Atenolol-Exffexor XR	Moderate
Drug-Drug	Atenolol-Motrin	Moderate
Drug-Drug	Motrin-Effexor XR	Moderate
Drug-Drug	Atenolol-Novolin L	Moderate
Drug-Drug	Atenolol-Calcium	Moderate
Drug-Drug	Atenolol-Oxycodone	Moderate
Drug-Drug	Ranitidine-Glucophage	Moderate
Drug-Drug	Atenolol-Humulin R	Moderate
Drug-Drug	Atenolol-Lomotril	Moderate
Drug-Drug	Atenolol-Glucophage	Moderate

### Participant #16 (cont.)

Errors	Errors						
Туре	Event	Risk					
Drug-Drug	Aspirin-Calcium	Moderate					
Drug-Drug	Aspirin-Effexor XR	Moderate					
Drug-Drug	Aspirin-Humulin R	Moderate					
Drug-Drug	Atenolol-NovoLog	Moderate					
Drug-Drug	Lotrisone-Avandia	Moderate					
Drug-Drug	Aspirin-Protonix	Minor					
Drug-Drug	Atenolol-Synthroid	Minor					
Drug-Drug	Atenolol-Aspirin	Minor					
Drug-Drug	Lotrisone-Novolin L	Minor					
Drug-Drug	Lotrisone-Humulin R	Minor					
Drug-Drug	Lotrisone-Glucophage	Minor					
Drug-Drug	Lotrisone-Allegra	Minor					
Drug-Drug	Motrin-Ranitidine	Minor					
Drug-Drug	Ranitidine-Percocet 10/325	Minor					
Drug-Drug	Ranitidine-Fosamax	Minor					
Drug-Drug	Percocet 10/325-Lomotil	Minor					
Drug-Drug	Aspirin-Omeprazole	Minor					
Drug-Drug	Lotrisone-NovoLog	Minor					

- Monitor for signs of GI ulceration and bleeding; excessive or prolonged CNS depression and constipation (3); respiratory depression (2); hypoglycemia (15); additive CNS effects (2); excessive serotonergic activity; cardiovascular adverse events (2); systemic glucocorticoid effects; gastric ulcers; hypotension (2); hematologic complications; lactic acidosis; diminished or inadequate analgesic anti-inflammatory effects; bleeding; gastric adverse effects (2)
- Monitor TSH levels; serum glucose levels (9); blood pressure
- Dosing interval recommendations (4)
- Clinical significance unknown (6)

Sex Age		No. of	Total No. of		nge of Missin		No. of Self	No. of S	<b>^</b>
	-	Conditions	Meds/CAMs	Meds/C	AMs from So	ources	Prescribed	Mee	15
F	52	9	20	5-15 3 0					
		EMR (	-7)		Errors	-			1
				Туре	Event			Risk	
		5				Missing	/		-
	Frequency Missing							-	
Particip	ant		Ph	armacy1	0 0		one-Cymbalta		Major
(-5)			<b>T</b> `	(-15)			um chloride-C		Major
(	7	3					DS-Potassiu	ım chloride	Moderate
					Drug-Drug	Trazodo	one-Vicodin		Moderate
					Drug-Drug	Diovan	HCT-Caltrat	e + D	Moderate
			$\overline{\mathcal{D}}$		Drug-Drug	Bactrim	DS-Diovan	HCT	Moderate
					Drug-Drug	Potassiu	ım chloride-D	viovan HCT	Moderate
(	Chart				Drug-Drug	Reglan-	Cymbalta		Moderate
	(-15)				Drug-Drug	Compaz	zine-Cymbalt	a	Moderate
	/				Drug-Drug	Vicodin	-Cymbalta		Moderate
					Drug-Drug	Compaz	zine-Vicodin		Moderate
					Drug-Drug	Compaz	zine-Zofran		Moderate
					Drug-Drug	Diovan	HCT-Compa	zine	Moderate
							Compazine		Moderate
					<u> </u>	Ŭ	HCT-Trazod	lone	Moderate
					Drug-Drug				Moderate

Management:
 Monitor for development of signs of serotonin syndrome (2); upper GI injury; altered renal function; excessive or prolonged CNS and respiratory depression (3); torsades de pointes; hypotension (2)

Drug-DrugCompazine-Trazodone

Drug-DrugSynthroid-Caltrate + D

Drug-DrugCaltrate + D-Boniva

Drug-DrugSynthroid-Trazodone

Drug-DrugProtonix-Cymbalta

Drug-DrugCaltrate + D-Cymbalta

Drug-DrugDiovan HCT-Caltrate + D

Moderate

Moderate

Moderate

Moderate

Minor

Minor

Minor

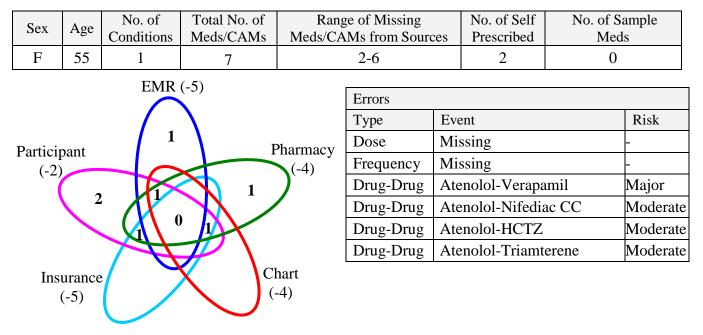
- Caution patients against self-medication prior to consulting healthcare provider (2)
- Interval dosing (2) and adjustment recommendation
- Clinical significance unknown (3)
- -

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	44	4	22	8-19	5	1

	EMR (-9)	
Participant		Pharmacy1
(-8) 7	$\frac{2}{3}$ 1	1)(-14)
Chart		
(-19)		

Errors Type E	Event	Risk
<i>2</i> 1	lissing	-
Frequency M		_
	upropion-Trazodone	Major
Drug-DrugB	upropion-Interferon Beta 1B	Major
	tenolol-Hyzaar	Moderat
	lagyl-NuvaRing	Moderat
	spir-Low-Celebrex	Moderat
	yzaar-Celebrex	Moderat
Drug-DrugX	anax-Wellbutrin SR	Moderat
Drug-DrugX	anax-Trazodone	Moderat
	razodone-Celebrex	Moderat
	lagyl-Celebrex	Moderat
	rovigil-Nexium	Moderat
	uvaRing-Provigil	Moderat
	rovigil-NuvaRing	Moderat
	tenolol-Xanax	Moderat
Drug-DrugA	tenolol-Wellbutrin SR	Moderat
Drug-DrugA	tenolol-Trazodone	Moderat
	anax-Hyzaar	Moderat
	ellbutrin SR-Hyzaar	Moderat
Drug-DrugH	yzaar-Trazodone	Moderat
Drug-Drug Ti	razodone-Hyzaar	Moderat
	spir-Low-Hyzaar	Moderat
Drug-DrugH	yzaar-Celebrex	Moderat
	tenolol-Aspir-Low	Minor
Drug-DrugX	anax-NuvaRing	Minor
	uvaRing-Ester-C	Minor
	anax-Provigil	Minor
	razodone-Provigil	Minor
	spir-Low-Nexium	Minor

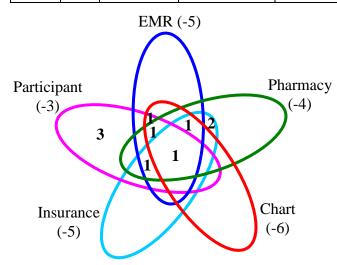
- Monitor for signs of altered renal function; hypotension (8); bleeding (3); GI ulceration; increased seizure activity (2); excessive or prolonged CNS effects; celecobix toxicity
- Monitor serum potassium levels, blood pressure (2), blood glucose; renal function
- Concomittant administration not recommended (3)
- Dosing interval and adjustment recommendations (1)
- Clinical significance is unknown (6).



\*Not included in the figure is Pharmacy 2 – 1 observation listed; 6 missing observations

- Monitor for hemodynamic response and tolerance (2);
- Monitor serum potassium levels (2); blood pressure (2); blood glucose (2)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
М	71	4	10	3-6	3	0



Errors		
Туре	Event	Risk
Dose	25 mg/day (Pt) versus	
Dose	50 mg/day (EMR, Chart, Pharm)	_
Frequency	Missing	-
Drug-Drug	Aspirin-Asacol	Moderate
Drug-Drug	Toprol-XL-Centrum	Moderate
Drug-Drug	Levoxyl-Centrum	Moderate
Drug-Drug	Toprol-XL-Aspirin	Minor
Drug-Drug	Toprol-XL-Levoxyl	Minor

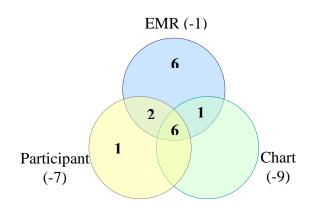
- Monitor renal function
- Dosing interval recommendation (2)
- Clinical significance unknown (2)

Sex	Age	No. of	Total No. of		nge of Missing				Sample	
BUA	Age	Conditions	Meds/CAMs	Meds/C	AMs from Source	ces	Prescribed	М	leds	
F	53	2	11		4-10		3		0	
		EMR	(-4)	[	Errors					
					Туре	Eve	Event		Risk	
		2			Dose	Mis	ssing	-		
Particip	ant		Р	harmacy	Frequency	Mis	Aissing		-	
(-4)				)(-8)	Compliance	Par	ticipant not ta	iken med	-	
	3 $1$				Drug-Drug	Adv	Advil-Aspirin		Major	
				Drug-Drug	Ate	tenolol-Advil		Moderate		
		4	$\mathcal{P}$		Drug-Drug	Hyo	drocodone-De	etrol	Moderate	
Spe	cialist			art	Drug-Drug	Zoc	cor-Zetia		Moderate	
(	(-9)		(-	8)	Drug-Drug	Ate	nolol-Aspirin	1	Minor	
			$\sim$		Drug-Drug	Ace	etaminophen-	Detrol	Minor	

\*Not diagrammed is the Insurance Company – is 1 of the 2 drugs shared with EMR, Participant, Specialist, and Pharmacy, missing from the Insurance Company is 10 drugs

- Potential additive GI toxicity advised to report signs and symptoms
- Monitor for prolonged CNS depression and constipation; antihypertensive response
- Monitor laboratory work, blood pressure

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	77	7	16	1-9	0	0



Errors			
Туре	Event	Risk	
Dose	Missing	-	
Frequency	Missing	-	
Compliance	Part. threw out med.	-	
Drug-Drug	Prednison-Avelox	Major	
Drug-Drug	Methadone-Avelox	Major	
Drug-Drug	Diltiazem-Methadone	Moderate	
Drug-Drug	Celebrex-Avelox	Moderate	
Drug-Drug	Iron Polysach-Avelox	Moderate	
Drug-Drug	Salmeterol-Avelox	Moderate	
Drug-Drug	Prednisone-Celebrex	Moderate	
Drug-Drug	Oxycodone-Celebrex	Moderate	
Drug-Drug	Methadone-Salmeterol	Moderate	
Drug-Drug	Lanoxin-Prednisone	Moderate	
Drug-Drug	BuSpar-Prednisone	Moderate	
Drug-Drug	Diltiazem-BuSpar	Moderate	
Drug-Drug	Methadone-BuSpar	Moderate	
Drug-Drug	Diltiazem-Lanoxin	Moderate	
Drug-Drug	Diltiazem-Oxycodone	Moderate	
Drug-Drug	Methadone-Oxycodone	Moderate	
Drug-Drug	BuSpar-Oxycodone	Moderate	
Drug-Drug	Diltiazem-Prednisone	Moderate	
Drug-Drug	Prednisone-MiraLax	Moderate	
Drug-Drug	Probenecid-Avelox	Minor	

- Caution is recommended of concomitant administration (6)
- Clinical monitoring for signs of CNS stimulation/depression (3); digoxin toxicity; hypokalemia
- Clinical monitoring of electrolyte levels; hypotension; blood pressure; body weight
- Dosing interval recommendations

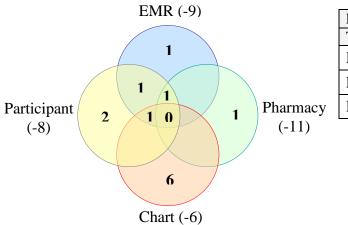
	Nev Are		ige of Missing AMs from Sources		No. of Self No. Prescribed		f Sample Ieds			
	F	57	2	9	Wieds/ CI	1-7		0	0	
	EMR (-1)					Errors				
	$\sim$				Туре	Eve	ent		Risk	
		2		2		Dose	Mis	ssing		-
Pa	rticip	ant		Ph	armacy1	Frequency	Mis	ssing		-
	(-2)				(-7)	Drug-Drug	Asp	Aspirin-Fluoxetine		Moderate
		1 2		Drug-Drug		Ate	tenolol-HCTZ		Moderate	
		$\searrow$				Drug-Drug	Flu	Fluoxetine-HCTZ		Moderate
				$\mathcal{P}$		Drug-Drug	Ate	enolol-Valsart	an	Moderate
Pharm (-6					Drug-Drug	Asj	Aspirin-Valsartan		Moderate	
		6)			4)	Drug-Drug	Ate	enolol-Aspirir	1	Minor

Management:

Participant #25

- Caution is recommended of concomitant administration (3)
- Monitoring serum potassium; blood pressure (2), blood glucose; antihypertensive response
- Recommends concomitant administration avoided in heart failure patients

Sex		Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
]	F	68	3	13	6-11	2	0



	Errors		
	Туре	Event	Risk
	Dose	Missing	-
	Frequency	Missing	-
у	Drug-Drug	Hyzaar-Calcium	Moderate

Management

- Cautioned against self-medication without first consulting Healthcare Provider

Sex	Age	No. of Conditions	Total No. of Meds/CAMs		ge of Missing Ms from Sourc	26	No. of Self Prescribed		o. of Sample Meds
F	73	3	17	Wieus/CF	4-16		2		0
		EMR							
		$\cap$			Errors				
					Туре	Ev	ent		Risk
Particip	<b>–</b>		2		Dose	Mi	issing		-
(-5)	am			pecialist (-6)	Frequency	Mi	issing		-
(3)					Drug-Drug	La	six-Albuterol		Moderate
	1				Drug-Drug	La	asix-Advair		Moderate
	$\mathbf{i}$	3 4			Drug-Drug	La	six-Lexapro		Moderate
		XH			Drug-Drug	K-	Dur-Avapro		Moderate
Dhor	maaul		Ins	urance	Drug-Drug	Av	apro-Lexapro		Moderate
	macy1 10)	1 /		(-7)	Drug-Drug	Za	ntac-Tylenol		Minor
(-	10)		$\sim$		Drug-Drug	Za	ntac-Os-Cal		Minor

\*Not diagrammed are: Chart - 1 listed (6 missing) and Pharmacy#2 - 4 listed (13 missing) Management:

- Caution is recommended for concomitant administration (4)
- Monitor for signs of hyperkalemia
- Dosing interval recommendations

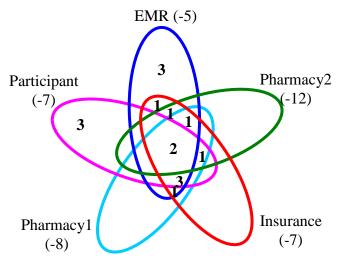
	Sex	Age	No. of	Total No. of		ge of Missing		No. of Self		f Sample
_	_		Conditions	Meds/CAMs	Meds/CA	AMs from Sou	irces	Prescribed		leds
	F	64	10	15		1-12		3		0
			EMR (	-7)		Errors				
			$\cap$			Туре				
-				DI	2	Dose	Missi	ng		-
Pa	articip	ant		Ph	armacy2 (-12)	Frequency	Missi	ng		-
	(-1)				(-12)	Drug-Drug	Napro	osyn-Plendil		Moderate
		3	X			Drug-Drug	Napro	osyn-Plavix		Moderate
		$\mathbf{i}$		1		Drug-Drug	Medr	ol Dosepak-A	valide	Moderate
			3 1 3			Drug-Drug	Napro	osyn-Avalide		Moderate
				7		Drug-Drug	Synth	roid-Centrum	n Silver	Moderate
	(	Chart		1 Pha	armacy1	Drug-Drug	Plendil-Centrum Silver			Moderate
		(-6)		$\smile$	(-8)	Drug-Drug	Avali	de-Calcium		Moderate
						Drug-Drug	Synth	roid-Calcium	1	Moderate
						Drug-Drug	Avali	de-Calcium		Moderate
						Drug-Drug	Plend	il-Calcium		Moderate
						Drug-Drug	Plend	il-Medrol Do	sepak	Moderate
						Drug-Drug	Napro	osyn-Medrol I	Dosepak	Moderate
						Drug-Drug	Lipito	or-Plavix		Moderate
						Drug-Drug	Medr	ol Dosepak-C	Calcium	Minor
						Drug-Drug	Napro	osyn-Calcium	l	Minor

- Monitoring blood pressure; electrolytes; body weight
- Monitoring for signs of NSAID toxicity; hypercalcemia; hypokalemia; GI ulceration; renal function
- Dosing interval recommendations (2)
- Cautioned against self-medication without first consulting Healthcare Provider

Sex	Age	No. of Conditions	Total No. of Meds/CAMs		nge of Missing AMs from Sou		No. of Self Prescribed	No. of S Med	<b>^</b>
F	59	4	15	111045, 0	5-8		3	0	
F Partici (-8	pant		15 (-5) 1 2 2	rmacy1 (-7)	5-8 Errors Type Dose Frequency Drug-Drug Drug-Drug Drug-Drug Drug-Drug Drug-Drug Drug-Drug Drug-Drug Drug-Drug Drug-Drug Drug-Drug Drug-Drug	Event Missi Oxyc Oxyc Oxyc Oxyc Benic Benic Atrop Atrop Benic	3 ng odone-Cymba odone-Benica odone-Hyzaar odone-Robinu ar HCT-Serev ar HCT-Albu ar HCT-Roxi ine-Robinul ine-Robinul ine-Roxicet ar HCT-Robi	0 alta ar HCT r al vent Diskus terol cel nul	Risk 
					Drug-Drug	1		Minor	
					Drug-Drug	Roxicet-Robinul		Minor	
					Drug-Drug	Roxic	et-Atropine		Minor

- Monitoring for signs of excessive serotonergic activity; hypotension (2); CNS depression (2); anticholinergic intoxication;
- Monitoring potassium level (2)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
М	82	5	16	5-12	3	0



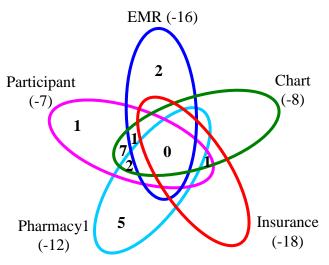
Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Naprosyn-aspirin	Moderate
Drug-Drug	Naproxyn-Nexium	Moderate
Drug-Drug	Avapro-Citalopram	Moderate
Drug-Drug	Ambien-Citalopram	Moderate
Drug-Drug	Doxazosin-Citalopram	Moderate
Drug-Drug	Temazepam-Citalopram	Moderate
Drug-Drug	Prilosec-Citalopram	Moderate
Drug-Drug	Aspirin-Citalopram	Moderate
Drug-Drug	Naprosyn-Citalopram	Moderate
Drug-Drug	Ambien-Avapro	Moderate
Drug-Drug	Naprosyn-Prilosec	Moderate
Drug-Drug	Temazepam-Doxazosin	Moderate
Drug-Drug	Doxazosin-Ambien	Moderate
Drug-Drug	Naprosyn-Avapro	Moderate
Drug-Drug	Aspirin-Avapro	Moderate
Drug-Drug	Temazepam-Avapro	Moderate
Drug-Drug	Aspirin-Prilosec	Minor
Drug-Drug	Aspirin-Nexium	Minor
Drug-Drug	Citalopram-Nexium	Minor

Management:

\_

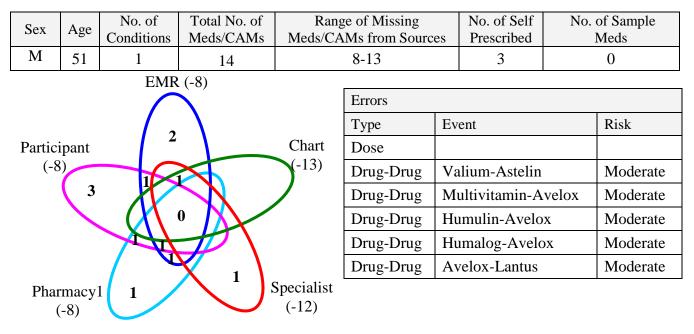
- Concomitant administration not recommended (3)
- Co-administration can result:
  - o additive effects (6) hypotension
  - o sub-therapeutic effects (1)
- Monitored for potentially excessive or prolonged CNS and respiratory depression. (1)
  - Close monitoring is recommended clinical and laboratory (2)
    - Excessive seronergic activity i.e. CNS irritability, altered consciousness, etc. (1)
      - Hematologic complications i.e. signs of bleeding (2)
      - Impaired renal function (1)
- Clinical significance is unknown (3)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
М	63	4	19	7-18	3	0



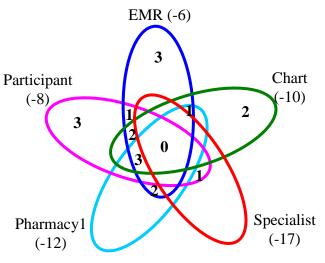
Errors		
Туре	Event	Risk
	Missing	-
Frequency		-
	Acetaminophen-Phenytoin	Moderate
Drug-Drug	Prochloroperazine-Keppra	Moderate
Drug-Drug	Phenytoin-Zofran	Moderate
Drug-Drug	Prochloroperazine-Zofran	Moderate
	Morphine-Transderm Scop	Moderate
	Phenytoin-Camptosar	Moderate
Drug-Drug	Dexamethasone-Camptosar	Moderate
	Vitamin E-Camptosar	Moderate
Drug-Drug	Colace-Camptosar	Moderate
Drug-Drug	Vitamin E-Temodar	Moderate
	Morphine-Kappra	Moderate
Drug-Drug	Prochloperazine-Hytrin	Moderate
Drug-Drug	Morphine-Hytrin	Moderate
	Pepcid-Phenytoin	Moderate
Drug-Drug	Phenytoin-Lorazepam	Moderate
0	Phenytoin-Dexamethasone	Moderate
	Phenytoin-Morphine	Moderate
Drug-Drug	Lorazepam-Morphine	Moderate
Drug-Drug	Phenytoin-Prochlorperazine	Moderate
	Lorazepam-Prochloroperazine	Moderate
	Morphine-Prochlorperazine	Moderate
Drug-Drug	Lorazepam-Hytrin	Moderate
Drug-Drug	Dexamethasone-Hytrin	Moderate
	Acetaminophen-Transderm Scor	Minor
Drug-Drug	Prochlorperazine-Camptosar	Minor
	Pepcid-Vitamin B12	Minor
Drug-Drug	Dexamethasone-Vitamin E	Minor

- Monitoring liver function; serum hydantoin levels; blood pressure, weight
- Monitoring for signs of CNS and respiratory depression (7); reduced antiemetic effects; increase risk of ventricular arrhythmias; anti-tumor activity may be reduced (3); increased heart failure; bowel movement changes (2); hypotension; phenytoin toxicity (2); reduced corticosteroid dosages;
- Dosing interval recommendation (2)



- Monitored for potentially excessive or prolonged CNS and respiratory depression
- Blood glucose should be monitored (4)
- Decrease absorption (1)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	72	3	18	6-17	2	0



Errors	Errors						
Туре	Event	Risk					
Dose	Missing	-					
Frequency	Missing	-					
Drug-Drug	Clarithromycin-Lipitor	Moderate					
Drug-Drug	Darvocet-N 100-Trazodone	Moderate					
Drug-Drug	Synthroid-Estradiol	Moderate					
Drug-Drug	HCTZ-Calcium	Moderate					
Drug-Drug	Atenolol-HCTZ	Moderate					
Drug-Drug	Atenolol-Valsartan	Moderate					
Drug-Drug	Darvocet-N 100-Valsartan	Moderate					
Drug-Drug	Atenolol-Detrol LA	Moderate					
Drug-Drug	Clarithromycin-Detrol LA	Moderate					
Drug-Drug	Synthroid-Calcium	Moderate					
Drug-Drug	HCTZ-Calcium	Moderate					
Drug-Drug	Atenolol-Calcium	Moderate					
Drug-Drug	Atenolol-Darvocet-N 100	Moderate					
Drug-Drug	HCTZ-Darvocet-N 100	Moderate					
Drug-Drug	Atenolol-Trazodone	Moderate					
Drug-Drug	Clarithromycin-Trazodone	Moderate					
Drug-Drug	HCTZ-Trazodone	Moderate					
Drug-Drug	Darvocet-N 100-Detrol LA	Moderate					
Drug-Drug	Estradiol-Lipitor	Minor					
Drug-Drug	Synthroid-Trazodone	Minor					
Drug-Drug	Tylenol-Detrol LA	Minor					
Drug-Drug	Atenolol-Synthroid	Minor					
Drug-Drug	HCTZ-Detrol LA	Minor					

- Monitor increased muscle toxicity; CNS adverse events (3); hypotension (3)
- Monitor serum thyrotropin; serum potassium levels; blood pressure; blood glucose; laboratory monitoring; serum TSH levels
- Caution self-treatment prior to consulting healthcare professional (2)
- Cautions co-administration

Sex			ge of Missing Ms from Sources		No. of SelfNo. ofPrescribedMe		-		
F	72	3	5		0-3		0	0	
		EMR	(-0)		Errors				
					Туре	Ev	ent		Risk
Participant Chart					Dose	Mis	Missing		-
(-0)				(-1)	Frequency	Missing			-
(					Drug-Drug	Asp	pirin-Calcium carbonate		Moderate
			Drug-Drug		Ava	valide-Calcium carbonate		Moderate	
			15		Drug-Drug	Asp	oirin-Avalide		Moderate
	macy 3)		In	surance (-4)					

- Monitored for diminished or inadequate analgesics or anti-inflammatory effects; renal impairment
- Cautioned self-medication prior to consulting a healthcare professional

#### No. of Total No. of Range of Missing No. of Self No. of Sample Sex Age Meds/CAMs from Sources Conditions Meds/CAMs Prescribed Meds F 79 4 3-4 0 0 12 EMR (-3) Errors Event Risk Type Dose Missing Pharmacy Frequency Missing Participant 1 1 (-4) Drug-Drug Celexa-Lexapro (-3) Moderate 1 1 2 4 Drug-Drug Avalide-Calcium carbonate Moderate Drug-Drug Avalide-Celexa Moderate Drug-Drug Avalide-Lexapro Moderate 1 Drug-Drug Calcium carbonate-Norvasc Moderate Drug-Drug Norvasc-Centrum Silver Moderate Chart (-3) Drug-Drug Gabapentin-Celexa Moderate Drug-Drug Gabapentin-Lexapro Moderate Drug-Drug Avalide-Celexa Moderate Drug-Drug Avalide-Lexapro Moderate Drug-Drug Aspirin-Lexapro Moderate Drug-Drug Aspirin-Celexa Moderate Drug-Drug Atenolol-Avalide Moderate Drug-Drug Atenolol-Calcium carbonate Moderate Drug-Drug Atenolol-Norvasc Moderate Drug-Drug Atenolol-Centrum Silver Moderate Drug-Drug Atenolol-Celexa Moderate Drug-Drug Atenolol-Lexapro Moderate Drug-Drug Aspirin-Calcium carbonate Moderate Drug-Drug Aspirin-Norvasc Moderate Drug-Drug Aspirin-Avalide Moderate Drug-Drug Avalide-Norvasc Minor Drug-Drug Atenolol-Aspirin Minor

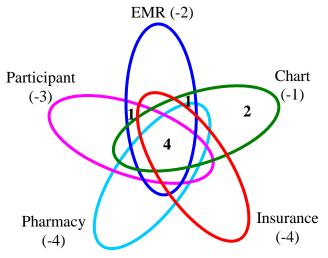
### Participant #33

- Monitor for CNS and respiratory depression (3); hypotension (4); calcium channel blocker therapy (2); hematological complications (2); diminished or inadequate analgesic and anti-inflammatory effects
- Caution self-treatment prior to consulting healthcare professional
- Monitor serum potassium levels, blood pressure (3), blood glucose
- Dosing interval recommendations (2)

Sex	Age No. of Total No. of Conditions Meds/CAMs			Range of Missing Meds/CAMs from Sources		No. of Self Prescribed	No. of S Me	-	
F	F 49 2 12			4-10		1	0		
		EMR (	-10)		Errors				
					Туре	Event		Risk	
		2			Dose	missing		-	
					Frequency	missing		-	
Particip	ant	0	Pha	rmacy	Drug-Drug	Cepha	Cephalexin-Junel Fe 1/20		Moderate
-	$\begin{array}{c c} 1 & \text{anterpant} \\ \hline (-4) & 5 & 3 & 2 \end{array} $ (-7)					Junel	Fe 1/20-Leve	othyroxine	Moderate
					Drug-Drug	Levothyroxine-Calcium		Moderate	
					Drug-Drug	Calci	um-Lisinopri	1	Moderate

- Alternative or additional methods should be considered \_
- Monitor serum thyroxine \_
- Monitor increased risk of hypermagnesemia May decrease bioavailability of drug -
- -

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	67	4	8	1-4	1	0



Errors					
Туре	Event	Risk			
Dose	Missing	-			
Frequency	Missing	-			
Drug-Drug	Aspirin-Glipizide	Moderate			
Drug-Drug	Aspirin-Actonel	Moderate			
Drug-Drug	Glipizide-Lisinopril	Moderate			
Drug-Drug	Actonel-Lisinopril	Moderate			

- Monitor for signs of hypoglycemia (2); diminished or inadequate analgesic and antiinflammatory effects; renal function assessment
- Dosing interval recommendations (2)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs		ge of Missing Ms from Sources	No. of Self Prescribed	No. of Sample Meds		
F	42	3	5		0-4	2	1		
		EMR	(-3)		Errors				
		0			Туре	Event	Risk		
						missing	-		
Particip	/		Cha		Frequency	missing	-		
(-0)		2 1		r)	Drug-Drug	Atenolol-Asp	irin Moderate		
		Pharmac	y (-3)						

Management: - Clinical significance unknown

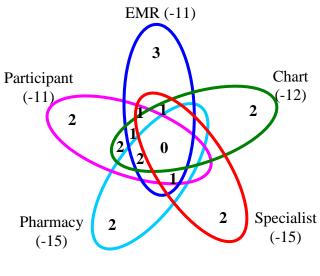
#### No. of Total No. of Range of Missing No. of Self No. of Sample Sex Age Conditions Meds/CAMs Meds/CAMs from Sources Prescribed Meds 3-10 F 45 2 0 1 12 EMR (-6) Errors Type Event Risk 2 Missing Dose Frequency Missing Participant Chart Drug-Drug Prednisone-Novolin Moderate (-10) (-3) Drug-Drug Prednisone-Humalog Pen Moderate 2 Drug-Drug Prednisone-Celebrex Moderate 1 Drug-Drug Albuterol-Novolin R Moderate Drug-Drug Albuterol-Humalog Pen Moderate 2 Drug-Drug Claritin-Celebrex Moderate Drug-Drug Effexor-Celebrex Moderate Insurance Pharmacy Drug-Drug Prednisone-Vitamin E Minor (-6)(-6)Drug-Drug Prednisone-Calcium + D Minor

### Participant #37

\*Not diagrammed are observation (present,missing) from the Pharmacy 2 (1,11), Pharmacy 3 (3,9) Pharmacy 4 (1, 11), and Pharmacy 5 (5,7)

- Monitor for signs of hypoglycemia (3); GI ulceration and bleeding;
- Dosing adjustment recommendations (2)
- Clinical significance unknown (2)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	73	6	20	11-15	1	1



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Motrin-Aspirin	Major
Drug-Drug	Atenolol-Motrin	Moderate
Drug-Drug	HCTZ-Calcium Acetate	Moderate
Drug-Drug	Atenolol-Calcium acetate	Moderate
Drug-Drug	Aspirin-Calcium acetate	Moderate
Drug-Drug	Synthroid-Calcium Acetate	Moderate
Drug-Drug	Motrin-HCTZ	Moderate
Drug-Drug	Atenolol-HCTZ	Moderate
Drug-Drug	Atenolol-Synthroid	Moderate
Drug-Drug	Atenolol-Calcium Acetate	Minor
Drug-Drug	Atenolol-Aspirin	Minor
Drug-Drug	Aspirin-Niacin	Minor

- Monitor for signs of additive GI toxicity; diminished or inadequate analgesic and antiinflammatory effects; renal function
- Monitor blood pressure (3); serum potassium levels; blood glucose
- Cautions self-medication prior to consulting healthcare provider
- Dosing interval recommendations (3)
- Clinical significance unknown (2)

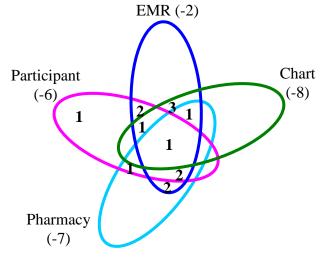
Sex	Age	No. of Conditions	~ ~		e of Missing Ms from Sources		No. of Self Prescribed	No	o. of Sample Meds
Μ	66	3	10		2-8		0		0
		EMR (-	6)		Errors				
	2					Event			Risk
					Dose	Missing			-
					Frequency	Mis	ssing		-
Particip	ant		Pharm	-	Drug-Drug	Asj	pirin-Vitamir	n E	Moderate
(-2)		2	(-8)	)	Drug-Drug	Asj	pirin-Calciun	n	Moderate
6				Drug-Drug	Hyzaar-Calcium		1	Moderate	
				Drug-Drug	Aspirin-Hyzaar			Moderate	

Management:

- Caution self-medication prior to consulting healthcare provider (3)
- Monitor for signs of diminished or inadequate analgesic or anti-inflammatory effects
- Monitor blood pressure; renal function

Participant #40

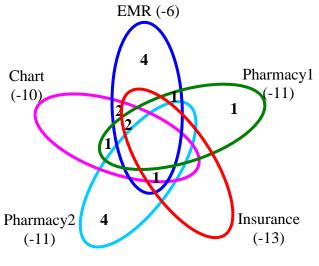
Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
М	66	2		2.8	0	0
IVI	00	5	14	2-8	0	0



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Aspirin-Cosopt	Major
Drug-Drug	Aspirin-Azopt	Major
Drug-Drug	Biaxin XL-Viagra	Major
Drug-Drug	Baxin XL-Zocor	Major
Drug-Drug	Niacin-Zocor	Major
Drug-Drug	Zocor-Vytorin	Moderate
Drug-Drug	Aspirin-Triamcinolone	Moderate
Drug-Drug	Biacin XL-Triamcinolone	Moderate
Drug-Drug	Biacin XL-Allegra	Minor
Drug-Drug	Aspirin-Niacin	Minor

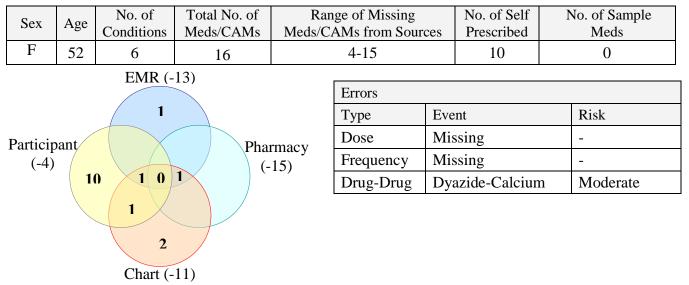
- Concomitant administration not recommended (3)
- Monitor for signs of musculoskeletal toxicity (3); GI ulceration and bleeding; adrenal function
- Clinical significance unknown (2)

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	80	3	16	6-11	0	0



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Aspirin-Cosopt	Major
Drug-Drug	Clarithromycin-Zocor	Major
Drug-Drug	Clarithromycin-Prochlorperazine	Moderate
Drug-Drug	Trazodone-Lyrica	Moderate
Drug-Drug	Prochlorperazine-Lyrica	Moderate
Drug-Drug	Maxzide-Cosopt	Moderate
Drug-Drug	Viactiv Calcium-Fosamax	Moderate
Drug-Drug	Trazodone-Neurontin	Moderate
Drug-Drug	Prochlorperazine-Neurontin	Moderate
Drug-Drug	Trazodone-Maxzide	Moderate
Drug-Drug	Prochlorperazine-Maxzide	Moderate
Drug-Drug	Prochlorperazine-Trazodone	Moderate
Drug-Drug	Maxzide-Trazodone	Moderate
Drug-Drug	Clarithromycin-Trazodone	Moderate
Drug-Drug	Maxzide-Prochlorperazine	Moderate
Drug-Drug	Neurontin-Lyrica	Moderate

- Concomitant administration not recommended
- Monitor for signs of musculoskeletal toxicity; torsades de pointes; excessive or prolonged CNS and respiratory depression (3); hypotension (5)
- Monitor serum potassium levels (2); blood pressure (2); blood glucose (2)
- Dosing interval recommendation (2)

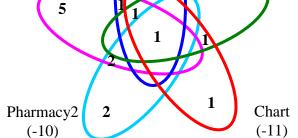


Management:

- Monitor for signs of hypercalcemia (2)
- Caution for self-medication prior to consulting a healthcare provider \_

Participant #43

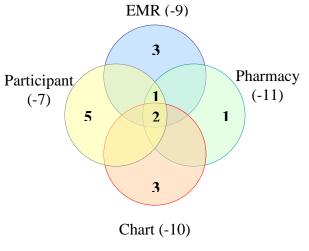
	Sex	Age	No. of Conditions			ge of Missing Ms from Sources		No. of Self Prescribed		f Sample Ieds
	М	56	3	15	5-12		5		0	
			EMR (-1	1)		Errors				
						Туре	Eve	nt		Risk
			1			Dose	Mis	ssing		-
Pa	rticipa	nt			rmacy1	Frequency	Mis	ssing		-
	(-5)				(-12)	Drug-Drug	Ate	nolol-Ibuprof	fen	Moderate



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Atenolol-Ibuprofen	Moderate
Drug-Drug	Atenolol-Lorazepam	Moderate
Drug-Drug	Atenolol-Ambien	Moderate
Drug-Drug	Lorazepam-Ambien	Moderate
Drug-Drug	Atenolol-Centrum Silver	Moderate

- Monitor blood pressure \_
- Monitor for signs of hypotension (2); CNS and respiratory depression \_
- Dosing interval recommendations \_

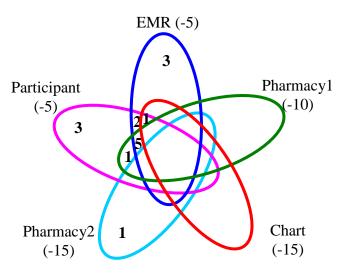
Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	73	3	15	7-11	5	1



Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Naprosyn-Lopressor	Moderate
Drug-Drug	Aspirin-Gingko Biloba	Moderate
Drug-Drug	HCTZ-Citracal	Moderate
Drug-Drug	Lopressor-Citracal	Moderate
Drug-Drug	HCTZ-Lisinopril	Moderate
Drug-Drug	Aspirin-Lisinopril	Moderate
Drug-Drug	Naprosyn-Lisinopril	Moderate
Drug-Drug	Aspirin-Vitamin E	Moderate
Drug-Drug	Lopressor-HCTZ	Moderate
Drug-Drug	Naprosyn-HCTZ	Moderate
Drug-Drug	Naprosyn-Aspirin	Moderate
Drug-Drug	HCTZ-Gingko biloba	Moderate
Drug-Drug	Lopressor-Aspirin	Minor

- Monitor blood pressure (5); electrolytes; serum potassium levels; blood glucose
- Monitor for signs of hematologic complications; diuresis; renal function (4); bleeding
- Caution against self-medication without first consulting a healthcare provider (2)
- Dosing interval recommendations
- Concomittant administration not recommended
- Clinical significance unknown

Sex		Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
	Μ	M 73 5 16		5-15	2	0	



Errors							
Туре	Event	Risk					
Dose	Missing	-					
Frequency	Missing	-					
Drug-Drug	Clonidine-Lopressor	Moderate					
Drug-Drug	Aspirin-Avapro	Moderate					
Drug-Drug	Lopressor-Glucophage	Moderate					
Drug-Drug	Lasix-Glucophage	Moderate					
Drug-Drug	Percocet 5/325-Neurontin	Moderate					
Drug-Drug	Clonidine-Neurontin	Moderate					
Drug-Drug	Prilosec-Zocor	Moderate					
Drug-Drug	Oxycodone-Norvasc	Moderate					
Drug-Drug	Aspirin-Norvasc	Moderate					
Drug-Drug	Lopressor-Norvasc	Moderate					
Drug-Drug	Lopressor-Oxycodone	Moderate					
Drug-Drug	Lasix-Oxycodone	Moderate					
Drug-Drug	Clonidine-Oxycodone	Moderate					
Drug-Drug	Lasix-Lopressor	Moderate					
Drug-Drug	Oxycodone-Avapro	Moderate					
Drug-Drug	Aspirin-Prilosec	Minor					
Drug-Drug	Lopressor-Aspirin	Minor					
Drug-Drug	Lasix-Aspirin	Minor					

- Monitoring blood pressure (3); blood glucose (3);
- Monitor for signs of CNS and respiratory depression (2); musculoskeletal toxicity; hypotension (6); hemodynamic response and tolerance

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	Range of Missing Meds/CAMs from Sources	No. of Self Prescribed	No. of Sample Meds
F	72	6	10	2-9	0	0

	EMR (-2)	
Participant (-2)		Pharmacy1
	4	
Specialist (-3)		Chart (-2)

Errors		
Туре	Event	Risk
Dose	Missing	-
Frequency	Missing	-
Drug-Drug	Aspirin-Plendil	Moderate
Drug-Drug	Caltrate-Actonel	Moderate
Drug-Drug	Prednisone-Avalide	Moderate
Drug-Drug	Aspirin-Avalide	Moderate
Drug-Drug	Avalide-Calcium	Moderate
Drug-Drug	Plendil-Calcium	Moderate
Drug-Drug	Avalide-Caltrate	Moderate
Drug-Drug	Caltrate-Plaquenil sulfate	Moderate
Drug-Drug	Avalide-Caltrate	Moderate
Drug-Drug	Plendil-Caltrate	Moderate
Drug-Drug	Aspirin-Caltrate	Moderate
Drug-Drug	Avalide-Prednisone	Moderate
Drug-Drug	Plendil-Prednisone	Moderate
Drug-Drug	Aspirin-Prednisone	Moderate
Drug-Drug	Calcium-Actonel	Moderate
Drug-Drug	Prednisone-Calcium	Minor

\* Not included in the diagram is the Insurance Company which shares 1 observation with all the sources, and is missing 9 observations; Specialist 2 which shares 1 observation and is missing 9.

- Monitor blood pressure (3); electrolyte levels (2); body weight (2)
- Dosing interval recommendation (2)
- Monitor renal function; effectiveness of calcium channel blocker (2); hypokalemia; GI ulceration
- Caution self-medication without first consulting healthcare provider (2)

	Sex	Nev Are		ge of Missing AMs from Sour	ces	No. of Self Prescribed	No. of Sample Meds			
	М	61	6	15		7-10		2		0
EMR (-7)						Errors				
			$\frown$			Туре	Eve	nt		Risk
		4				Dose	Mis	Missing		-
_				D	harmacy	Frequency	Mis	sing		-
ł	Participa				(-10)	Drug-Drug	Ate	Atenolol-Lorazepam		Moderate
	(-7)	2	2		(-10)	Drug-Drug	Dio	van HCT-Lez	kapro	Moderate
		4				Drug-Drug	Asp	oirin-Lexapro		Moderate
					Drug-Drug	Lor	azepam-Lexa	pro	Moderate	
				$\mathcal{D}$		Drug-Drug	Ate	nolol-Lexapro	0	Moderate
				7		Drug-Drug	Asp	oirin-Valsarta	n	Moderate

Drug-Drug

Drug-Drug

Drug-Drug

Drug-Drug

Drug-Drug

Drug-Drug

Drug-Drug

Atenolol-Valsartan

Lorazepam-Reglan

Reglan-Lexapro

Aspirin-Nexium

Atenolol-Aspirin

Lorazepam-Diovan HCT

Atenolol-Diovan HCT

Moderate

Moderate

Moderate

Moderate

Moderate

Minor

Minor

### Participant #47

Management:

Chart

(-10)

2

- Monitor for signs of hypotension (4); CNS and respiratory depression (2); excessive serotonergic activity

Insurance

(-10)

- Monitor blood glucose; potassium levels; blood pressure
- Manufacturer recommends avoiding combination of drugs
- Clinical significance unknown (2)

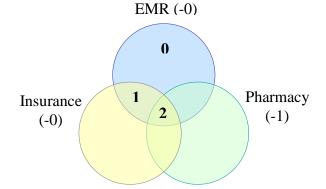
Sex	Age	No. of	Total No. of		nge of Missing	0 0			of Sample
	0	Conditions	Meds/CAMs	Meds/C	AMs from Sour	ces	Prescribed	1	Meds
F	51	3	7		1-4		1		0
		EMR	(-1)		Errors				
					Туре	Eve	nt		Risk
		2			Dose	Mis	Missing		-
Partici	nant /		Ph	armacy	Frequency	Mis	Missing		-
(-2)	<u>۲</u>			(-4)	Drug-Drug	Asp	Aspirin-Lisinopril		Moderate
( 2)	<b>′</b>	1 3			Drug-Drug	HC	HCTZ-Lisinopril		Moderate
					Drug-Drug	Zan	Zantac-Glucophage		Moderate
					Drug-Drug	HC	HCTZ-Glucophage		Moderate
					Drug-Drug	Lisi	Lisinopril-Glucophage		Moderate
		Chart	(-3)						

Management:

- Monitor renal function (2); blood pressure; electrolytes; blood glucose;
- Monitor for signs of possible signs of lactic acidosis; hypoglycemia; diuresis

### Participant #49

Sex	Age	No. of Conditions	Total No. of Meds/CAMs	8 8		No. of Sample Meds
М	52	2	3	0-1	0	0



Errors	Errors							
Туре	Event	Risk						
Dose	Missing	-						
Frequency	Missing	-						
Drug-Drug	Aspirin-Prinivil	Moderate						

### Management:

- Monitor blood pressure and renal function assessments.

Sex Age		No. of Conditions	Total No. of Meds/CAMs		ge of Missing AMs from Sour	ces	No. of Self Prescribed		f Sample Ieds
F	51	6	7	Wieds/ CI	1-5		0		0
	_		,		-				-
		EMR	(-1)		Errors				
					Туре	Eve	ent		Risk
		1			Dose	Mis	ssing		-
Particip	bant		P	Pharmacy1	Frequency	Mis	issing		-
(-5)		-		(-5)		Ate	Atenolol-Ibuprofen		Moderate
			$\sim$		Drug-Drug	Ate	Atenolol-HCTZ		Moderate
					Drug-Drug	Ibu	profen-HCTZ		Moderate
					Drug-Drug	Ate	nolol-Triamte	erene	Moderate
		X	$\mathbf{D}$		Drug-Drug	Ibu	profen-Triam	terene	Moderate
					Drug-Drug	Ate	nolol-Vaictiv	<sup>r</sup> Calcium	Moderate
Pharr	nacy2		$\sim$	Chart					
	4)		$\sim$	(-3)					

\* Not included in the figure are Pharmacy 3 and 4 – both with 1 observation, 4 missing.

Management:

- Monitor blood pressure (5); serum potassium levels (3); blood glucose (3); renal function (2)

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