Prevalence of Potentially Inappropriate Medications Use Among Recently Admitted Geriatric Patients in Rural Hospitals

by

Haya Al-Shamri

A thesis
presented to the University of Waterloo
in fulfilment of the
thesis requirement for the degree of
Master of Science
in
Pharmacy

Waterloo, Ontario, Canada, 2014

Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Potentially inappropriate medications (PIMs) are prescribed most often to elderly patients and can cause serious adverse effects. Older adults tend to use multiple medications, and age-related physiological changes can make some medications inappropriate. The aims of this study are to determine the prevalence of PIMs use for older patients admitted to rural hospitals; to identify the most frequently prescribed PIMs in this population; to compare the number of PIMs identified using two tools, STOPP criteria and Beers' criteria; and to identify the total number of PIMs identified when using both sets of criteria. Secondly, this study explores the factors associated with PIMs use in this group. These objectives were examined through an observational study design involving patients aged 65 years and above at rural hospitals. Of the 178 patients enrolled, the median age was 80 and 93 participants (52.2%) were female. The collected data included demographic patient information, medical histories and current diagnoses, number and type of PIMs, and total number of prescribed medications. Using Beers' criteria, the prevalence of taking at least one PIM was 62.92% among the population, with 112 older adults using 202 PIMs. Using the STOPP criteria, the prevalence of receiving at least one PIM was 69.10%, with 123 patients using 240 PIMs. When both sets of criteria were applied, the proportion using one or more PIMs increased to 73.03%, representing 130 patients using 330 PIMs. Bivariate logistic regression models showed no predictable associations between PIM use and gender, number of illnesses, or age when using both the STOPP and combined criteria models. In contrast, a positive association was found between PIM use and the number of medications, the presence of neurological or urogenital diseases, and age using Beers' criteria. This study provided insight into the higher prevalence of PIMs in rural healthcare settings. The

higher prevalence and number of PIMs under STOPP criteria compared to the Beers criteria were due to differences in their features, while these variances were eliminated when both criteria were concurrently applied. The continued use of PIMs among older patients is a crucial issue that requires further research to discover the underlying reasons of continued prescription of PIMs particularly in rural regions, and to determine an ideal approach that prevents PIM-related problems.

Keywords: Potentially inappropriate medications, STOPP criteria, Beers' criteria, older adults, rural hospitals

Acknowledgements

There are many individuals to whom I owe thanks for their contributions and efforts in assisting me to conduct this research. First, I would like to express appreciation to my supervisor Dr. Feng Chang for her countless hours of mentoring and guidance over the past two years of my master's degree study. My sincere gratitude goes to my committee thesis members, Dr. Carlos Fernandez and Dr. Leilei Zeng, for providing their precious time, knowledge and insightful advice and comments. Special thanks and eternal gratitude to Dr. Jonathan Blay for his vigorous support and assistance to all graduate students. I owe many thanks to the pharmacy faculty and staff, especially Sara Rae for her helpful advice and assistance with administrative work. Also, many thanks to my colleagues for sharing their friendship and experience in postgraduate studies.

This project would have been very difficult to complete without the permission of SBGHC and their support in using their site as a source of potential enrollment patients. I would like to extend my sincere thanks to healthcare providers in four hospitals, including directors, coordinators, physicians, nurses, and remaining inpatient department staff for their cooperation and time. Special warm thanks and gratitude to the pharmacy department for their friendly support and time, including the clinical pharmacy director and her staff. This project would not have been possible without participation by the wonderful older adults. I gratefully acknowledge those one hundred seventy-eight patients and their families for understanding and cooperation with the researcher to optimize health care. Last but not least, warm gratitude for my incredible parents, fabulous brothers, lovely sister, and sweetheart niece for supporting me morally, financially, and constantly encouraging me to complete my postgraduate studies.

Dedication

To my parents: my father, Mukhlef Al-Shamri and my mother, Shima Al-Shamri.

Unlimited heartfelt thanks for the sacrifices you made so I could pursue higher education, and for encouraging me to achieve my ambitions no matter what obstacles stand in my way. My career would not be possible without your love, understanding, support, and inspiration.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

Abbreviation	Definition
AChIs	Acetylcholinesterase Inhibitors
ADEs	Adverse Drug Events
BPH	Benign Prostatic Hyperplasia
CCBs	Calcium Channel Blocker
CHF	Congestive Heart Failure
COPD	Chronic Obstructive Pulmonary Disease
GI	Gastrointestinal
HTN	Hypertension
ICD-10	International Classification of Diseases, version.10
MAI	Medication Appropriateness Index
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
OTC	Over The Counter
PIMs	Potentially Inappropriate Medications
PPIs	Proton-Pump Inhibitors
SNRIs	Serotonin and Norepinephrine Reuptake Inhibitors
SSRIs	Selective Serotonin Reuptake Inhibitors
START	Screening Tool to Alert to Right Treatment
STOPP	Screening Tool of Older Persons' Prescriptions
TCAs	Tricyclic Antidepressants

Chapter 1: Introduction

1.1 Definition

The optimization of prescribed medications for the elderly is a global concern for health care providers and researchers who attempt to improve the safety of medications. One of the foci of pharmaceutical research is the standardization of the selection of medications to be prescribed for this population. Appropriate medication use for older adults is a major challenge encountered by prescribers, even with medications not considered contraindicated. Some medications, if prescribed under certain conditions, will probably harm one's health. So, a consensus of health care professionals, researchers, and specialists in geriatric care are working to eliminate this problem that may contribute to worsening of complex diseases in older adults. Particular medications administered under specific conditions have been categorized and identified as potentially inappropriate medications (PIMs). A PIM is defined as a medication that can create serious problems when the risks of adverse drug reactions outweigh the benefits of the medication compared with alternative treatments, especially if an alternative treatment is available and safer for the same condition (Beers et al., 1991; Gallagher & O'Mahony, 2008; Keith et al., 2013).The prescription of PIMs has negative clinical and economic outcomes, especially among the elderly. PIMs are widely prevalent around the world, and the estimated percentage of the prevalence of PIMs is approximately 6% to 41% (Kaur et al., 2009).

1.2 Reasons to consider a medication as a PIM

After a comprehensive review of literature, it is found that there are two main factors that cause different reactions to medications and contribute to worsening elders' conditions, and that make those medications inappropriate.

1.2.1 Aging and physiological changes

Many medications are considered inappropriate for older patients due to age-related physiological changes. Despite inter-individual variants among elders, generally the functions and compositions of body systems are changed from youth. These changes continue with advancing age, often leading to adverse effects from medications not seen in younger patients, even among safer drugs. Age-related physiological changes encompass and affect both pharmacokinetic and pharmacodynamic processes as detailed in the following section.

1.2.1.1 Age-related physiological change: Pharmacokinetics Pharmacokinetic processes consist of drug absorption, distribution, metabolism, and excretion.

1.2.1.1.1 Drug absorption. Age-related physiological changes include reductions in the surface of the intestinal epithelium, gut motor function, splanchnic blood flow, and possibly stomach acid. However, the bioavailability of most drugs is not affected by these changes because most drugs are absorbed via passive diffusion.

A few drugs are affected by a decreased rate of absorption due to aging, such as indomethacin, prazosin, digoxin (Turnheim, 2003). Some drugs require an acidic environment for absorption and any changes in the gastric environment due to aging will affect the bioavailability of some

compounds that require an acidic environment in order to be ionized, such as ketoconazole, ampicillin esters, and iron compounds (McLean & LeCouteur, 2004). Supplements such as calcium, iron, and vitamins are absorbed by the intestinal epithelium through specific carrier-mediated transport mechanisms. Seniors may experience a reduction in absorbability for these specific transport mechanisms, affecting the bioavailability of those nutrients (Turnheim, 2003; Mangoni & Jackson, 2004).

The normal aging process leads to degeneration of the epidermis and dermis. Tissue blood perfusion, specifically, and general barrier functions of the skin are reduced. The transdermal drug absorption rate may therefore decrease with age (Turnheim, 2003). However, drug absorption as a function of aging does not decrease to any clinically relevant extent for most drugs.

1.2.1.1.2. Drug distribution. Medication distribution is dependent on many factors that might change with aging including blood flow, plasma protein binding, and body composition (DiPiro et al., 2014). Aging leads to decreases in body mass, especially skeletal muscle mass. The total body water content also declines by 10-15%. For this reason, the distribution volume of hydrophilic, or water-soluble, drugs (e.g. aspirin, tubocurarine, edrophonium, famotidine, and lithium) decreases. Consequently, the volume of distribution for water-soluble drugs decreases, but the serum concentrations increase. Total body fat, on the other hand, increases with age. Body fat among females increases by 33-45%, while body fat among males increases by 18-36%. When the volume of distribution is increased, the plasma half-life of lipid-soluble drugs is increased as a result. Examples of lipid-soluble drugs are amiodarone, diazepam, teicoplanin, and verapamil (Turnheim, 2003).

Drugs in the blood bind to plasma protein, and only the free fraction of drugs is pharmacologically active. When plasma albumin levels decrease to a certain level in older people, the concentration of α1-glycoprotein (which binds alkaline drugs) increases or remains unchanged. When the free (unbound) drug concentration increases, drug elimination rises as well. Therefore, these changes in plasma protein binding due to aging are not clinically important. It is noticed that slight decrease in the binding of plasma proteins and increase in unbound drugs could be occur in older patients with specific conditions such as renal or hepatic dysfunction as well as malnourishment in older patients with late-stage cancers. In fact, it is necessary to emphasize that these changes in protein binding are not due to aging but some diseases or conditions lead to small alterations in protein concentration (Turnheim, 2003; Mangoni & Jackson, 2003).

1.2.1.1.3 Drug metabolism: Liver. Hepatic drug metabolism during the aging process is not fully understood. The liver structure changes and liver size decreases by approximately 25-35% in old age. The endoplasmic reticulum is weakened so that hepatic extracellular space increases. Moreover, hepatic blood flow decreases by 40%, which subsequently reduces bile flow and the synthesis of proteins, lipids, and glucose. In vivo, the metabolic clearance for some drugs may decrease by 20-40% or remain unchanged depending on the extraction ratio for each drug. Inter-individual variations have a greater effect on metabolic drug processes than do aging changes related to drug metabolism (Turnheim, 2003).

Blood flow and extraction ratio, which determine the level of drug clearance in the liver, are important factors in monitoring the toxicity of drugs (Mangoni & Jackson, 2003). The extraction ratio is based on the liver's capacity to metabolize drugs. With advancing age,

blood flow may decrease and affect liver clearance. This process mainly affects high extraction ratio drugs such as chlormethiazole, dextropropoxyphene, glyceryl nitrate, lignocaine, pethidine, and propranolol (Turnheim, 2003). Aging has no effect on phase-II or conjugation reactions while aging does affect the action of the membrane-bound cytochrome P450 microsomal cytochrome P450 enzymes (CYP), which are oxidative enzymes and regulate the phase-I metabolism. Moreover, some CYP 450 isoforms have decreased activity with advanced age, while others remain unchanged (Schwartz & Abernethy, 2009).

1.2.1.1.4. Drug excretion: Kidney. The physiology and structure of the kidney change with age. The number of glomeruli, which is part of the nephron, and renal blood flow decreases with advanced age (after age 40). Renal blood flow decreases approximately 1% decrement per year due to factors such as increased angiotensin-II and endothelin levels and decreased prostaglandin concentrations (Turnheim, 2003). Furthermore, intra-renal vascular changes in the kidney (except in the medullary vasculature area, in which there is no change) contribute to this decrease in renal blood flow. Kidney mass generally decreases with age (Mangoni & Jackson, 2003). The efficiency of renal clearance and the glomerular filtration rate decreases in older people. After age 20, the glomerular filtration rate reduces by 25% to50%. This decline in glomerular filtration rate can induce drug side effects for drugs that are mainly excreted by the kidney (Turnheim, 2003).

1.2.1.2 Age-related physiological change: Pharmacodynamics. Pharmacokinetics deals with the effects of drug concentration on actions, whereas pharmacodynamics deals with the effects that drugs have on the body and how the drugs exert these effects. The changes in pharmacodynamics among older people may impact drug receptor numbers, receptor affinity, or homeostatic mechanisms (Turnheim, 2003; DiPiro et al., 2014). Most studies examined these alterations in the cardiovascular and nervous systems.

Decreasing receptor response to the substrate or drugs has been observed in the cardiovascular system. For example, reduced β-adrenoceptors affinity to agonists is reported in older people. In particular, the receptors' sensitivity in the myocardium to catecholamine is poor. The nervous system also changes with age. Between the ages of 20 and 80, brain weight decreases by 20% and neuron loss occurs, leading to a change in brain structure. A reduction in the number of synapses is also reported. Nervous system changes in compositions and responses, including reductions in the number of dopaminergic neurons and dopamine D_2 receptors and cholinergic neurons and receptors are reported in older individuals. In addition, the central nervous system has a higher sensitivity to the action of benzodiazepines in older people than in younger people. These changes in the nervous system contribute to adverse drug side effects (Turnheim, 2003).

1.2.2 Polypharmacy

Due to age-related increases in pathological conditions, older individuals are more likely to consumption of multiple medications (polypharmacy). Polypharmacy is (generally-not everyone agrees) defined as the administration of five or more medications (Bregnhoj et al., 2009; Bushardt et al., 2008). Despite benefitting many patients, polypharmacy is also the most frequent cause of PIM-related problems due to the risk of drug–drug interactions or drug–disease

interactions (Pitkala et al., 2012). This was demonstrated by Goldberg and colleagues who found that the risk of adverse drug–drug interactions for patients taking two medications is 13%, 38% for patients taking four drugs, and 82% for patients taking seven or more medications (Goldberg et al., 1996). When polypharmacy is used to treat multiple chronic conditions, even relatively safe drugs can interact in dangerous ways. Hospitalized patients who are administered five to seven drugs have a 58% higher risk of developing adverse drug events (ADEs) than patients who use fewer than five medications and quadruples for patients taking eight or more drugs (Onder et al., 2010; Scott et al., 2012). Furthermore, many disabled older adults dependent on others have difficulty adhering to a medication treatment plan (Bergqvist et al., 2009). Overall, patients taking a larger number of medications are more likely to have PIMs.

1.3 Consequences of Prescribed PIMs

1.3.1 Adverse drug reactions

While the causes of ADEs are well-documented in older adults, the first version of the Beers' criteria drew researchers and caregivers to investigate the association between PIMs and ADEs, and this research is ongoing.

The most common side effects of PIMs are conditions such as orthostatic hypotension, cognitive impairment, falls, and fractures. This is exemplified by an American report that showed that cognitive deficit results from taking PIMs among patients with mild cognitive impairment (Weston et al., 2010). Most hip fractures and admissions in hospitals of older adults result from falls, which can be caused by PIMs (Agashivala & Wu, 2009). The risk of falling rises meaningfully per use of potentially inappropriate psychotropic medications of the Beers' criteria

in nursing home settings, with an increased risk of approximately 20.5% in patients receiving potentially inappropriate psychotropic medications compared to patients receiving other psychoactive medications, and this percentage increased to 60.3% when compared to patients not receiving any kind of psychoactive medications (Agashivala & Wu, 2009). This finding was confirmed in a French evaluation of all inappropriate medications leading to falling, that found that use of those medications by older adults increased the risk of falling, especially with long-acting benzodiazepines, psychotropics, and anticholinergic medications (Berdot et al., 2009).

Previous research attempts to determine ADEs associated with use of PIMs evaluated the decline of the health status in general (Fu et al., 2004). An association between PIMs and serious side effects that resulted in a general decline in functionality was identified in two studies conducted in Italy. These studies had different results, probably due to variance in the study setting and unadjusted potential confounders. The first study shows a strong relation between the use of PIMs and physical disability in community-dwelling, frail, older adults (Landi et al., 2007), while the second study found no associations between functional disability in older patients and use of PIMs in acute medical wards (Corsonello et.al, 2009). Regardless, most ADEs could have been prevented and reduced by reviewing and assessing the appropriateness of the medication prescribed per older adult (Gurwitz et al., 2003).

Furthermore, an association exists between increased use of health services and ADEs resulting from PIMs, such as increased outpatient visits (Fillenbaum et. al., 2004) and presentation to the emergency department (Nixdorff et al., 2008). A recent pilot Canadian study determined that 65% of patients receiving PIMs lead them to frequent emergency department visits (Wong et al., 2014). Likewise, an Irish study noted a prevalence of PIMs of about 50% among patients who

were older than 70 years and visiting the emergency department due to falls (McMahon et al., 2014). The greater number of hospitalizations in older adults can be attributed to PIMs. For example, a large population-based study in Australia found that the risk of unplanned hospitalizations of older adults increased with the number of PIMs consumed (Price et al., 2014).

A relationship between ADEs and hospital readmissions was determined in a study that found that 10–30% of hospital readmissions among older adults are due to drug-related problems (Bonnet-Zamponi et al., 2013). Moreover, many of these readmissions to hospital for drug-related problems could have been prevented (Bero et al., 1991). Thus, ADEs of inappropriate prescriptions are common in hospitalized older patients with polypharmacy.

Finally, there is an association between increasing mortality among older adults and ADEs. Up to 18% of inpatient deaths may be attributable to ADEs, with most caused by inappropriate prescription medications (Scott et al., 2012; Gallagher et al., 2007). Studies set in nursing homes observed that residents who had at least one PIM in the prior year had an increased risk of being hospitalized and an increased risk death (Lau et al., 2005 ; Dedhiya et al., 2010).

1.3.2 Health care expenditures

PIMs also increase the cost of drug-related problems. While few studies have investigated the relationship between PIMs and their expenses for health care systems in particular, Irish retrospective studies measured the costs of prescribing PIMs. A first study on the national population found that one-third of the study's older population used at least one PIM, resulting in a cost of 9% (€45,631,319) of the total pharmaceutical expenditures in 2007 (Cahir et al., 2010). A second study determined the prevalence of PIMs in 2009/2010 in Northern Ireland (applying

the STOPP criteria) to be 34%. Moreover, those medications prescribed for people aged 70 and over roughly cost €6,098,419 or approximately 5.38% of the total pharmaceutical expenditures (Bradley et al., 2012). These studies agree that the most frequently prescribed PIMs are proton pump inhibitors (PPIs), non-steroidal anti-inflammatory drugs (NSAIDs), and long acting benzodiazepines (Bradley et.al, 2012; Cahir et al., 2010). Similarly, an American survey study conducted from 2000 to 2001 showed that the use of PIMs cost approximately $7.2 billion in US health care expenditures (Fu et al., 2007).

1.4 Assessment Tools Used to Identify PIMs

There are a large number of different criteria to describe PIMs that can be considered tools for evaluation, education, and detection. All were developed and reviewed by experts who specialize in and practice geriatric care and are based on evidence-based guidelines and published reviews. These tools are based on explicit and implicit criteria.

Implicit criteria, which are based on clinicians' judgment, include general questions that alert clinicians to factors associated with PIMs. An example is the Medication Appropriateness Index (MAI), but it may be difficult and complicated to apply (Pitkala et al., 2012). Implicit criteria depend upon healthcare decision-makers who have comprehensive and sufficient knowledge and practice in geriatrics to identify and prescribe appropriate medications. So, a large number of implicit tools are very time-consuming (Gokula & Holly, 2012). In contrast, explicit criteria include lists of drug-related problems and include medications that interact with drug-disease or conditions that should be avoided by elderly people. The main advantage of explicit criteria is that they are easily applied; drug or disease oriented, and require little or no clinical judgment

(Pitkala et al., 2012). However, explicit tools may not necessarily be applicable to specific elderly people because individual patients have unique conditions that require customized treatments. Explicit tools that are commonly used to evaluate PIMs are the Screening Tool of Older Persons' Prescriptions (STOPP), the Screening Tool to Alert to Right Treatment (START), and Beers' Criteria.

1.4.1 Beers' Criteria

Beers' criteria were the first criteria developed to determine the appropriateness of a prescribed medication for geriatric patients and became widely used in United States (Beers et al., 1991). They were initially developed by Beers and his colleagues to identify PIMs for older adults in nursing homes. These criteria were modified and revised in 1997 and 2003 to comprise all healthcare settings for older adults receiving PIMs (Beers et al., 1991; Beers, 1997; Dedhiya et al., 2010; Fick et al., 2003; Fu et al., 2007; Gurwitz et al., 2003; Gokula & Holly, 2012). In 2012, Beers' criteria were updated via the consensus of an 11-member interdisciplinary expert panel in geriatrics care and pharmacotherapy (Campanelli, 2012) using the most current comprehensive review evidence and ranking these reviews based on quality and strength of evidence. Beers' criteria were supported and published with the support of the American Geriatrics Society in 2012 (see Appendix A). The updated Beers' criteria include fifty-three medications or medication classes divided into three categories: potentially inappropriate medications and classes, potentially inappropriate medications and classes to avoid in geriatric patients for specific diseases and syndromes, and medications to be used with caution in geriatric patients (Campanelli, 2012).

1.4.2 STOPP and START criteria

The STOPP and START criteria are commonly used in Europe (see Appendix A). In 2008, these criteria were created by an interdisciplinary team of 18 experts in geriatric medicine, clinical pharmacology, clinical pharmacy, psychiatry, and primary care in Ireland (Gokula & Holly, 2012; O'Mahony et al., 2010). These criteria involve two parts. STOPP includes sixty-five drugs that are indicators to detect PIMS by a list of drug-drug and drug-disease interactions that worsen the medical condition of older patients (O'Mahony et al., 2010; Chang & Chan, 2010; Gokula & Holly, 2012). The medications are categorized based on human physiologic systems and by drug classes (O'Mahony et al., 2010; Gokula & Holly, 2012). The START criteria tool is comprised of twenty-two medications that are frequently omitted by prescribers (O'Mahony et al., 2010; Gokula & Holly, 2012; Chang & Chan, 2010). In essence, the "STOPP" division is concerned with potential errors of prescribing commission which includes list of medications to be avoided, while the "START" division covers potential errors of prescribing omission. In this study, "STOPP" criteria are used along with Beers' criteria to determine the inappropriateness of medication prescriptions.

1.5 Previous Comparative Studies between STOPP and Beers' Criteria

1.5.1 Differences in the features of these tools

These two explicit criteria have multiple differences, including the specialist teams who created the lists, the number of medications listed, and their reasons for considering these medications as PIMs. However, the most notable difference is the classification of these therapeutic drugs and the frequency of use or availability of drugs worldwide. These two aspects

were drawbacks of the 2003 version of Beers' criteria. In comparison, the STOPP criteria was more applicable as it divided drugs into groups based on physiological systems and included frequently prescribed drugs among older adults. However, the updated Beers' criteria of 2012 included three new classifications of drugs: (1) drugs to be avoided regardless of diagnosis, (2) drugs to be avoided in the presence of certain diseases or syndromes, and (3) drugs to be used with caution, as well as omitting medications and adding some to new lists. All weaknesses documented by numerous critics were modified and improved by the American Geriatrics Society (Fick & Semla, 2012) using evidence-based approaches to update their findings. These changes make the Beers' criteria more clear, reasonable, and feasible to apply on a daily basis among health care providers, even if the health professionals have not specialized in geriatric medicine (Corsonello et al., 2012; Fick & Semla, 2012).

1.5.2 Studies comparing STOPP with Beers' criteria

From 2003 to 2012, most studies that compared the number of PIMs identified using the STOPP and 2003 version of Beers' criteria obtained markedly different results regarding the number of PIMs identified, adverse drug reactions related to PIMs, or resultant hospital admissions. Therefore, it is very important to present an overview of the differences in the previous results. In 2007, an Irish teaching hospital conducted a prospective study that enrolled 715 admitted critically ill patients transferred from emergency departments, with a total of 4,403 prescribed medications. The numbers of PIMs identified by STOPP and Beers' 2003 criteria were 336 and 226, respectively. Moreover, the most frequent PIMs prescribed by STOPP were long-acting benzodiazepine, tri-cyclic anti-depressants (TCAs), and antihistamines, followed by medications that increased the risk of falls. The prevalence of PIMs was higher by STOPP (35%)

than by Beers' (25%) criteria (Gallagher & O'Mahony, 2008). Thus, STOPP criteria were more sensitive than Beers' (2003) criteria in determining adverse effects of these medications leading to hospital admissions. Furthermore, the identified PIMs contributed to 11.5% (STOPP) and 6% (Beers) hospital admissions of the study population (Gallagher & O'Mahony, 2008). Likewise, the prevalence of PIMs in an Irish study of emergency department visits by patients over the age of 70 due to falls were 44% (Beers' criteria) and 53% (STOPP criteria) (McMahon et al., 2014).

In 2008, at a Spanish nursing home, a retrospective six-month study of 81 older adults using 416 drugs determined that the prevalence of PIMs was 25% and 48% based on Beers' (2003) and STOPP criteria, respectively (Ubeda et al., 2012).

Differences in the prevalence of PIMS using the STOPP and Beers' criteria (2003 version) were respectively presented as being 21% versus 13–18% in primary care, 34–50% versus 25–32% in hospital care at point of admission, and 60% versus 37% in nursing home care in a study of Irish healthcare for the elderly (O'Mahony et al., 2010). Another Irish study, published in 2011, collected data from two different areas of Ireland at home-care and long-term facilities and applied the two sets of criteria at each site. The results also showed a high prevalence and higher detection of PIMs by STOPP than by Beers' (2003) criteria (Byrne et al., 2011). Interestingly, in an American study, the prevalence of PIMs (using 2003 Beers' criteria) was 21.3% to37% among outpatients (Zhan et al., 2001; Steinman, et al.,2006), but up to 50% in nursing home residents (Lau et al., 2004), and 16.8 in those visiting the emergency department (Meurer et al., 2010).

In contrast to these findings, a 2009–2010 prospective observational study in an Indian tertiary-care hospital was conducted. It concluded that among 540 patients aged ≥60 years, the median

number of medications used was 10 drugs. The study also found that 150 drugs and 79 drugs were detected by Beers' (2003) criteria and STOPP criteria, respectively, which provided a higher prevalence with Beers' criteria (24.6%) than STOPP criteria (13.3%) (Vishwas et al., 2012). In 2011, a comparative study was conducted in Malaysian nursing homes that involved 211 patients using 989 medications. That study also displayed that Beers' (2003) criteria detected more PIMs than STOPP criteria, 33% versus 24% (Chen et al., 2012).

A large European study covered different teaching hospitals that provide geriatric services to both urban and rural patients in six countries: Switzerland, Spain, Belgium, Italy, the Czech Republic, and Ireland. Overall, the average prevalence of PIMs was 51% according to STOPP, greater than that detected by Beers' (2003) criteria (30%) (Gallagher et al., 2011). According to Beers' and STOPP criteria, the range of PIMs differed between cities, with Prague at 22.7% and 34.7% having the lowest number of PIMs, while Geneva had the highest at 43.3% and 77.3%, respectively, confirming the applicability of STOPP in some European countries (Gallagher et al., 2011).

These differences across the published literature regarding performance of these criteria to identify PIMs and adverse drug reactions are due to the difference in the features of these criteria studies as well as differing elements within each study that affects net results, such as study population, study setting, and formulated medications lists for that region (Vishwas et.al, 2012). Therefore, any researchers or professionals intending to use or compare the Beers' and STOPP criteria must consider these factors in their observations. Overall, the range of PIMs identified by STOPP versus Beers criteria to summarize the aforementioned literature review.

However, the new version of the Beers' criteria is more realistic and accounts for most of the same reasons to consider medications as PIMs (Fick & Semla, 2012). Nonetheless, there are still minor differences between the criteria, which made an interesting insight for research to continue to evaluate their validity and applicability.

1.6. PIMs in a rural setting

There are remarkable differences between rural areas in terms of health status and the utilization of health services, leading to discrepancies in life expectancy, physician visits, and access to health services. It is clear then, that residents who live in urban areas have fewer challenges regarding health care needs than their rural counterparts. Compared to urban residents, rural dwellers have less diverse services, support, and caregivers, in addition to demographic differences in education and socioeconomic conditions, which are influential factors in health (Forbes & Edge, 2009). Thus, rural dwellers have poorer health care statuses and shorter life expectancies (Pong et al., 2011)**.**

By 2021, the percentage of older adults will have increased and it is assumed that one in four elders will live in a rural zone. In fact, older adults aged 65 and older will comprise 30% to 40% of the population of rural dwelling (Forbes & Edge, 2009). Furthermore, Brundisini and colleagues' (2013) review found that the precarious condition of people with multiple illnesses has greater potential to worsen if rurally domiciled.

Aside from increasing the vulnerability of the elderly, rurality should be evaluated as a remarkable factor that may affect health care outcomes. Firstly, "rural" has been defined in different manners to serve specific purposes; however, Statistics Canada defines "rural areas" as

zones that are located outside of urban centers with populations of at least 10,000. Classification depends on the type of rural community and accounts for those close to urban cities where advanced health care services are provided. Furthermore, it is subdivided into four categories based on a census of rural areas (Pong et al., 2011).

The literature related to the impressions of family physicians and specialists who work in remote and rural settings is considerable, providing a rich image of their needs and satisfactions, as well as the prevalence of diseases, frequency of utilization of heath care services, and characteristics of rural populations, but not their risk of PIMs (Sibley & Weiner, 2011; Toguri et al., 2012).

Chapter 2: Study Rationale & Objectives

2.1 Rationale for Conducting the Study

The underlying purpose of this research is to assess the quality of medication use among older patients. It is clear that special care should be taken when prescribing medications to older patients since inappropriate treatment for older adults leads to ADEs, which are still a major challenge facing the health care system, leading to frequent hospitalizations, increasing the burden on the health care system. Therefore, continuing research to evaluate and attenuate the problem of PIMs is necessary to diminish the burden of ADEs.

A review of the literature reveals that educating prescribers about the appropriateness of the medication prescribed leads to a decrease in the use of inappropriate drugs. The frequency of inappropriate medications prescribed has been well-documented worldwide over the past twenty-five years using a variety of tools. However, the assessment of this problem using updated criteria is rare throughout Canada, but especially in rural settings. Therefore, this study attempts to determine the extent of inappropriately prescribed medications for the older rural adult.

In this study, the use of both geriatric assessment criteria is unique, as previously, prevalence was measured using either STOPP or Beers' criteria (2003 version), not both concurrently. Since STOPP criteria are quite different from Beers' criteria, prevalence depends on the type of PIM criteria used in the research, making comparisons of the data difficult. However, the updated Beers' criteria (2012 version) have many modifications that improve its deficiencies and drawbacks, but its relatively recent availability means that few studies have used this updated

version yet. Therefore, this study will use the updated version of the Beers' criteria in addition to the STOPP criteria to identify as many PIMs as possible, to derive a truer picture of the prevalence of PIMs.

Previous studies have focused their efforts in various urban health care settings, or do not differentiate rural from urban patients, but few studies are concerned with rural health care settings when measuring the prevalence of PIM use among older patients. For example, studies of medications prescribed to rural populations and the quality of treatment are rare. In this study, we attempt to provide information about medication use in multiple hospitals in rural Ontario.

Overall, this study is motivated by the inequity between rural and urban centers' health care to evaluate the appropriateness of medication use in those rural settings and to gain insight on vulnerable patients who suffer from chronic diseases. Using the updated Beers' criteria and comparing it to the STOPP criteria to determine the appropriateness of medications use provides novelty in this research since previous studies used the outdated version of the Beers' criteria. In addition, insufficient research has been conducted in a Canadian context. Finally, we focus on inpatients, rather than the more commonly studied facilities, making this research unique.

2.2 Objectives and Research Question

The aims of the study are as follows:

1) Estimate the prevalence of PIMs use among older patients who are admitted to rural hospitals using STOPP and Beers' criteria.

    a. Identify the most frequent PIM category prescribed.

    b. Compare the number of PIMs identified by STOPP to Beers' criteria as well as the total number of PIMs identified by both criteria.

2) Explore and determine the factors associated with PIMs use in rural elderly inpatients, including patient characteristics.

This study will answer the following question:

Is the use of PIMs prevalent among older patients who are admitted in rural hospitals?

Chapter 3: Methods

3.1 Literature Review Strategy

The literature review was conducted using two databases: Medline (PubMed) and Embase (Ovid), using the following keywords as synonyms for "elderly" (known as "Mesh Terms" in Medline): geriatrics, geriatric, aged, aged 80 and over, senior, elderly, or older. Searches for "inappropriately prescribed medications" were based on suggested acronyms from these databases: inappropriate prescribing, inappropriate medication, and inappropriate prescription. Also, searches were conducted using the following terms in combination with or without the previously mentioned keywords: prevalence, epidemiology, rural, health, medication, drug, tools, criteria, STOPP/ START, Beers' criteria, comparison, difference, Ontario, and Canada. All of these keywords were used to assure that all articles related to this subject were reviewed.

3.2 Research Ethics Clearance

This study was reviewed and approved by the Research Ethics Office of the University of Waterloo and the ethics committee of South Bruce Grey Health Centre (SBGHC) institutional review board (see Appendix B).

3.3 Study Setting

This study conducted in multiple rural hospitals. The setting of this study is the SBGHC, which is comprised of four hospitals in southwestern Ontario in the towns of Chesley, Durham, Kincardine, and Walkerton.

3.4 Study Population

All patients aged 65 and over admitted to the four hospitals were included during the study period. However, re-admitted patients in the same hospital or in other sites of study were excluded to avoid recording patient information twice that would result in inaccurate calculations of prevalence. Older patients who declined to sign a consent form were eliminated from the study population. Otherwise, there were no selection criteria and all older patients were asked to participate in this study throughout the study periods.

3.5. Study Design

This study was designed as an observational cross-sectional study. The prevalence of PIMs use was evaluated once patients were admitted. Patients' medication profiles were reviewed and analyzed carefully to find the required data. In addition, if the health site had electronic medical records database facilities, the patients' medications were screened from there while the patient was still hospitalized. Both PIMs screening tools (updated Beers' and STOPP criteria) were used for each patient's medication lists. Overall, this study was carried out within three months (mid-January to mid-April, 2014).

3.6 Study Protocol

3.6.1 Data collection

The data were collected when the patient arrived at the hospital (i.e., the data were recorded either from a combination of electronic or paper-based medical charts). The home

medication lists from each patient was reviewed, as well as the admission medication list. Collected data included clinical and demographic patient characteristics:

- Patient name
- Age and gender
- Medical history and current diagnoses (reasons for admission)
- Number and type of PIMs from home medications as well as admission lists were reviewed and recorded to confirm the complete lists of home medications (reasons for any missing information were documented)
- Total number of prescribed medications per patient

These data were collected upon hospital admission. The medication data included previously prescribed medications and over-the counter (OTC) medicines that the patient was administering daily just prior to hospital admission.

3.6.2. Processes of the data collection

Information was collected through multiple steps at each hospital as follows:

1. One site had all the admissions lists for all four hospitals. These admissions lists were provided and updated on a daily basis and included patient name, age, hospital ID, patient room number, and a briefing of the diagnosis upon admission. This method helped assess all the admitted patients in all four hospitals until the end of the specified study period. Those admissions lists were screened to identify patients aged 65 or older. Once new admissions were observed, the researcher went to the site to meet the patients. Often, there were

admissions in four sites at the same time so the researcher took rounds through all of these sites to recruit patients.

2. Participants signed the provided the patient consent form (see Appendix C). Based on patients' requests, sometimes the consent letters were left with patients to think about and discuss with their family members. Since the target population was of older adults, some were not familiar with the requirements of conducting clinical research. Once permission was granted, a feedback and appreciation letter was given to the patient (see Appendix D).
3. Located and assessed patient information from their medical charts.
4. Excluded the patients who were re-admitted to avoid any duplication in the data by screening full patient name and age from the research laptop.
5. Obtained answers and clarifications from nurses or health records in case of questionable information.
6. Reviewed admission/home medication lists carefully and detected PIMs using Beers' and STOPP criteria.
7. Recorded other required patient information (as mentioned above) by filling out the Microsoft's spreadsheet software Excel in the research laptop.

3.6.3 Obtaining informed consent from geriatric patients

The recruiting of hospitalized older adults and asking them to sign a consent form was not an easy task in practice. While some were in reasonable health with the competence to sign consent forms, most elderly patients admitted to hospital were not well-oriented, so unable to do so. This made it unethical to ask for their permission while they were in critical condition. Aside from their complex conditions, some were in isolation areas, which increased the difficulty of

obtaining consent letters. Additionally, other minor challenges were faced in circulating consent forms to the patients. These challenges were overcome by waiting for patients to become conscious and for their condition to improve to ask them for permission before their discharge. Searching for patients' family members was an alternate solution. In some cases, there were no relatives, so powers of attorney were contacted.

Before asking patients to sign consent forms, explanations of the purpose of the project, the reasons to consent, the kind of information being collected, and the risks and benefits of conducting of this research were explained, and all of the patients' concerns and questions were answered. Because of the variety of patients, both acceptances and objections were expected. When patients or their relatives refused to take part in study even though the benefits and risks of this project had been explained and clarified, their decisions were respected and patients or their relatives were never encouraged to change their decisions. However, the reasons for participants' objections were requested and documented if applicable.

3.6.4 Procedures for screened medications and reported PIMs

Once a patient was admitted and the consent form was completed, about 25 minutes were spent to read and record required information into a research laptop computer. Each case was comprehensively studied and the required information completed, because in some cases, the home medication list and reason for admission was not confirmed or documented at the time of admission, which required rechecking from time to time. Once the entire patient information was recorded, a second revision of the patient profile was always done in case some of the required information changed.

After completion of these steps to ensure the dataset was accurate, each criterion was applied separately. Then, each PIM identified was highlighted using different colors for each criteria and the criterion used to consider the medication as a PIM was also recorded. If both criteria were identified as the same medication, it was highlighted with a different color and the different or same reasons from both criteria were documented. At that point, the number of PIMs was counted for each case. At the end of each week of the study period, all data recorded on the Excel sheet on the research laptop were reviewed to ensure the required patient data were detected and that the counted PIMs were accurate and complete.

Data collection and consent form accumulation continued, until data for 50 patients was achieved. The data entry was then re-evaluated before closing the excel file. At the end of the research period, the entire patient dataset was coded and classified based on electronic International Classification of Diseases, v. 10 (ICD-10 codes). At this step, patient information, reason for admission, and the number of PIMs were reviewed thrice at different times. Finally, a last revision was done when reasons for considering a medication as a PIM and the number of PIMs were sorted in criteria tables as presented in the next chapter.

3.7 Information Security Protocol

3.7.1 Data security procedures designed for this study

According to the University of Waterloo Information Security (Policy 8), guidelines and procedures were created to protect confidential information and privacy of research participants, thus helping the researcher to ensure and maintain information security when the individuals' data were collected and stored.

This study was concerned with two main direct personal identifiers: patient name and age. Other identification numbers (for example: health insurance numbers and patient profile numbers) were not collected. The full patient name and age (first, middle and last name) were required to avoid possible duplication in the data should the patient be admitted multiple times either in the same hospital, or other sites of this study.

This information and other data (medical histories and current diagnoses) were coded to be anonymized to diminish the risk of re-identification of participants. Personal information was not recognized when the data was released for analysis purposes, sharing, or presenting study results. The following processes were implemented to confirm data security:

- The site of study where the patient was admitted was recorded as a letter; for example, the first hospital or site A was registered as letter A in the database and so on for the remaining sites.

- Each patient at each hospital was registered as a sequentially alphanumeric case; for example, the first patient who was admitted to the first site of study had a code 1A and the second patient who was admitted to the same hospital had a code 2A, and so on.

- Knowledge of medical conditions was required to determine the appropriateness of using medications with that medical diagnosis. For this reason, diseases were entered and encoded using the ICD-10 codes.

- The collected data was entered in the research laptop using Microsoft Excel. The data analysis spreadsheets were password protected. Moreover, the data were not shared with others, and patients were not recognized in either the data analysis or reporting.

- At all times, data set was stored in a secure place and in secure data-encrypted form.

3.7.2 Information security followed in this study

3.7.2.1 Physical security The principal investigator was responsible for keeping the research laptop in a safe and secure place during transportation and storage. The laptop was stored in a locked cabinet in a locked office located in a secure building (School of Pharmacy). Only the principal investigator had access to the secure location using physical and electronic keys. During data collection, the laptop was logged out or shut down during periods when the principal investigator left the office for any reason. Login accounts and other software passwords were never shared with anyone.

3.7.2.2 Software security Spyware and antivirus software were installed to protect the database from any threats. Also, the research laptop was not connected to the internet for any reason nor used for personal purposes. Furthermore, data was encrypted on the laptop using Truecrypt software. This software protected the confidential files from theft. Once the data was encrypted, a password or key was required to access the documents.

Complex passwords were created for the computer. As well, any documents or servers that were used during data collection such as Microsoft's Excel, were password protected. A password-protected screen saver was applied to ensure that the laptop locked automatically

when it was not active within a specified time. Finally, direct identifier data was erased and destroyed in a secure manner to protected privacy (e.g.: secure digital destruction program).

3.8 Statistical Analysis

Firstly, the prevalence of PIMs use was measured by collecting the total number of patients who had been prescribed at least one PIM, as the numerator divided by the total number of patients enrolled in this study within the three month period as the denominator.

Secondly, the possible factors associated with PIMs use including demographic patient characteristics, age, gender, and clinical patient characteristics (number and type of diseases and number of medications prescribed) were assessed. These data were expressed as a mean and percentages (%). The association between these factors that lead to the use of PIMs was identified using logistic regression analysis. The odds ratio with a 95% confidence interval (CI) was reported for each of the explanatory variables. A p-value of 0.05 was considered significant. Statistical analyses were performed using the IBM SPSS (Statistical Package for the Social Sciences), version 22.

Chapter 4: Results

4.1. Study Population Size

During the three month study period, all 215 age-eligible patients that were admitted at one of the four sites were considered for participation in this study, within which 178 signed consent forms. However, 31 of 178 were readmitted later within the same study period but excluded from eligibility at the second admission to avoid duplication of data. Thirty seven patients declined or were unable to provide consent and were excluded. In brief, some patients objected because they did not wish to release their information or were enrolled in other research. Furthermore, some patients were excluded because they were at the end stage of life or were not competent, or did not have relatives or power of attorney to provide consent.

4.2 Participant Demographics

Of the study population, 93 (52.2%) were female and 85 (47.8%) were male. The mean patient age was 79.09 ± 8.270. The median age of the participants was 80 (65–97) years. Most of the patients aged 85 years and older were female (see Figure1). The patient's demographic characteristics are represented in Table 1.

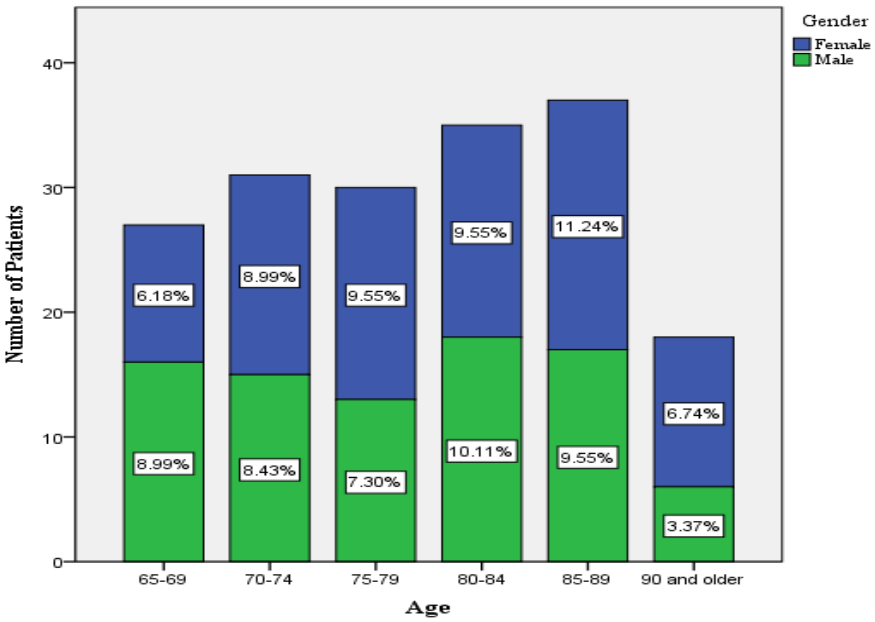


Figure 1. Distribution of the study population by age and gender

Table 1. Patient demographics

Patient Characteristic	**Female N= 93 (52.2%)**	**Male N= 85 (47.8%)**	**Total N=178 (100%)**
Age			
Mean (SD)	79.90 ± 8.195	78.20 ± 8.309	79.09
Median	80	79	80
Age range			
65-69	11 (6.2%)	16 (9.0%)	27 (15.2%)
70-74	16 (9.0%)	15 (8.4%)	31 (17.4%)
75-79	17 (9.6%)	13 (7.3%)	30 (16.9%)
80-84	17 (9.6%)	18 (10.1%)	35 (19.7%)
85-89	20 (11.2%)	17 (9.6%)	37 (20.8%)
90 and more	12 (6.7%)	6 (3.4%)	18 (10.1%)
Risk factors			
Current Smoking	7 (3.9%)	4 (2.2%)	11 (6.2%)
Non-smoking	86 (48.3%)	81 (45.5%)	167 (93.8%)
Alcoholic intake	7 (3.9%)	7 (3.9%)	14 (7.9%)
Non-alcoholic intake	86 (48.3%)	78 (43.8%)	164 (92.1%)
Obese	9 (5.1%)	5 (2.8%)	14 (7.9%)
Non-obese	84 (47.2%)	80 (44.9%)	164 (92.1%)

4.2.1. Health conditions of patients

Table 2 demonstrates that 54.5% of the participants had six or more diseases. The mean number of illnesses of the study population was 6.16 ± 3.259. Furthermore, most patients aged 80-89 years had more chronic conditions compared to the other aged groups.

Table 2. Number of patients in categories of comorbidities by gender and age group

	0-2 disease(s) N = 23(12.9%)	**3-5 diseases N = 58 (32.6%)**	**≥ 6 diseases N = 97 (54.5%)**	**Total**
Gender				
Female	11 (6.2%)	32 (18%)	50 (28.1%)	93 (52.2%)
Male	12 (6.7%)	26 (14.6%)	47 (26.4%)	85 (47.8%)
Age range				
65–69	3 (1.7%)	11 (6.2%)	13 (7.3%)	27 (15.2%)
70–74	3 (1.7%)	11 (6.2%)	17 (9.6%)	31 (17.4%)
75–79	6 (3.4%)	12 (6.7%)	12 (6.7%)	30 (16.9%)
80–84	6 (3.4%)	7 (3.9%)	22 (12.4%)	35 (19.7%)
85–89	3 (1.7%)	12 (6.7%)	22 (12.4%)	37 (20.8%)
90 and over	2 (1.1%)	5 (2.8%)	11 (6.2%)	18 (10.1%)
Total	**23 (12.9%)**	**58 (32.6%)**	**97 (54.5%)**	**178 (100%)**

More than half of the study population had six or more diseases; of whom 51.55% (50/97) were female and 48.45% (47/97) were male (Figure 2). Among all of the age groups, the number of patients approximately increased with the number of diagnoses. Consequently, roughly higher percentages of all age groups had six or more diseases than did patients with fewer diseases (Figure 3). The percentages of patients with six or more diseases were approximately similar for patients aged 80 to 84(22/35= 62.9%), those aged 85 to 89 (22/37= 59.5%), and those aged 90 and over (11/18=61.1%). These three age groups had the highest proportions of individuals with six or more diseases, compared with the other age groups.

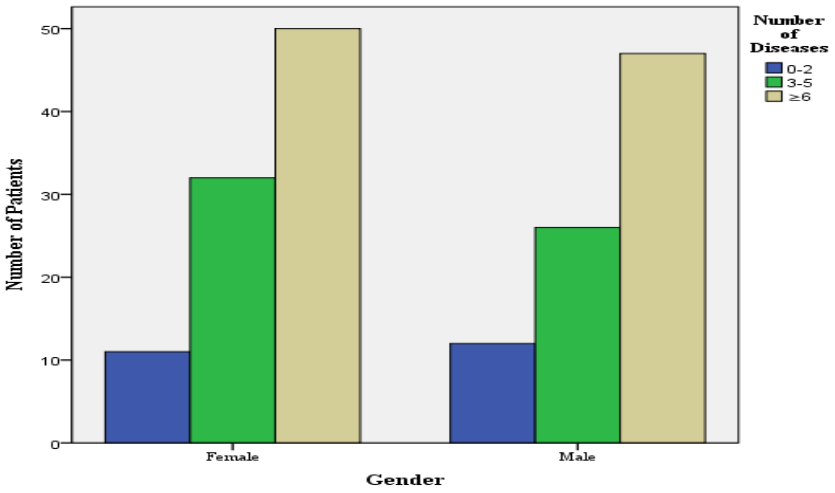


Figure 2. Distribution of the number of diseases per patient by gender

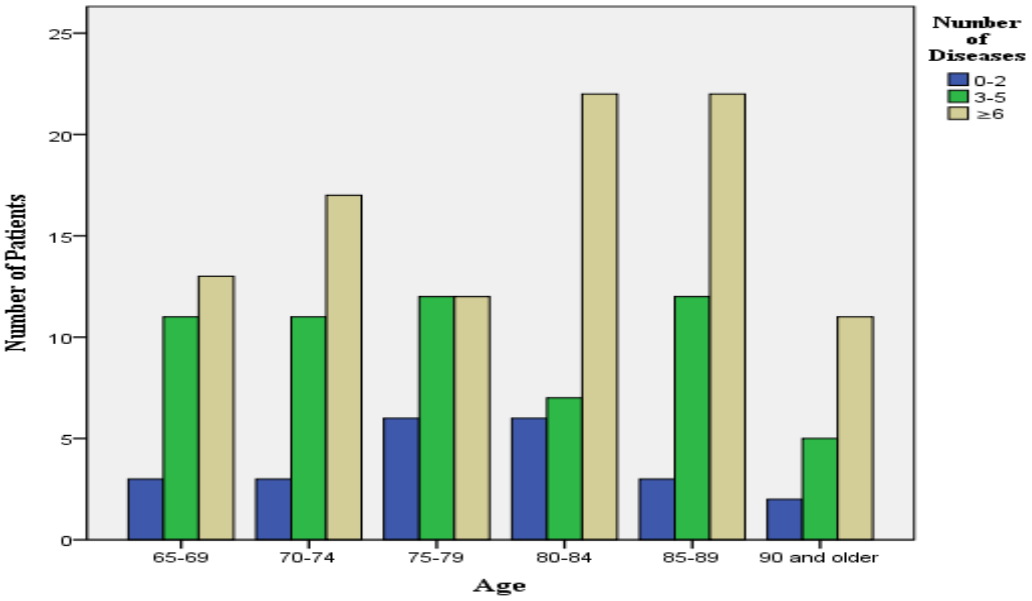


Figure 3. Distribution of the number of diseases per patient by age group

The most commonly reported diseases were a history of cardiovascular disease (160/178=89.9%), followed by endocrine diseases (81/178=45.5%), musculoskeletal diseases (72/178=40.4%), gastrointestinal diseases (66/178=37.1%), neurological diseases (57/178=32%), respiratory diseases (52/178=29.2%), cancer and immune diseases (36/178=20.2%), urogenital diseases (34/178=19.1%), and renal diseases (16/178=9%). The distribution of morbidity and comorbidity among the study population is represented in Table 3.

Table 3. Distribution of chronic diseases among the study population

Disease	**No. cases (%)**	**Disease**	**No. cases (%)**
Cardiovascular		**Gastrointestinal**	
HTN	123 (69.10)	GERD	36 (20.22)
Hyperlipidemia	64(35.96)	Diverticular of intestine	12 (6.74)
Arrhythmia unspecified	47(26.4)	Liver disorder	6 (3.37)
CAD unspecified	40(22.47)	Constipation	5 (2.81)
HF	26 (14.61)	Inflammatory bowel diseases	4 (2.25)
MI/ Heart Attack	24 (13.48)	Irritable Bowel Syndrome	4 (2.25)
Stroke/CVA	24 (13.48)	Gall bladder, biliary tract and pancreas disorder	4 (2.25)
TIA	11(6.18)		
Aortic disorders	7 (3.93)	GI Haemorrhage	3 (1.69)
DVT	6 (3.37)	PUD	3 (1.69)
Peripheral vascular disease	5(2.81)	Diarrhea	1 (0.56)
Cardiomyopathy	4 (2.25)	**Renal**	
		CKD	13 (7.30)
Neurologic		AKD	4 (2.25)
Depression	20 (11.24)	Fluid and electrolyte imbalance	4 (2.25)
Dementia	17 (9.55)		
Sleep disorders	11 (6.18)	**Urogenital disease**	
Anxiety/ Stress	10 (5.62)	BPH	15 (8.43)
Cognitive disorder	9 (5.06)	Urinary incontinence	8 (4.49)
Pain unspecified	21(11.79)	UTI	5 (2.81)
PD	5(2.81)	Prostate disorder	2 (1.12)
Bipolar disorder	2 (1.12)	**Endocrine**	
Epilepsy	1 (0.56)	DM2	45 (25.28)
		Thyroid disorder	31 (17.42)
		DM1	13 (7.30)
		Addison crisis	2 (1.12)

Table 3 cont'd

Disease	No. cases (%)	Disease	No. cases (%)
Musculoskeletal		**Respiratory**	
Osteoarthritis	49 (27.53)	COPD	36 (20.22)
Rheumatoid arthritis	35 (19.66)	Other disorder	10 (5.62)
Osteoporosis	23 (12.92)	Asthma	8 (4.49)
Gout	17 (9.55)	Pneumonia	6 (3.37)
DDD	4 (2.25)	TB	2 (1.12)
Bursitis	3 (1.69)		
Polymyositis	2 (1.12)		
Cramps	2 (1.12)		
Infection		**Hematologic**	
Sepsis	2 (1.12)	Anaemia	9 (5.06)
Other infection	3 (1.69)		
Ophthalmic disease		**Skin disease**	
Cataract	20 (11.24)	Cellulitis	7 (3.93)
Glaucoma	14 (7.87)	Other	8 (4.49)
Other eye disorders	8 (4.49)		
Cancer and immune system		**Falls**	36 (20.22)
Skin cancer	7 (3.93)	**Fractures**	24 (13.48)
Kidney cancer	6 (3.37)		
Colon cancer	6 (3.37)	**Other**	
Prostate cancer	5 (2.81)	Edema	5 (2.81)
Breast cancer	5 (2.81)	Nutrition disturbance	4 (2.25)
Leukemia /Myelodysplasia	5 (2.81)	Off balance/vertigo	2 (1.12)
Lung cancer	4 (2.25)	Syncope	2 (1.12)
Tumor, Unspecified	4 (2.25)	Failure to cope	2 (1.12)
Lupus	2 (1.12)	Allergic rhinitis	2 (1.12)
Liver cancer	2 (1.12)	Dehydration	2 (1.12)
		Rare diseases	2 (1.12)
		Gangrene	1 (0.56)

AF; atrial fibrillation, AKD; acute kidney disease, BPH; benign prostatic hyperplasia, HF ;congestive heart failure, CAD; coronary artery disease, CKD; chronic kidney disease, COPD; chronic obstructive pulmonary disease**,** CVA; cerebral vascular accident, DDD; degenerative disc disease, DM: diabetes mellitus, DVT; deep vein thrombosis, GERD; gastroesophageal reflux disease, GI; gastrointestinal, HTN; hypertension, MI; myocardial infraction , PD; Parkinson's Disease, PUD; peptic ulcer disease, TIA; transient ischemic attack, TB; tuberculosis, UTI; urinary tract infection

The underlying reason for patient admission or patient diagnose upon admission was carefully recorded. Table 4 provides a summary of patient conditions with numbers of cases and percentages of patients satisfying the condition. Falls (10.76%) and fractures (14.61%) are common reasons for geriatric admissions leading to repairs or replacements of hips or other limbs; subsequently the number of surgeries increased as seen below in Table 4. As well, a high percentage of seniors were admitted with the condition "Failure to cope" (11.80%), which is being commonly diagnosed in most of the older adults upon admission, indicating the severity of elders' conditions.

Table 4. Reasons for hospital admission

Disease/condition	**No. (%)**	**Disease/condition**	**No. (%)**
CVA/Stroke	10 (5.62)	Gastrointestinal hemorrhage	4 (2.25)
TIA	5 (2.81)	Bowel diseases	7 (3.93)
Acute coronary	4 (2.25)	Gallbladder, biliary tract and	4 (2.25)
Myocardial infraction	7 (3.93)	Renal failure	4 (2.25)
Angina	3 (1.69)	electrolyte imbalance/edema	5 (2.81)
Heart failure	10 (5.62)	Dehydration	7 (3.93)
Cardiac arrhythmia	14 (7.87)	COPD/Asthma	3 (1.69)
HTN	3 (1.69)	Pulmonary disorder	5 (2.81)
Syncope/Off balance	13 (7.30)	Pneumonia	18 (10.11)
Stress/anxiety	3 (1.69)	UTI	7 (3.93)
Delirium	2 (1.12)	Infection	2 (1.12)
Dementia	5 (2.81)	Sepsis	5 (2.81)
Confusion	8 (4.49)	Anemia	5 (2.81)
Failure to cope	21 (11.80)	Skin disease	9 (5.06)
Tremor	1 (0.56)	Gout/arthritis	3 (1.69)
Headache/Migraine	2 (1.12)	Post-surgery/rehabilitation	22 (12.36)
Weakness	17 (9.55)	Metastatic cancer- possible	5 (2.81)
Pain	17 (9.55)	Fall	19 (10.67)
Glucose disturbance	8 (4.49)	Fracture	26 (14.61)

COPD; chronic obstructive pulmonary disease, CVA; cerebral vascular accident, HTN; hypertension , TIA; transient ischemic attack, UTI; urinary tract infection.

4.2.2. Medication use

The total number of medications administered was 2,024. The median number of medications used was 10 and the mean was 10.96 ± 5.732. The number of medications used among the cohort ranged between 0-27 drugs. The number of medications grouped into different intervals to determine the polypharmacy in the study population (see table 5). It shows that most of older participants are receiving multiple medications, approximately more than five medications. Furthermore, most patients used these medications regularly, because there were fewer medications (203) to be used as needed (PRN) than used on a daily basis. In addition, patients used 53 non-prescribed OTC medications, some of which (multivitamins, vitamin D, etc.) were used on a regular basis as well. Additional details concerning the number of medications prescribed for each patient, the drug classifications, and frequency of medications used are found in Appendix E.

Table 5. Number of patients in categories of medication use by gender and age group

	<5 medications	**5-9 medications**	**≥10 medications**	**Total**
	No. patients (%)	**No. patients (%)**	**No. patients (%)**	
Gender				
Female	14 (7.9)	23 (12.9)	56 (31.5)	93 (52.2)
Male	10 (5.6)	31 (17.4)	44 (24.7)	85 (47.8)
Total	24 (13.5)	54 (30.3)	100 (56.2)	178 (100)
Age range				
65-69	4 (2.2)	6 (3.4)	17 (9.6)	27 (15.2)
70-74	3 (1.7)	11 (6.2)	17 (9.6)	31 (17.4)
75-79	4 (2.2)	8 (4.5)	18 (10.1)	30 (16.9)
80-84	4 (2.2)	8 (4.5)	23 (12.9)	35 (19.7)
85-89	5 (2.8)	16 (9.0)	16 (9.0)	37 (20.8)
90 and over	4 (2.2)	5 (2.8)	9 (5.1)	18 (10.1)
Total	24 (13.5)	54 (30.3)	100 (56.2)	178 (100)

As shown in Table 5, only 13.5% of patients used less than five medications, whereas 86.5% of patients used five or more medications. More than half of the older adults (n = 100, 56.2%) consumed ten or more medications, of whom 56% were female and 44% were male (Figure 4). The number of medications used increased in each age group, peaking in the 80-85 group, and then declining in the 85–89 group and over 90 group. All age groups contained more people who used ten or more medications than those who used few medications (Figure 5).

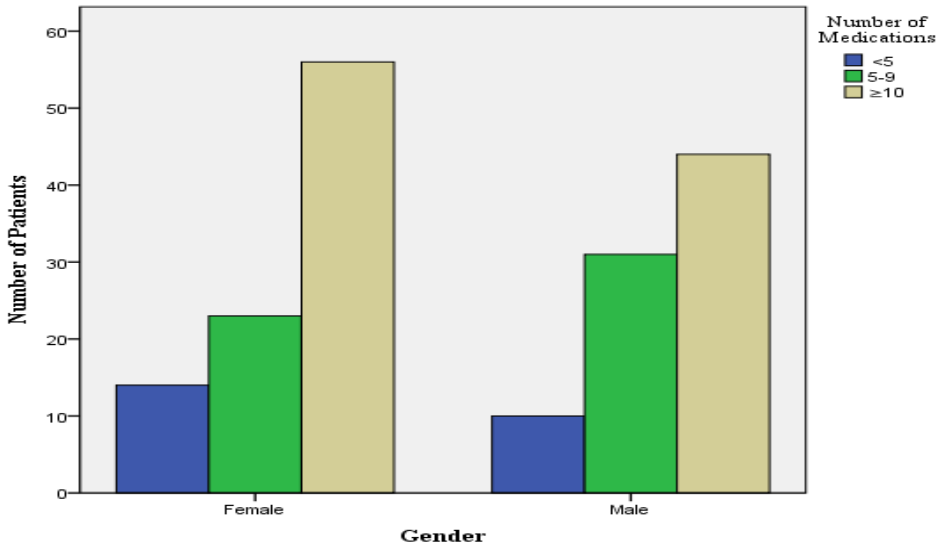


Figure 4. Distribution of the number of medications used per patient by gender

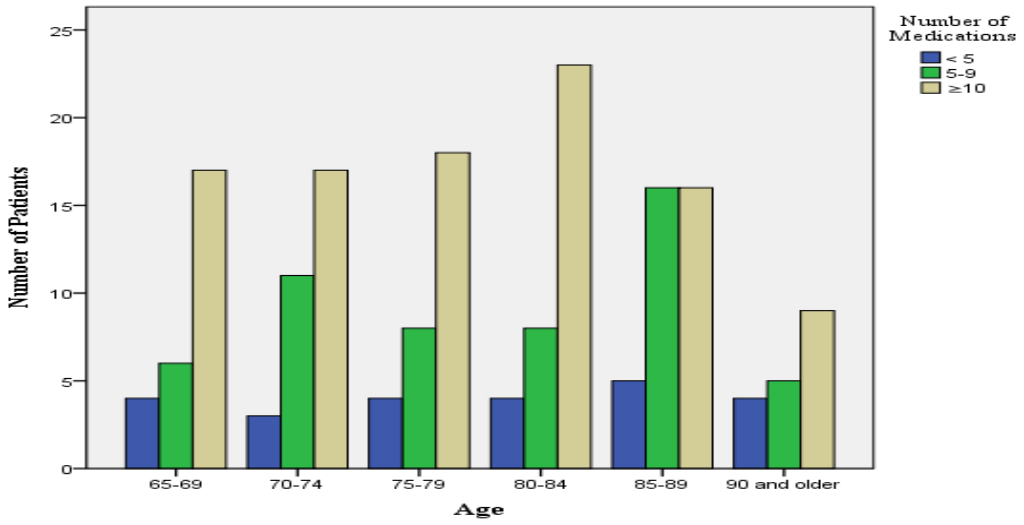


Figure 5. Distribution of the number of medications used per patient by age group

4.3 Potentially Inappropriate Medication Use

4.3.1 Prevalence of PIMs by STOPP, Beers' and both sets of criteria

The prevalence of using at least one PIM among the older adults in this study was 62.92% (112/178) based on Beers' criteria, while the prevalence of receiving at least one PIM was 69.10% (123/178) by STOPP criteria. When both criteria were used concurrently, the proportion of using at least one PIM was 73.03% (130/178). Table 6 presents the differences between the number of patients administering multiple PIMs compared with types of screening criteria, whether these criteria are used individually or together.

From Figure 6, the concurrent use of both criteria resulted in an increased number of PIMs detected per patient, which is equal to the total number of PIMs identified by each set of criteria minus the number of medications that both criteria agree upon and considered as PIMs (the overlap in the number of PIMs between both criteria), in order to avoid duplication in results.

Table 6. Number of patients receiving PIMs using Beers', STOPP, or both sets of criteria

	Beers' criteria No. patients (%)	STOPP criteria No. patients (%)	Beers' & STOPP No. patients (%)
Patient does not receive PIMs	66 (37.1)	55 (30.9)	48 (27.5)
Patient receives one PIM	51 (28.7)	55 (30.9)	34 (19.1)
Patient receives two PIMs	40 (22.5)	36 (20.2)	40 (22.5)
Patient receives three PIMs	14 (7.9)	22 (12.4)	26 (14.6)
Patient receives four PIMs	6 (3.4)	4 (2.2)	18 (10.1)
Patient receives five PIMs or more	1 (0.6)	6 (3.4)	12 (6.7)
Total	178 (100)	178 (100)	178 (100)

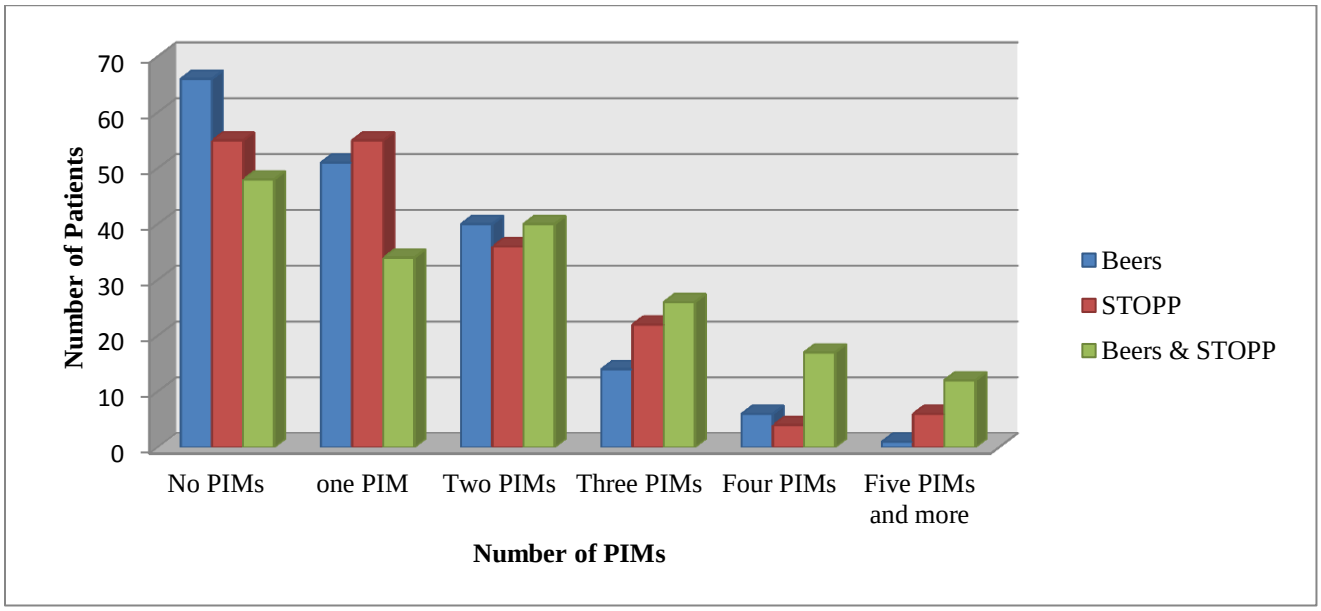


Figure 6. Distribution of patients by PIM frequency using Beers, STOPP, or both criteria

4.3.2. Number of PIMs in each category identified using STOPP, Beers', or both criteria.

To detect the medications that should be avoided, 25 of 48 Beers' criteria were used (29 of 53 criteria were used to determine medications that should be avoided or used with caution), whereas 53 of 65 STOPP criteria were used. As a result, the total number of PIMs identified by Beers' criteria is 202 PIMs (see Table 7), and by STOPP criteria is 240 PIMs (see Table 8).

Table 7. Number of PIMs identified by Beers Criteria

Therapeutic Category or Drug	Number of PIMs (%)
Anticholinergic Drugs	
1. First-generation antihistamines	11 (5.4)
2. Antispasmodics	1 (0.49)
Anti-infective	
3. Nitrofurantoin	1 (0.49)
Cardiovascular	
4. Antiarrhythmic drugs (Class Ia, Ic, III)	2 (0.99)
5. Digoxin >0.125 mg/day	3 (1.48)
6. Spironolactone >25 mg/day	7 (3.46)
Central Nervous System	
7. Tertiary TCAs, alone or in combination	4 (1.98)
8. Antipsychotics, 1st-(conventional) & 2nd (atypical) generation	12 (5.94)
9. Benzodiazepines; short, intermediate and long-acting	26 (12.87)
Endocrine system	
10. Insulin, sliding scale	6 (2.97)
11. Sulfonylureas, long acting	3 (1.48)
Gastrointestinal	
12. Metoclopramide	6 (2.97)
Pain Medications	
13. Meperidine	2 (0.99)
14. Non-COX-selective NSAIDs, oral	11 (5.4)
15. Indomethacin	2 (0.99)
Ketorolac, includes parenteral	1 (0.49)
16. Skeletal muscle relaxants	2 (0.99)

Table 7 cont'd

Medications with specific diseases or syndromes	
17. Heart failure with	
NSAIDs and COX-2 inhibitors	7 (3.46)
Nondihydropyridine CCBs	5 (2.47)
Pioglitazone	2 (0.99)
18. Syncope with	
AChEIs	2 (0.99)
Tertiary TCAs	1 (0.49)
19. Dementia & cognitive impairment	
Anticholinergics	9 (4.45)
Benzodiazepines	4 (1.98)
H2-receptor antagonists	1 (0.49)
Antipsychotics, chronic and as-needed use	5 (2.47)
20. History of falls or fractures	
Anticonvulsants	7 (3.46)
Antipsychotics	2 (0.99)
Benzodiazepines	13 (6.43)
TCAs	5 (2.47)
SSRIs	17 (8.41)
21. Parkinson's disease	
Antipsychotics	2 (0.99)
22. Chronic constipation with	
Oral antimuscarinics for urinary incontinence	5 (2.47)
Nondihydropyridine CCB	4 (1.98)
23. History of gastric or duodenal ulcer	
Non–COX-2 selective NSAIDs	3 (1.48)
24. Chronic kidney disease	
NSAIDs	2 (0.99)
25. Lower urinary tract symptoms with	
Benign prostatic hyperplasia	
Inhaled anticholinergic agents	6 (2.97)
Total	**202 (100)**
Medications used with Caution	
26. Aspirin for primary prevention of cardiac events	8 (15.09)
27. Dabigatran	6 (11.32)
28. Mirtazapine	9 (16.98)
SNRIs	15 (28.30)
SSRIs	13 (24.52)
29.Vasodilators	2 (3.77)
Total	**53 (100)**

AChIs; acetylcholinesterase inhibitors, CCB calcium channel blocker, NSAID**;** nonsteroidal anti-inflammatory drug, SSNI; serotonin and norepinephrine reuptake inhibitors SSRI; selective serotonin reuptake inhibitor, TCA: tri-cyclic antidepressant

Table 8. Number of PIMs identified by STOPP Criteria

Therapeutic Category or Drug	No. PIMs (%)
Cardiovascular System	
1. Digoxin >0.125mg with impaired renal function	1 (0.41)
2. Loop diuretic as first line monotherapy for HTN	7 (2.91)
3. Thiazide diuretic with a history of gout	5 (2.08)
4. Non selective beta blocker with COPD	1 (0.41)
5. Diltiazem or verapamil with NYHA Class III/IV heart failure	5 (2.08)
6. CCB with constipation	7 (2.91)
7. Aspirin and warfarin without H2 R antagonist or PPI	1 (0.41)
8. Aspirin with history of PUD	3 (1.25)
9. Aspirin with doses > 150mg/day	6 (2.5)
10. Aspirin with no history of coronary, cerebral or peripheral vascular disease	6 (2.5)
11. Warfarin >12 mo. for first uncomplicated pulmonary embolism	1 (0.41)
12. Aspirin, clopidogrel, dipyridamole, or warfarin with concurrent bleeding disorder	1 (0.41)
Central Nervous System and Psychotropics	
13. TCAs with dementia	1 (0.41)
14. TCAs with glaucoma	1 (0.41)
15. TCAs with cardiac conduction abnormalities	2 (0.83)
16. TCAs with constipation	1 (0.41)
17. TCAs with opiate or calcium channel blocker	4 (1.66)
18. TCAs with prostatism or urinary retention	1 (0.41)
19. Long term benzodiazepines (>1 month)	5 (2.08)
20. Long term neuroleptics with Parkinson's (>1 month)	2 (0.83)
21. Long term neuroleptics as long term hypnotics	13 (5.41)
22. Anticholinergics to treat extra-pyramidal neuroleptic symptoms	1 (0.41)
23. SSRIs with hyponatremia	14 (5.83)
24. >1 week use first generation antihistamines	11 (4.58)
Gastrointestinal System	
25. Diphenoxylate, loperamide, or codeine for diarrhea of unknown cause	3 (1.25)
26. Diphenoxylate, loperamide, or codeine for infective gastroenteritis	1 (0.41)
27. PPI for PUD at full therapeutic dose >8 weeks	22 (9.16)
28. Anticholinergic, antispasmodics with constipation	1 (0.41)
Respiratory System	
29. Systemic vs. inhaled corticosteroids for moderate-severe COPD	3 (1.25)

Table 8 cont'd.

Musculoskeletal System	
30. NSAIDs with history of PUD or GI bleeding	2 (0.83)
31. NSAIDs with moderate to severe HTN (>160/100)	2 (0.83)
32. NSAIDs with heart failure	7 (2.91)
33. NSAIDs long term for mild joint pain in OA	6 (2.5)
34. NSAIDs with warfarin	1 (0.41)
35. NSAIDs with chronic renal failure	2 (0.83)
36. Long term corticosteroids (>3mo) as monotherapy for RA, OA	2 (0.83)
37. Long term NSAID or colchicine for gout (if allopurinol okay)	9 (3.75)
Endocrine system	
38. Beta blockers in DM and frequent hypoglycemic episodes	1 (0.41)
39. Oestrogens without progestogen in patient with intact uterus	2 (0.83)
Urogenital System	
40. Bladder antimuscarinics with dementia	1 (0.41)
41. Antimuscarinic with constipation	5 (2.08)
42. Antimuscarinic with prostatism	2 (0.83)
43. Alpha blockers in males with frequent incontinence	7 (2.91)
Drugs that adversely affect those prone to falls (≥ 1 fall/3mo)	
44. Benzodiazepines	11 (4.58)
45. Neuroleptics	6 (2.5)
46. 1st generation antihistamines	5 (2.08)
47. Vasodilators causing hypotension with postural hypotension	2 (0.83)
48. Long-term opiates with recurrent falls	7 (2.91)
Analgesics	
49. Long-term powerful opiates first line for mild to moderate pain	1 (0.41)
50. Regular opiates > 2 weeks with constipation and no laxative	3 (1.25)
51. Long-term opiates with dementia unless for palliative care	1 (0.41)
52.Duplicate Drug Class	
Two concurrent benzodiazepine drugs	5* (2.08)
Two concurrent NSAID	1 (0.41)
Two concurrent antipsychotic drugs	2 (0.83)
Two concurrent opioid drugs	9 (3.75)
Two concurrent regular use of anticholinergic inhalers	1 (0.41)
Two concurrent regular use of corticosteroids inhalers	1 (0.41)
Two concurrent PPI drugs	1 (0.41)
Two concurrent thiazide diuretic drugs	1 (0.41)
Two concurrent regular long acting beta blocker inhaler	1 (0.41)
Two concurrent CCB	1 (0.41)
Two concurrent antihistamine drugs	2 (0.83)
Total	**240 (100)**

*One triple. AChIs; Acetylcholinesterase inhibitors, CCB; calcium channel blocker, COPD; chronic obstructive pulmonary disease, GI; gastrointestinal, H2 R; histamine H2 receptor, HTN; hypertension, OA; osteoarthritis, PPI; proton-pump inhibitors , PUD peptic ulcer disease, NSAIDs; nonsteroidal anti-inflammatory drugs, RA; rheumatoid arthritis, SSRI; selective serotonin reuptake inhibitors, SNRI; serotonin and norepinephrine reuptake inhibitors, TCA; tricyclic antidepressant.

However, the number of identified PIMs increased to 330 medications used among 130 patients (18 + 7 + 105 = 130) when the medications were screened by both criteria (See Table 9). This number (330 PIMs) indicates the total number of PIMs but included the overlap number of PIMs on which both criteria agreed. Once these duplications were eliminated, the combined criteria yielded 112 medications (see Table 11) that were used by 85 patients (see diagram below). Those PIMs are detected by common reasons between two criteria. Even though there are a few differences between the criteria, in this case they agree that particular medications should be considered PIMs. The exact differences and similarities are elucidated extensively in the discussion section.

Table 9. Cross tabulation of patients identified using Beers' and STOPP criteria

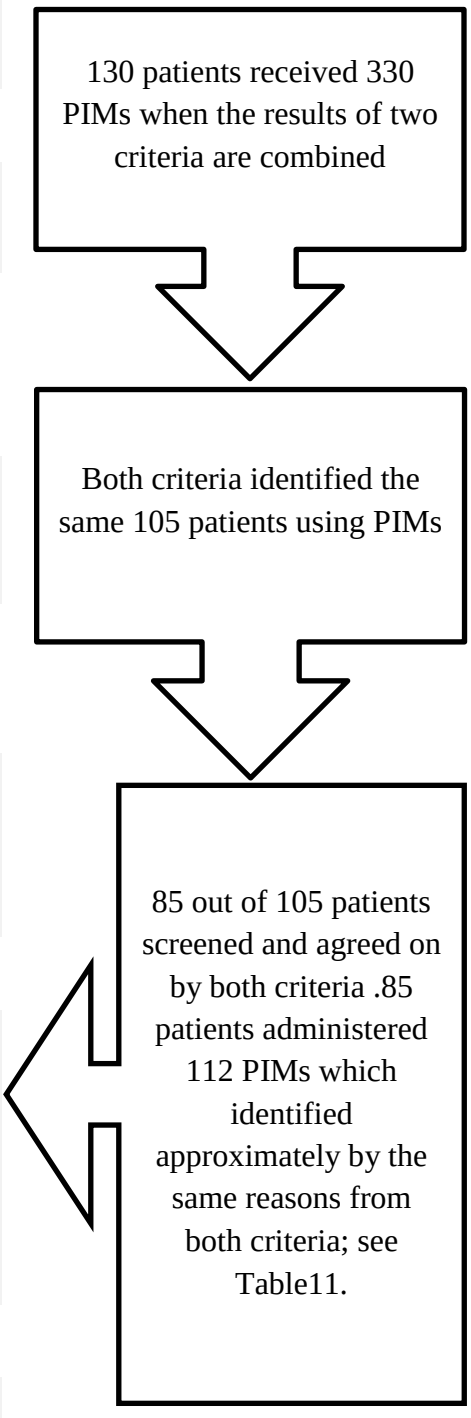
		STOPP Criteria		
		No	**Yes**	**Total**
Beers' Criteria	**No**	48	18	66
	Yes	7	105	112
	Total	55	123	178

Yes: number of patients taking PIMs
No: number of patients not taking PIMs

Table 10. Common rationalizations between the two criteria

Therapeutic categories identified by both criteria	No. PIMs	Total
Nondihydropyridine CCB		10
With constipation	5	
With heart failure	5	
Antispasmodics		1
With constipation	1	
Antimuscarinics		5
With constipation	4	
With cognitive decline/dementia	1	
NSAID		21
With history of PUD or GI bleeding	11	
With heart failure	7	
With chronic renal failure	2	
Warfarin + long term use for OA	1	
Antihistamines		17
Long term use	5	
With falls and fractures	5	
With dementia or cognitive impairment	7	
Benzodiazepines		18
With long acting and long term use	8	
With falls	9	
With dementia	1	
Antipsychotic drugs		21
Falls and fractures	5	
As hypnotics drugs	10	
Parkinson's disease	2	
Dementia	4	
SSRI's		8
With falls or fractures and low Na level	8	
Tricyclic Antidepressants		10
With dementia/syncope	1	
With cardiac conduction abnormalities	2	
With constipation	2	
With glaucoma	1	
With history of falls	2	
With CCB or opiates	1	
With prostatism or urinary retention	1	
Digoxin > 0.125 mg with impaired renal function	1	1
Total	**112**	**112**

CCB; calcium channel blocker, GI; gastrointestinal, PUD; peptic ulcer disease, OA; osteoarthritis, SSRI; selective serotonin reuptake inhibitor



4.3.3. PIM classification: most frequent PIMs

There is disagreement between two criteria in determining the rank of frequent medication classes. The most frequently-used medication in both tools is represented by numbers and percentages that are calculated by the total number of potentially inappropriate therapeutic drug classes divided by the total number of PIMs detected by each tool. As depicted in two pie charts (Figures 7 and 8), Beer's criteria detected benzodiazepines (43) as a frequently prescribed inappropriate medications, followed by anticholinergics (33), NSAIDs (26), antipsychotics (21), antihypertensive/antiarrhythmic (21), selective serotonin reuptake inhibitors (SSRIs) (17), antidiabetics (11), TCAs (10), anticonvulsants (7), and antiemetics (6).

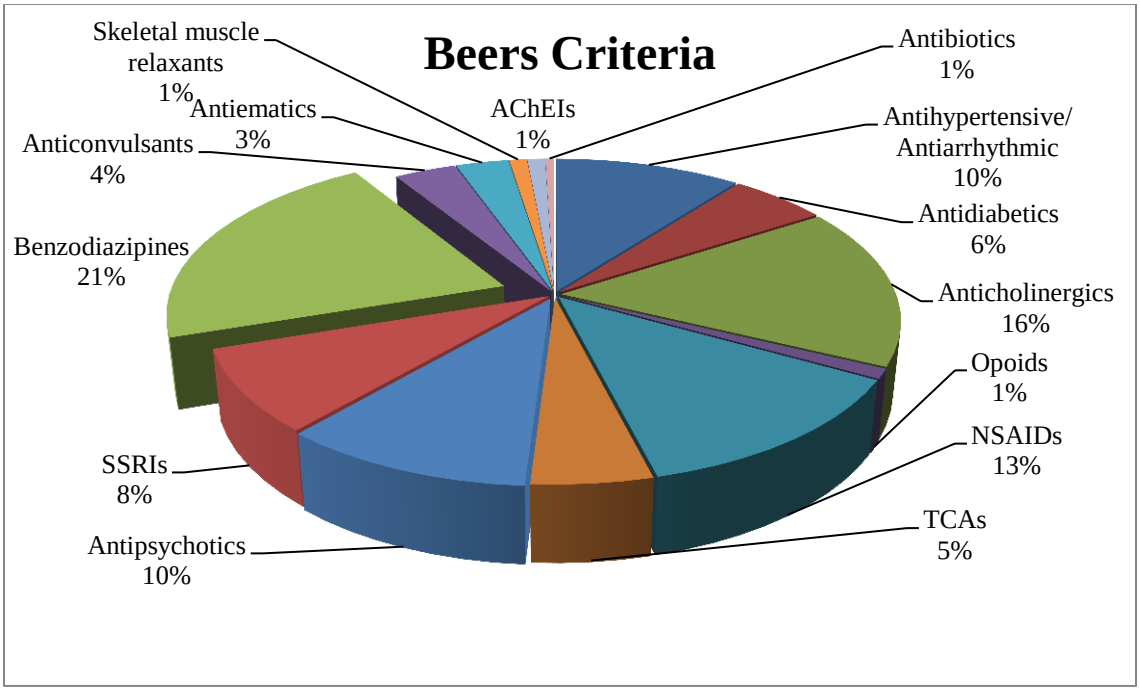


Figure 7. Frequency of classes of PIMs identified by Beers' criteria

On the other hand, STOPP criteria show a different arrangement and classification than Beers' criteria. Inappropriate antihypertensive/antiarrhythmic drugs (38) were found to be most commonly prescribed, followed by NSAIDs (30), anticholinergics (29), PPIs (23) and antipsychotics (23), opioids (21) and benzodiazepine (21), SSRIs (14), antiplatelets/ anticoagulants (12), TCAs (10), anti-gout (7), corticosteroids (6), and antidiarrheal drugs (4).

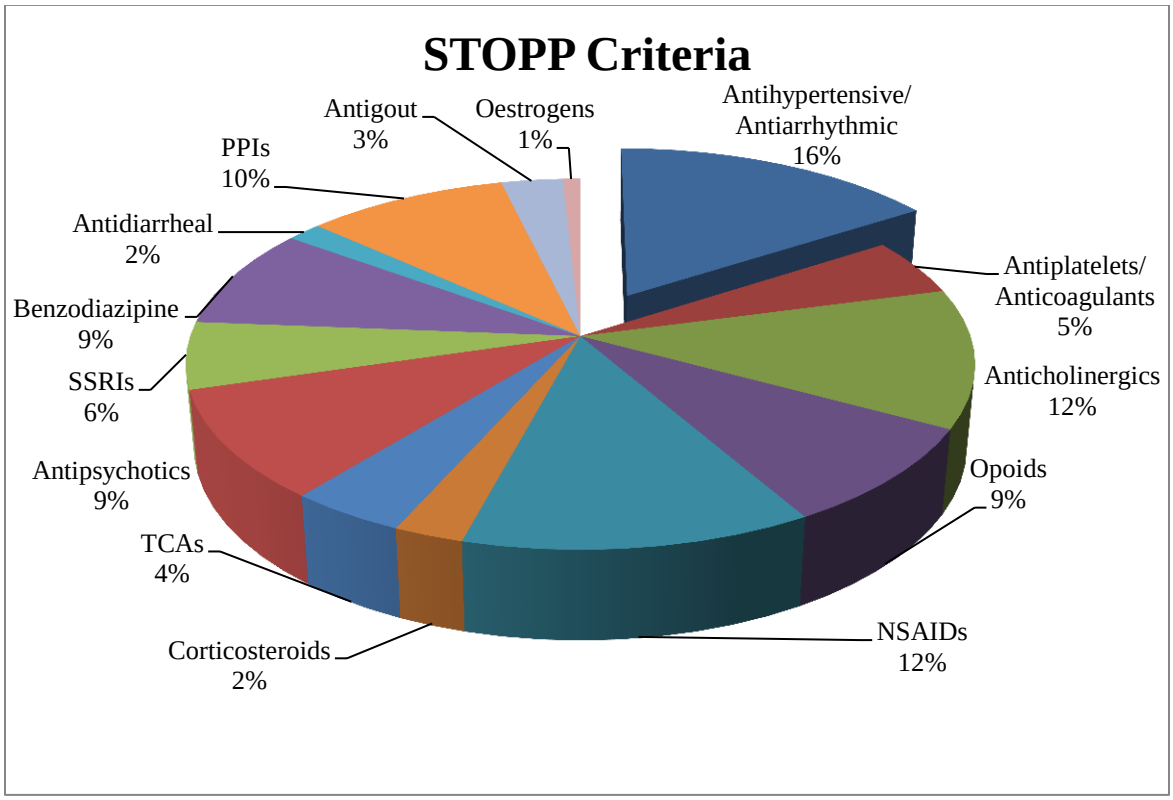


Figure 8. Frequency of classes of PIMs identified by STOPP criteria

4.4 Factors Associated with PIMs Use

4.4.1 Logistic regression

Regression models are beneficial to explore the relationship between a dependent or response variable and one or multiple independent or predicator variables of interests (Forthofer et al., 2007). In this study, three regression models were built to analyze the associations between the PIMs screening tools and multiple independent variables, including gender, age, type and number of illnesses, and number of medications used. These explanatory predictors were tested with the dependent variables, which are Beers' criteria, STOPP criteria, and both sets of criteria used together. Binary logistic regression was selected because the dependent variables' outcomes or responses are dichotomous. Logistic regression uses either 0 or 1 to code dependent variables. Here, "1" means that the patients use PIMs, while "0" means they do not (Dobson & Barnett, 2008). Thus, binary logistic regression can predict the relationship between the use of PIMs based on different criteria used and the different expected independent variables. This relationship can be interpreted in term of odds ratios and its significance can be tested using Wald- tests.

4.4.2 Interpretation of the results from the three models

Two of the five independent variables—the number of medications and illnesses—are grouped into four classes based on their quartiles. The quartile calculation depends on the percentiles of the data distribution, with the first quartile being the 25^{th} percentile or less, the second being the 25^{th}–50^{th} percentile, the third quartile being the 50^{th}–75^{th} percentile, and the last comprising the $>75^{th}$ percentile). However, the number of medications was not solely divided into quartiles; it was also divided based on the definition of polypharmacy (Bushardt et al., 2008). The first

quartile was originally 0–7 medications, but it was changed to 0–4 in order to include only those who used few medications (see Table 11 for illustrations of complete classes for each categorical variable)**.** Moreover, histograms were built for the categorical variables in order to confirm that the variables' distributions were equally divided into four groups (see Appendix F). The interpretation is based on Table 11, which summarizes the three logistic regression model outputs. The odds ratios, confidence intervals (95%), and statistical significance Wald-tests associated with each of the explanatory variables are reported in Table 11.

Table 11. Binary logistic regression outputs for each model

	Beers' criteria			**STOPP Criteria**			**Combined criteria**		
	OR	**95% CI**	**P value**	**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Gender[1] Male	1.226	0.508-2.959	0.650	1.140	0.470-2.765	0.772	1.508	0.612-3.719	0.372
Age[2]									
65-69	15.306	2.448-95.713	0.004**	8.395	1.387-50.828	0.021**	5.674	0.953-33.771	0.056*
70-74	16.638	2.894-95.648	0.002**	8.881	1.566-50.365	0.014**	5.952	1.079-32.833	0.041**
75-79	14.744	2.677-81.211	0.002**	5.662	1.070-29.960	0.041**	4.438	0.864-22.807	0.074*
80-84	5.124	1.052-24.963	0.043**	3.071	0.633-14.909	0.164	2.059	0.451-9.387	0.351
85-89	7.331	1.489-36.084	0.014**	3.352	0.706-15.920	0.128	2.352	0.528-10.477	0.262
Overall			**0.028****			**0.177**			**0.308**
Disease Cardiovascular	1.175	0.282-4.898	0.825	0.987	0.241-4.036	0.985	1.037	0.241-4.455	0.961
Neurological	2.552	0.926-7.034	0.070*	3.016	1.019-8.928	0.046**	2.804	0.905-8.690	0.074*
Gastrointestinal	0.502	0.189-1.334	0.167	0.785	0.287-2.152	0.638	0.998	0.361-2.758	0.997
Respiratory	1.741	0.657-4.610	0.264	2.451	0.816-7.360	0.110	2.022	0.667-6.127	0.213
Musculoskeletal	1.044	0.417-2.616	0.927	2.079	0.781-5.530	0.143	2.375	0.888-6.352	0.085*
Urogenital	5.180	1.234-21.740	0.025**	16.554	2.561-107.01	0.003**	9.712	1.550-60.870	0.015**
Kidney	1.579	0.338-7.383	0.561	3.295	0.545-19.931	0.194	1.660	0.302-9.119	0.560
Endocrine	1.069	0.440-2.593	0.883	0.841	0.330-2.142	0.717	0.908	0.352-2.344	0.842

Cancer and immune	1.753	0.620-4.960	0.290	0.574	0.207-1.588	0.285	0.929	0.325-2.657	0.890
No. illnesses[3]									
4-5	0.587	0.166-2.075	0.408	1.111	0.319-3.868	0.868	0.859	0.241-3.063	0.814
6-8	0.628	0.156-2.524	0.512	0.738	0.172-3.174	0.683	0.708	0.167-3.002	0.640
≥9	0.447	0.074-2.682	0.378	0.269	0.037-1.931	0.192	0.321	0.047-2.196	0.247
Overall			**0.812**			**0.426**			**0.649**
No. of drugs[4]									
5-9	3.382	0.952-12.006	0.059*	2.060	0.634-6.691	0.229	3.007	0.922-9.807	0.068*
10-13	5.493	1.423-21.195	0.013**	2.412	0.700-8.309	0.163	3.899	1.120-13.571	0.032**
≥ 14	52.384	9.535-287.785	0.00***	21.722	3.939-119.788	0.00***	20.728	3.907-109.96	0.00***
Overall			**0.00*****			**0.005****			**0.005****

Footnotes for Table 11

[1] Female is selected as reference

[2] 90 and over is selected as reference

[3] (0-4 medications) is selected as reference

[4] (0-3 illness) is selected as reference

*P (0.05-0.10): marginally significant

**P < 0.05: statistically significant

***P < 0.001: statistically highly significant

4.4.2.1 Interpretation of predictor: gender. The three logistic models corresponding to Beers' criteria, STOPP criteria, and combined both sets of criteria respectively provide no evidence of associations between gender and occurrences of PIMs, when controlling for other variables.

4.4.2.2 Interpretation of predictor: age. Overall, when Beers' criteria is used, there is a statistically significant, association between age and PIMs use (P=0.028), when the other independent variables are controlled. Specifically, all sub age groups under 90 have significantly higher risks of PIMs than the 90 years and older age group. The highest odds ratio was seen in patients aged 70–74 years, who had odds of taking PIMs about 16 times higher than the patients aged 90 and over. This significant and strong association is also obvious with patients aged 65–69 and 75–79. These groups had odds of using PIMs approximately 15 times higher than patients aged 90 and older. Similarly, the odds of using PIMs was significantly higher among patients

aged 80–84 and 85–88, compared with patients over 90, although not as strongly as the previous ranges of ages.

Under the STOPP criteria, age is overall not associated with the occurrence of PIMs when holding other variables constant. The results are insignificant for the prediction of PIM usage by age. However, variations among different age groups exist. For example, patients aged 65–69, 70–74, and 75–79 have significantly higher risks of taking PIMs than patients aged 90 and above, but no difference was found between aged 80–89 or over 90.

When combined, both sets of criteria provide relatively similar results as the STOPP criteria alone. When all other variables are controlled, age is insignificant and does not seem to be associated with PIMs use. An internal comparison between age ranges only shows significantly higher PIM usage for participants aged 70–74, compared with participants aged 90 and older. However, the 65-69 and 75-79 age groups are marginally significant and are insignificant at all compared with the reference groups.

4.4.2.3 Interpretation of predictor: type and number of illnesses. Diverse diseases were included in the three models to discover any associations with PIMs use when other independent variables are controlled for. Cardiovascular disease is a highly insignificant predictor of PIMs, irrespective of the criteria applied. Likewise, endocrine, gastrointestinal, immune system diseases and cancer do not predict use of PIMs. The associations between respiratory disease or kidney disease and taking PIMs are weak and insignificant, regardless of the criteria used. However, while musculoskeletal disease was not associated with the occurrence of PIMs when either the Beers' or STOPP criteria were used, it approached significance and was positively

associated with PIMs when both criteria were applied simultaneously (OR: 2.375, CI: 0.888–6.352, $p = 0.085$*).

Neurological and urogenital diseases are significantly associated with the likelihood of PIM use. Based on the STOPP criteria, the odds of taking PIMs for patients with urogenital diseases is 16.5 times higher than for patients without this disease; this finding is statistically significant when the remaining diseases and other independent variables are controlled for. Under the Beers' criteria or combined criteria, the odds of taking PIMs for patients with urogenital illness are about 5.9 times than the one for patients without the disease, which is lower than the result under STOPP criteria but it is still significant. On the other hand, the odds of taking PIMs for patients with neurological diseases are about three times the odds of those without the disease, as detected by the STOPP criteria. When the Beers' criteria or the combined criteria were used to determine the occurrence of PIMs, a predictable association between neurological disease and PIMs use still existed but with marginal significance.

Whether both sets of criteria were applied separately or concurrently, there was no predictable association between the PIMs used and number of illnesses when the other independent variables were controlled for. Regardless of the type of criteria used, when the different subclasses of number of illnesses were compared with the baseline subclass, the association was not present; demonstrating that unlike the type of illness, the number of illnesses does not predict PIMs. However, number of illnesses and number of medications can be highly correlated; hence only one of these two factors may show significance when both are included in a regression model.

4.4.2.4 Interpretation of predictor: number of medications. Overall, when controlling for other variables, the number of medications is significantly associated with PIMs regardless of the criteria used. Patients who consumed 5 or more drugs were already on multiple medications; they were further classified into the following sub-categories:

0–4 Minimal number of medications used (reference subgroup)

5–9 Low number of medications used

10–13 Moderate number of medications used

≥ 14 High number of medications used

When Beers' criteria and combined criteria were used to determine the occurrence of PIMs, patients who used a low number of medications (5–9) had roughly 3 times the odds of taking PIMs, compared to patients with minimal medications (0-4), when holding other variables constant, but the power of this association was marginally significant. This association became insignificant when STOPP criteria were used to determine the occurrence of PIMs. When using the STOPP criteria, no difference in the number of PIMs taken was found between patients with less than 5 medications and patients with a low (5-9) or moderate (10-13) number of medications. On the other hand, when Beers' and the combined criteria were used, patients who received 10–13 medications had significantly higher risks of PIMs than patients with minimal medication use (0-4). More specifically, under the Beers' criteria, patients who received 10–13 medications had about 5.5 times the odds of taking PIMs compared to patient receiving ≤4 medications (P=0.013). Furthermore, when PIMs were determined by both sets of criteria, the odds of taking PIMs for patients consuming 10–13 medications were approximately four times that of patients who took ≤4 medications (P=0.032).

Remarkably strong predictors of PIMs were observed in patients who consumed ≥14 medications, compared to patients who received ≤ 4 medications when other variables were controlled for, regardless of the criteria used. Under Beer's criteria model, the odds of taking PIMs for patients who consumed high numbers of medications (≥14) were about 52 times the odds of patients who used minimal medication (≤4 medications). Based on the STOPP criteria, patients who used ≥14 medications had roughly 22 times the odds taking PIMs of those who took minimal medication. Finally, when both sets of criteria were used, patients who took high numbers of medications had approximately 21 times the odds taking PIMs than those who consumed minimal medications. Indeed, consuming ≥14 medications leads to the highest odds of taking PIMs among all of the independent variables.

4.4.3. Diagnostic tests for three models

When analysis is performed using SPSS, the outputs include results and accuracy measurements of the model. In addition, the output is provided in two blocks, as discussed below. The logistic regression model was fitted by including all selected independent variables in the model at a single step without removing insignificant variables.

4.4.3.1 Overall test of the significance of the fitted model. Comparing the three fitted logistic models including all the independent variables with the logistic model with only an intercept, the fitted models demonstrated more statistically significant improvement than the constant models (Beer's criteria chi square = 72.090, df = 21, P <0.000), (STOPP criteria chi-square = 65.489, df = 21, P <0.000), (Combined criteria chi-square = 56.565, df = 21, P <0.000).

4.4.3.2 Model summary table From the model summary table, the Nagelkerke R square reflects the percentage of the variation in the response that can be explained by all included predictor

variables. It equals 45.5% and 43.4% when using Beers' criteria and STOPP criteria respectively, while in the model of combined criteria, it is 39.5%.

4.4.3.3 Deviance residual and residual plots Residual means that the observed and predicted probabilities were compared for all possible covariate patterns in order to check the model adequacy. One of the residual tests used to examine the fitting of model is deviance residuals (Forthofer et al., 2007; Dobson & Barnett, 2008). This test is applied with a p-value to indicate the goodness of the fit of the model to the data. A small p- value indicates that the predicted probabilities diverge from the observed probabilities, so the fitted logistic regression model does not adequately predict the observed outcomes. Thus, the larger the p-value leads to the conclusion that the model fits the data well.

From Table 12, the p- value is greater than 0.05, so we accept the null hypothesis that three logistic regression models fit the data well. The deviance residuals are plotted by participants for the three logistic regression models (Forthofer et al., 2007; Dobson & Barnett, 2008). The residuals are overall very small and randomly scattered between -2 and 2, which again support the fitted logistic regression models. (Figures 9, 10, and 11)

Table 12. Deviance residual test (deviance testing using t-test)

	N	Mean	Std. Deviation	Std. Error Mean
Beers Criteria Model				
Deviance value	178	.0485208	.95736032	.07175719
STOPP Criteria Model				
Deviance value	178	.0675237	.93219470	.06987095
Combined Criteria Model				
Deviance value	178	.0899696	.91908605	.06888841

	Test Value = 0					
	t	df	2-tail significance	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Beers Criteria						
Deviance value	.676	177	.500	.04852084	-.0930889	.1901306
STOPP Criteria						
Deviance value	.966	177	.335	.06752374	-.0703636	.2054111
Combined Criteria						
Deviance value	1.306	177	.193	.08996963	-.0459787	.2259180

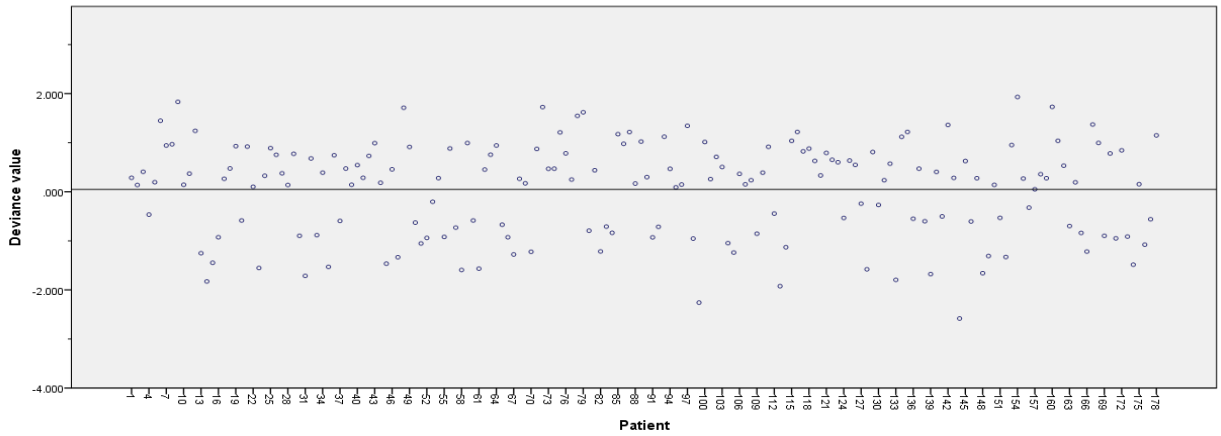


Figure 9. Residual plot for Beers' criteria model

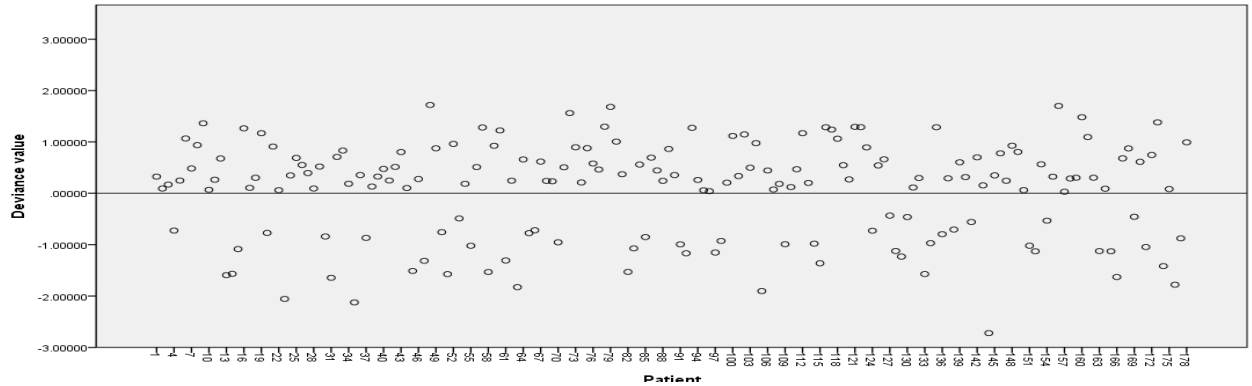


Figure 10. Residual plot for STOPP criteria model

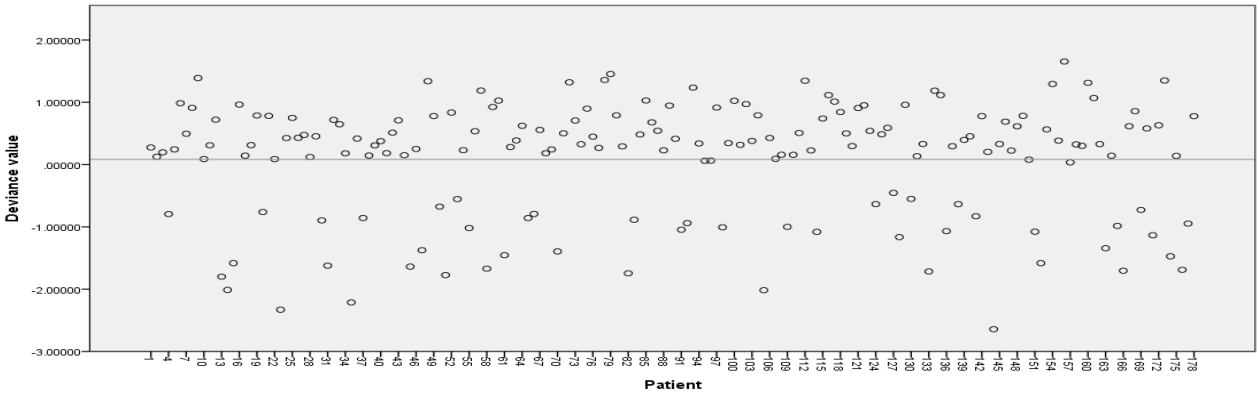


Figure 11. Residual plot for combined sets of criteria model

Chapter 5: Discussion & Conclusion

5.1 Prevalence of PIMs When Using Two Criteria Independently

From among the 178 rural elderly patients enrolled in this study, over 60% used at least one PIM regardless of the criteria applied. The prevalence of PIMs truly depends on the criteria used; the percentage of PIMs among older adults based on STOPP (69%) is higher than PIMs identified by the Beers' criteria (63%).

As presented in the literature review, most previous studies used the old version of Beers' criteria (2003) in comparison studies with STOPP criteria, with the result that STOPP criteria identified more PIMs than did Beers' criteria when used in different healthcare settings (Gallagher & O'Mahony, 2008; Ubeda et al., 2012; Byrne et al., 2011; Gallagher et al., 2011). Other non-European studies showed the opposite, finding that Beers' criteria detected more PIMs than STOPP (Vishwas et al., 2012; Chen et al., 2012). Despite applying the same criteria, the conflict between the results exists due to differences in drug formularies and healthcare settings. Aside from this variance, these studies cannot be compared with the present study because of the differences between the previous and updated versions of Beers' criteria. These modifications to the latest version released in 2012 identify more patients with PIMs than did the 2003 version (Undela et al., 2014). The restructuring and modification of Beers' criteria by adding new therapeutic drugs and removing other medications is based on clinical evidence and availability on the market (Campanelli, 2012).

Three current studies, with slightly different objectives, but comparing PIMs criteria identified using STOPP and the 2012 version of Beers' criteria were located. Two of these studies reported that patients taking PIMs are more readily detected by STOPP than by Beers' criteria, even though they were applied in diverse areas and settings. The first study was carried out in Ireland

at 14 long-term care facilities where 732 older adults' medication profiles were screened and reviewed to detect PIMs. The study showed that the predominance of PIMS was higher using STOPP (63.7%) than Beers' (42%) criteria (O'Sullivan et al., 2013). An Australian study evaluated the medication profiles of 570 ambulatory patients using three criteria, of which two match our criteria. In this study, STOPP was used to detect 1,032 PIMs used by 79% of the patients, while Beers' criteria identified 399 PIMs used by 48% of the patients (Curtain et al., 2013). In contrast, Italian research provided a disagreement with the previous two studies when the two sets of criteria were applied separately. Beers' criteria detected more PIMs (58.4%) than STOPP (50.4%) criteria (Tosato et al., 2014). However, the remarkable idea here is that even though these criteria were originally established in different areas; Beers' criteria in North America and STOPP in Europe, the results stand out as being opposite to what has been expected. It has been mentioned that these criteria detect more PIMs in the area where they were originally established, due to local medication usage. This was first noted in an Irish long-term study that posited that more PIMs were detected by STOPP criteria than by Beers' criteria due to the fact that STOPP was established based on an Irish setting (O'Sullivan et al., 2013). This general perspective is not absolutely true, especially after the updating of Beers, criteria, which was previously considered as the main reason for differences in applicability. In the context of this study's findings, the results of these articles raise important questions about the differences in detection of PIMs. Are the features of each tool and/or external inferences related to prescribers or health care settings that create disagreements about the performances of these criteria? This is discussed extensively below after elucidating the differences between the tools and the evaluations of the prevalence of PIMs among rural elders.

5.2 Prevalence of PIMs When Applying Two Criteria Concurrently

The prevalence of patients using at least one PIM exceeded 70% when both criteria were applied concurrently in the same setting. When STOPP and Beers' criteria were used together on the same population and setting, they detected 330 prescribed PIMs among 130 patients (73%); demonstrating that the sensitivity of detecting PIMs is increased by using these tools together. This finding was confirmed by only one recently published study (CRIteria to Assess Appropriate Medication Use among Elderly Complex Patients (CRIME)), where using both criteria led to the identification of 75% of the population as using PIMs, which approximates the present results (Tosato et al., 2014)

The detection of the proportion of a study population using PIMs is directly amplified when both criteria are used concurrently, compared with using each criteria individually. Since using both criteria together eliminates any differences between or shortcomings within the criteria, the subsequent detection of prevalence increases. According to epidemiological theory, this indicates that the net sensitivity is increased, while the net specificity is decreased, when compared to using each set criteria separately. In most health care settings, several tests are done concurrently upon admission to ensure correct test results for the patient. Using both criteria simultaneously increases the probability that a patient will have a positive result since a positive result can be found using either one or both of the criteria. Furthermore, the test result is considered negative when all tests provide negative results (Gordis, 2009). It is very important to apply both criteria concurrently when detecting PIMs on each individual since there are some differences between the criteria. This method will help decision-makers to note any medications that could be considered as PIMs, so that their decisions will be based on full knowledge about potential PIMs, regardless of differences between criteria used to detect them.

5.3 Rural Study Populations

The study population was comprised of acutely ill patients aged 65 years and older with a history of chronic diseases who presented to the in-patient departments of four hospitals. More than half of all patients had six or more chronic diseases, irrespective of gender. Generally, the most prevalent disease was cardiovascular disease and the main co-morbidity was hypertension (HTN), affecting approximately 70% of the patients. Most patients had other heart conditions or complications such as coronary artery disease (22.47%), arrhythmia (26.4%), history of stroke, and/or heart failure. Their history of chronic disease included endocrine disturbances largely due to the high prevalence of diabetes mellitus. Approximately comparable percentages of skeletal, muscle, and gastrointestinal (GI) diseases such as gastroesophageal reflux, arthritis, and/or osteoporosis were found. Similarly, neurological disorders and respiratory disease were distributed among this population. The majority of chronic neurologic diseases were mood disorders, including depression and anxiety, followed by dementia, and cognitive disorders. Chronic obstructive pulmonary disease (COPD) was the most common respiratory illness among the study population. It was noted that the distribution proportions of cancer and autoimmune diseases are roughly equal to the proportion of urogenital disorders, such as benign prostatic hyperplasia (BPH), urinary incontinence, and frequent urinary tract infections. While other diseases exist, they were not numerically comparable with the above-mentioned conditions.

A major factor leading to the risk of taking a PIM is the use of multiple medications. The participants in this study tended to take more than 10 medications, and this number rose to 27 in one case. As a result, polypharmacy is a significant problem that creates subsequent issues, for instance, drug-drug interactions or contraindications. There were many patients admitted with one of the categories of drug interaction which increased the toxicity of some medications (based

on Lexicomp, a compilation of clinical drug information to promote medication safety). For example, a patient who used tiotropium and ipratropium inhalers together, suffered from urinary retention, constipation, tachycardia, and dry mouth due to additive anticholinergic effects. Tiotropium was also prescribed with hydroxyzine, cetirizine, prochlorperazine, solifenacin, or haloperidol that also increased the risk of anticholinergic effects. Furthermore, it is important to mention that duplication of medications from the same therapeutic categories was taken, such as patients using concurrently three types of diuretics or antipsychotic drugs.

It is necessary to see admitting participants from different perspectives. The implication of geographic residency differences in terms of rural older people's health status is a very essential health concern. This study revealed the wide use of PIMs among rural people recently admitted to hospitals. This reflects and provides an overview image about medication management among older adults in rural areas and not specifically about those inside hospitals or discharged patients. Prescribing excess medications results in consequences of increased ADEs and unnecessary polypharmacy, which reduce patients' quality of life and the quality of healthcare.

5.4 Comparisons between Rural and Urban Data in the Literature

The prevalence of PIMs has been investigated in some regions in Canada. Some of the published studies reported different proportions of PIMs; for example, in 1995–1996, a study reported that 54.7% of 2,633 patients who live in 71 long-term care facilities in Quebec City were taking PIMs (Rancourt et al., 2004). A large retrospective study done in Ontario compared the prevalence of PIMs prescribed to community-dwelling and nursing home residents in 2001. It found that medications that should be always avoided or that are rarely appropriate were prescribed more often and were more prevalent in the community (3.31%) than in nursing homes (2.26%). The reason for the increased percentage of inappropriate medications prescribed in

community-dwellers was attributed to the medication review programs decreed in Ontario nursing homes (Lane et al., 2004). A study conducted in primary care in southern Ontario, including rural and urban patients found that 16.3% of 777 patients had at least one PIM (Howard et al., 2004). However, it is difficult to compare those data with that of the present study, due to the differences in criteria and methods that were used. Most of those studies are outdated as well. Recently, the Canadian Institute for Health Information (CIHI) published a report including the general results of a survey of the medications used by seniors across Canada. This report used updated Beers' criteria to find that the rate of using at least one PIM among older adults across Canada ranged from 20.1% to 39.1% and the rate of PIM use in Ontario was 22.6% in 2012 (Canadian Institute for Health Information, 2014). Again, a comparison could not be made with those results since the measurement of prescribed PIMs was conducted by rate and the presented study measured the proportion of PIMs that were prescribed.

Even though different studies have been conducted in rural areas in the world, each rural setting is diverse for many reasons. These differences start with the country in which the study was conducted and extend to other aspects; for example, the quality of healthcare, lifestyles, facilities, infrastructure, and access to healthcare, among others. Also, when attempting to use those studies for comparison, the studies' designs must be considered and analyzed, including such factors as sample size, setting, patients' demographics, and other considerations. Regardless of these variables, analyzing studies in different parts of the world enables the finding of clues about the increase in PIMs, especially in rural areas. For instance, using the latest version of Beers' criteria in a Nigerian rural tertiary hospital, the prevalence of PIMs was found to be 25.5% with 66 PIMs in 56 patients (Fadare et al., 2013). This outcome was much lower than what was detected in this study, despite a roughly similar sample size (220 patients). However, it

is very important to note that 837 drugs were utilized in the Nigerian study with the patients using a mean of 4 medications. In our study, the mean was 10 medications; a huge difference in terms of polypharmacy. Similarly, in a rural community health center in Taiwan, the prevalence of PIMs was low (27.5%, 2003 version Beers' criteria) with patients using an average of 4 drugs (Lin et al., 2011). Although these studies cannot be compared as equivalents, they collectively demonstrate that when the number of drugs prescribed increases per patient, the possibility of being prescribed a PIM also increases.

In addition, factors other than polypharmacy might contribute to the number of PIMs taken within a population. These factors are not related to patients' conditions, but are external factors that might contribute to an increase in the number of prescribed PIMs; and they vary based on regional differences. For example, a study in 2007 confirmed a difference between outpatients in rural settings, who used significantly more PIMs than did their urban counterparts. In addition, there were variations in the prescribing quality among rural areas, due to the variations in the quality and access to healthcare services (Lund et al., 2013).

The literature concerning differences between rural and urban areas, in terms of external factors that lead to an increase in the prescribing of PIMs, especially in rural Ontario is sparse. A retrospective study done in 2002 reported that researchers in a small rural hospital recommended increased access to diagnostic examinations and enhanced management of heart failure in primary care settings. (Sanborn et al., 2005) Another study conducted in 2004 compared urban and rural settings, in terms of the prevalence of pain among patients in southeastern Ontario. While there was a high prevalence of pain in both urban and rural areas, rural people used fewer healthcare services (Tripp et al., 2006). In addition, some studies evaluated the challenges and feelings of health care providers. One of these studies indicates that non-trained geriatric/family

physicians were more likely to prescribe multiple medications and PIMs than geriatric practitioners in a rural U.S. nursing home (Monroe et al., 2011), whereas another study of rural and urban family physicians in Ontario found that neither certification nor the amount of time elapsed since graduation were significantly associated with the prescribing of PIMs (Howard et al., 2004).

The literature was consistent, as all of these studies sought to demonstrate that rural areas demanded more attention and that probably some external factors related to PIMs' use existed only in rural and remote areas. As a result, some studies evaluated uncontrolled external factors that might contribute to the increase in the number of PIMs prescribed among rural older adults. This study has been designed in a manner to provide more perceptions about the magnitude of using PIMs among rural populations, not about the reasons why PIMs are prescribed or the occurrence of prescribed PIMs inside those four hospitals. However, these published articles that focus on rural areas provide some reasons to consider the differences between rural and urban areas. Further research was required in order to confirm if those external factors contributed to the increased number of PIMs used. Finally, it is very important to emphasize that this issue is not limited to rural areas, but is becoming a global concern.

5.5 Comparison Between Beers' and STOPP Criteria

5.5.1 Frequency of classes of PIMs identified by Beers' criteria

Our study's findings present the controversy of the types of frequent PIMs prescribed, according to the STOPP and Beers' criteria. After conducting our research, the PIMs were aggregated and categorized based on the therapeutic drug class for each set criteria, and ultimately 14 therapeutic categories were determined. However, the arrangement and types of

those classes are disputed due to the differences in the features of both Beers' and STOPP criteria. This is discussed in more detail.

First, benzodiazepine drugs represent the majority of PIMs prescribed, accounting for 21% of the total PIMs, based on Beers' criteria. Recently, the use of benzodiazepine as hypnotic drugs has increased, despite evidence in the literature that strongly recommends avoiding all types of benzodiazepines (from short- to long-acting ones) because older adults are more sensitive to them and take longer to metabolize them (see Appendix A for the full criteria under independent diagnosis). Benzodiazepines are also mentioned under the dependent diagnosis section (see Appendix A), where it is recommended to be avoided with dementia/cognitive impairment and delirium conditions, as well as in patients with a history of falls or fractures, according to Beers' criteria. In this study, it was observed that the following benzodiazepines were the most frequently prescribed: alprazolam, oxazepam, clonazepam, flurazepam, temazepam, diazepam, and chlordiazepoxide.

In the literature, benzodiazepines groups have been under scrutiny since the prescribing of these groups has increased and are being inappropriately used among the elderly. A 2003 study measured the prevalence of PIMs using different assessments and found short-acting benzodiazepine prescriptions are the most frequent PIMs in the long-term-care community in southern Ontario, Canada (Howard et al., 2004). A retrospective study done with elders in Quebec found that 44% of the elderly who received a benzodiazepine prescription had previously had at least one inappropriate benzodiazepine prescription. As a result, older adults are vulnerable to hospitalization or visiting emergency or ambulatory care and are at an increased risk of benzodiazepine interactions with other medications compared with patients who had appropriate benzodiazepine prescriptions. Inappropriate use of benzodiazepine leads to

significantly increased health costs per patient, which are estimated to be $3,076 per year compared with patient taking appropriately prescribed benzodiazepine (Dionne et al., 2013). This result was based on previous study data showing that nearly half of community-dwelling adults who used benzodiazepine used it inappropriately, and 23% of them had a second benzodiazepine prescription or another drug that interacted adversely with benzodiazepines. Also, it was found that the patient aged 75 and older were a higher risk of use benzodiazepines for long term than patients aged between 65 and 74 (Préville et al., 2011). Even after Beers criteria was updated and tremendous research efforts was conducted on benzodiazepines, benzodiazepines are still the most frequently prescribed PIMs.

The second most common PIMs are anticholinergic drugs, which consist of antihistamines, antispasmodic, antimuscarinics, and anticholinergic inhalers, which collectively comprise 16% of the PIMs identified in this study. Like benzodiazepine, these drugs are mentioned in different places in Beers' criteria under independent and dependent diagnoses including delirium and cognitive impairment in addition to chronic constipation, lower urinary tract symptoms and benign prostatic hyperplasia. The criteria provide a list of drugs with strongly anticholinergic properties that should be avoided with some conditions.

The third most common PIM category was NSAIDs, which account for 13% of the PIMs identified by Beers' criteria. These include diclofenac, indomethacin, ketorolac, ibuprofen, meloxicam, naproxen, and celecoxib. NSAIDs are found in two sections of Beers' criteria; in the dependent diagnosis section, NSAIDs are linked with heart failure, chronic renal disease, and history of gastric duodenal ulcer criteria.

Anti-depressant medications comprised thirteen percent of the PIMs identified by Beers' criteria, and they are divided into SSRIs (8%) and TCAs (5%) for study purposes. The main reason for this division is to enable a comparison when applying the two criteria. TCAs are found in all three sections of the Beers' criteria. They should be avoided with patients who have a history of falls and fractures and with patients suffering from orthostatic hypotension or delirium. In contrast, the avoidance of SSRIs is only mentioned in instances of falls and fractures. However, both should be used with caution because both enhance hyponatremia. Other drugs administered to this study population include escitalopram, citalopram, fluoxetine, paroxetine, and sertraline. Examples of frequently used TCAs are amitriptyline, nortriptyline, and imipramine.

Antipsychotic and antihypertensive/antiarrhythmic drugs each comprises ten percent of frequently prescribed PIMs, but they are mentioned in different places in Beers' criteria. Antipsychotics are not a good option for treating older adults, and Beers' criteria emphasize avoiding using these drugs, specifically mentioning them multiple times under two sections along with cognitive disorders, falls or fractures, and Parkinson's disease. Haloperidol, perphenazine, prochlorperazine, paliperidone, olanzapine, quetiapine, and risperidone are examples of PIMs. Antihypertensive/antiarrhythmic medications are listed under independent diagnoses such as antiarrhythmic drugs, digoxin, spironolactone, triamterene, and alpha blockers. Alpha blocker drugs should be avoided with syncope and urinary incontinence in women. Other antihypertensive/antiarrhythmic drugs such as non-dihydropyridine calcium channel blockers (CCBs) are listed with heart failure and chronic constipation. During the screening of the patients' medication profiles, amiodarone, sotalol, digoxin, spironolactone, alpha blockers, verapamil, and diltiazem were found.

The remaining groups such as anticonvulsant, anti-diabetic, and other drugs not comparable with STOPP criteria are categorized differently between the two criteria and are not frequently prescribed PIMs, so they will not discussed under frequently prescribed PIMs but under differences between criteria.

5.5.2 Frequency of classes of PIMs identified by STOPP criteria

Antihypertensive/antiarrhythmic drugs (16%) comprised nearly one-fifth of all PIMs identified by STOPP criteria, but are in fifth position in the Beers' criteria. Indeed, this is indicative of the differences in composition of the criteria, as will be discussed later in more detail. Briefly, STOPP includes extra criteria of therapeutic classes not found in Beers' criteria, such as diuretics and beta blockers, has duplication of treatment criteria that increases the number of PIMs for each group, as well as contributing to all following groups.

Importantly, both criteria agree that inappropriate anticholinergic or NSAIDs are prescribed most frequently. Using STOPP criteria, NSAIDs appear more often than anticholinergic drugs because STOPP recommends that it ought to be avoided in patients with severe hypertension, those taking warfarin, or for long duration use for gout or joint pain in osteoarthritis. Unlike in Beers' criteria, anticholinergic drugs are not mentioned often in STOPP, but do appear under important criteria that it should be avoided in patients prone to falls.

STOPP criteria present important drugs such as PPIs that are prescribed with equal frequency as antipsychotic drugs. The difference between the number of antipsychotic drugs identified by Beers' and STOPP criteria is because STOPP criteria counts duplications. Opioids composed 9% more of the identified PIMs by STOPP than Beers' criteria because STOPP criteria do not recommend using long-acting opioids as a first line treatment for non-severe pain. Long-term use

of opioids with a history of falls or complaints of dementia, or use of opioids with TCAs or by patients with chronic constipation without taking laxatives should be avoided.

In contrast, antidepressant drugs (SSRIs and TCAs) comprised 10% of all STOPP-identified PIMs, which is less than what was determined by Beers' criteria. This is because neither is considered as PIMs in patients prone to falls and fractures. However, the actual number of TCAs was not changed because STOPP criteria extensively includes TCAs with different conditions/drugs; for instance, avoid TCAs in patients with dementia, cardiac conduction abnormalities, prostatism, urinary retention, using opiates or CCBs, one or more of which is typically borne by most older adults. Therefore, omitting one important criterion (avoid use of TCAs in patients at risk of falls and fractures) does not affect the number of TCAs identified as PIMs as compared with those identified using Beers' criteria.

Antiplatelets/anticoagulants, anti-gout, and corticosteroids in the remaining groups are not comparable with Beers' criteria due to a difference in criteria. This is discussed comprehensively below. Overall, the frequency that medications are identified as PIMs depends on how many therapeutic drugs are emphasized and repeated under multiple criteria.

5.5.3 Number of criteria shared by Beers' and STOPP

Differences between the criteria should be analyzed in terms of detecting PIMs and identifying any disputes between them. It is fundamental to indicate the percentage of useful criteria of those assessments in this study setting. Firstly, 29 out of the total 53 Beers' criteria composed more than half of the criteria used (55%) when medications to be used with caution are counted. However, the percentage of Beers' criteria used to determine medications that should only be avoided if both independent and dependent diagnosis sections is reduced to 52%

(25/48 criteria). These criteria are identified 202 drugs used by 112 elderly patients. On the other hand, 80 % (52/65) of STOPP criteria were used to detect 240 drugs taken by 123 elderly patients. These differences in the number of criteria used result in a difference in the number of PIMs detected. Consequently, the prevalence of PIMs is extremely affected by these differences.

5.5.4 Differences in medications identified by Beers' and STOPP criteria

Despite the extensive updating of Beers' criteria, STOPP criteria still detect more PIMs. There are multiple explanations behind this discrepancy. First, there are various medications only listed in either Beers' or STOPP criteria. These differences are summarized in Table13 using the names of drugs that are found in one of these criteria only. For example, the most obvious difference is the PPI group, which is found under STOPP criteria but not in Beers' criteria. In this study population, PPIs such as rabeprazole, lansoprazole, pantoprazole, esomeprazole, and omeprazole were misused for a longer term and with higher daily dosage allowances.

The recent and notable changes to Beers' criteria make them more relevant today. These changes include a new list of medications such as thiazolidinediones, AChEIs, and non-benzodiazepines, and include newly marketed medications under medications prescribed with caution for the elderly based on recent clinical evidence, such as antithrombotics (dabigatran and prasugrel). Beers' criteria also include new conditions not discussed in STOPP criteria, such as delirium, syncope, and insomnia (Campanelli, 2012). In spite of these changes, Beers' criteria still fail to meet the standard set by STOPP due to infrequently used medications. For illustration, immediate release nifedipine is no longer used since it is less safe and effective than the extended release nifedipine. Another example is short-acting dipyridamole, which is always used in

Table 13. Medications listed by either Beers' Criteria or STOPP Criteria

Drugs that should be avoided with/without diagnosis	Beers' criteria	STOPP criteria
Antiparkinson agents	✓	
Antithrombotic: ticlopidine	✓	
Alpha agonists, central	✓	
Antiarrhythmic drugs	✓	
Disopyramide	✓	
Dronedarone	✓	
Nifedipine, immediate release	✓	
Spironolactone >25 mg/day	✓	
Clopidogrel with concurrent bleeding disorder		✓
Warfarin for first, uncomplicated deep venous thrombosis/pulmonary emboli		✓
Thiazide diuretic with a history of gout		✓
Loop diuretic for dependent ankle edema/first-line monotherapy for HTN		✓
Non-cardioselective beta-blocker with COPD		✓
Aspirin at dose>150mg/day- with no history of coronary, cerebral or peripheral arterial symptoms or occlusive arterial event- to treat dizziness not clearly attributable to cerebrovascular disease		✓
Aspirin >325 mg/ day	✓	
Beta blocker in combination with verapamil		✓
Antibiotic: nitrofurantoin	✓	
Thioridazine/ mesoridazine	✓	
Barbiturates	✓	
Chloral hydrate	✓	
Meprobamate	✓	
Non-benzodiazepine hypnotics	✓	
Ergot mesylates, isoxsuprine	✓	
Androgens	✓	
Desiccated thyroid	✓	
Growth hormone	✓	
Insulin, sliding scale	✓	
Megestrol	✓	
Sulfonylureas: glyburide	✓	
Glibenclamide with type 2 diabetes mellitus		✓
Beta blockers with diabetes mellitus and frequent hypoglycemic events		✓

Table 13. cont'd

Drugs that should be avoided with/without diagnosis	Beer's criteria	STOPP criteria
Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhea of unknown cause/ severe infective gastroenteritis		✓
PPI for peptic ulcer disease at full therapeutic dosage for>8 weeks		✓
Theophylline as monotherapy for COPD		✓
Colchicine for chronic treatment of gout if no contraindication to allopurinol		✓
Mineral oil, oral	✓	
Trimethobenzamide	✓	
Skeletal muscle relaxants	✓	
Heart failure with pioglitazone, rosiglitazone, and cilostazol	✓	
Syncope with AChEIs	✓	
Thioridazine with syncope, epilepsy, and delirium	✓	
Chlorpromazine with syncope, epilepsy, and delirium	✓	
Maprotiline, thiothixene, tramadol with epilepsy	✓	
Anticonvulsants with falls and fractures	✓	
Insomnia with oral decongestants, stimulants, theobromines	✓	
Chronic renal disease with triamterene	✓	
Duplicate drug classes		✓

AChEIs; Acetylcholinesterase inhibitor, COPD; chronic obstructive pulmonary disease, HTN; hypertension

combination with aspirin under the name of Aggrenox, but is no longer used alone. For a complete list of infrequent drugs, see the full list of Beers' criteria in Appendix A. Secondly, some criteria in the independent diagnosis section are repeated in the diagnosis section, although the new organization of Beers' criteria is better than the old and better than STOPP criteria.

5.5.5 Therapeutic categories listed by both criteria but for different reasons

It is also essential to emphasize that even though some therapeutic categories are documented in both criteria, they are mentioned under diverse clinical classifications. Regardless of independent diagnosis or similarities between criteria, there are differences found in the following groups of drugs with different diagnosis: TCAs, SSRIs, benzodiazepines, aspirin, corticosteroids, analgesic drugs (NSAIDs, and opioids). Firstly, TCAs have highly

anticholinergic effects and therefore should be avoided under the independent/dependent diagnosis of Beers' criteria. Beers' criteria stipulate that TCAs should be avoided in patients with a history of falls and fractures, delirium, and syncope, while STOPP criteria mentions cognitive deficiency, cardiac abnormalities, glaucoma, prostatism/history of urinary retention, and use with opiates/CCBs. Likewise, SSRIs are contraindicated in patients prone to falls/fractures in Beers' criteria and under caution when the patient has hyponatremia, while STOPP criteria require that it be avoided if the sodium level is less than 130 mmol/L. Thirdly, the benzodiazepine drugs identified by Beers' criteria include short acting and intermediate acting, and are linked with different diagnoses, such as dementia or delirium that are not recorded in STOPP criteria. Another example in Beers' criteria is that aspirin should be avoided if more than 325 mg/ day, and under caution with a patient aged 80 and over for primary prevention of cardiac events, whereas in STOPP, aspirin should be avoided at a dose of more than 150 mg/day and in patients with no history of coronary, cerebral, or peripheral arterial symptoms or occlusive arterial events.

Both criteria agree that the use of analgesic NSAIDs should be avoided in patients with heart failure, chronic renal disease, and history of GI ulcers. However, STOPP has additional criteria such as that NSAIDs should be avoided in patients taking warfarin, with moderate to severe hypertension, and for long-term use for gout and osteoarthritis. Opioids are other analgesics that are included in multiple STOPP criteria such as avoidance in patients with recurrent falls, dementia, and constipation, as well as use of long-acting opiates or use of opiates with TCAs, while Beers' criteria do not consider that opioids as a group should be regarded as PIMs. Only three of the analgesic narcotic medications are included in Beers' criteria; meperidine, pentazocine, and tramadol.

In STOPP, corticosteroid drugs are considered PIMs in two criteria; when used for long-term treatment for arthritis and when used systemically rather than inhaled in maintenance treatment of COPD, whereas in Beers' criteria, corticosteroids should be avoided only in patients with delirium. STOPP appears to be more specific with anticholinergic inhalers, which contraindicates only nebulized ipratropium in patients with glaucoma. In contrast, Beers' criteria stipulate that all anticholinergic inhalers should be avoided with BPH or lower urinary symptoms. Both criteria agree that oral antimuscarinic drugs have to be avoided in case of chronic constipation or dementia (Beers' criteria stipulate that anticholinergics should be avoided with delirium/dementia diagnosis) while STOPP has two more criteria for patients with chronic glaucoma/prostatism.

Even though both criteria indicate avoidance of metoclopramide in case of Parkinson's disease, Beers' criteria emphasizes this by mentioning metoclopramide in the independent diagnosis section. There are nearly similar criteria for both assessments regarding antipsychotics, but Beers' criteria have additional considerations, which emphasize awareness of those medications in patients with dementia/cognitive impairment. In spite of Beers' criteria mentioning anticholinergics more frequently than STOPP criteria, it misses an important criterion: anticholinergics should be avoided in patients at risk for falls/ fractures. STOPP includes the first generation of antihistamines, which are anticholinergic drugs, under that criterion. Another difference is in regard to alpha blocker drugs that STOPP criteria indicate should be avoided with urinary incontinence among males, Beers' criteria stipulate avoidance in females with urinary incontinence.

5.5.6 Other differences between criteria

Aside from these differences, STOPP criteria are superior to Beers' criteria in the last criterion, which is that any regular use of two concurrent medications of the same drug category should be avoided. Significant duplication of medication was observed during review of patient profiles. Therapeutic duplication has been documented and evaluated in multiple studies (Hajjar et al., 2007; Page et al., 2010). It might be that duplication of treatment is allowed and recommended based in practiced in North American countries compared to European countries. This criterion detected 25 duplicated medications considered to be PIMs. This is an important reason that enables STOPP criteria to detect more PIMs than Beers' criteria, resulting in the higher prevalence of PIMs when using STOPP criteria.

However, based on the medications prescribed with caution in Beers' criteria, three criteria used in the present study identified 53 drugs that should be prescribed with caution but not avoided. The criteria included a new anticoagulant drug that had been used by nearly 3% of the study population. This section includes anti-depressant drugs that were not found in other criteria, such as serotonin and norepinephrine reuptake inhibitors (SNRIs) and mirtazapine. However, there are some criteria that are already included under avoidance in the STOPP criteria that might increase the number of PIMs detected using STOPP, such as aspirin. Aspirin is recommended to be prescribed with caution to patients aged 80 and over. Also, if a patient takes SSRIs and has frequent drops in sodium levels, SSRIs should be avoided according to STOPP criteria. Therefore, STOPP criteria identify more PIMs because it includes some medications under avoidance while Beers' criteria list these medications under the cautionary section.

In the end, it is important to mention that STOPP criteria seem to be a more implicit tool than Beers' criteria because STOPP lists the general names of the pharmacological drug groups such

as antimuscarinic, CCBs, and opiates, while Beers' criteria lists the specific name of drugs such as darifenacin, verapamil, and meperidine of the same therapeutic group. Consequently, some medications cannot be considered as PIMs because this particular medication is not included in the drug formulary. For more illustration, non-benzodiazepine drugs have been mentioned as a PIM, but zopiclone is not listed under this group, while the other listed non-benzodiazepine drugs are marketed in the United States. It would be preferable to include zopiclone in Beers' criteria to be suitable for the Canadian drug market (Pharmacist's Letter/Prescriber's Letter, 2012).

5.6 Predicting Factors Associated with PIMs Use

Exploring the factors that might be associated with use of PIMs by the study population is another main aim of this research. Logistic regression models provide some positively predicted factors when PIMs were identified by Beers, STOPP, or both sets of criteria. There was no association between gender and the number or type of PIMs used, regardless of the tool used to identify them. This lack of gender association has been confirmed in multiple studies (O'Sullivan et al., 2013; Vishwas et al., 2012), but other studies show a positive association between female sex and using PIMs (Cahir et al., 2010; Gallagher & O'Mahony, 2008). However, Cahir et al. (2010) showed a negative association of gender when the odds ratio was adjusted which confirms the present result.

On the other hand, the occurrence of PIMs is significantly affected by the patient's secondary characteristics. Age was a predictor for patients using PIMs using Beers' criteria to detect PIMs, but it was an insignificant predictor using STOPP criteria or both sets of criteria. Regardless of the overall age predictions, the significance of the association varies between age ranges and the type of criteria used to compare between subjects. All of the criteria used to identify PIMs agree

that patients aged 70–74 were more susceptible to use of PIMs than those aged 90 and over. It was generally noted that patients aged 90 and older had a lower number of PIMs compared with those under 90, regardless of the criteria used. This might be because patients of advanced age were taking a lower number of medications compared to those of younger age, since the number of PIMs increases directly with the number of medications used. A previous study did find that the risk of receiving PIMs decreases with aging (Rancourt et al., 2004). Another explanation could be that those patients might be healthier than others or that prescribers preferred to reduce the number of medications prescribed for patients in advanced age (Rancourt et al., 2004). Further research is required since the number of patients who aged 90 and older were enrolled in this study is small.

Heterogeneity in the literature makes it difficult to consider age as a predicting factor of using PIMs. While some emphasize negative associations (O'Sullivan et al., 2013; Cahir et al., 2010; Bradley et al., 2012; Byrne et al., 2011) others disagree (Vishwas et al., 2012; Ubeda et al., 2012; Undela et al., 2014). Nonetheless, it is not possible to compare these results with the present study due to multiple factors: some considered elderly people as those aged 60 and over, which results in different PIMs (Undela et al., 2014; Vishwas et al., 2012). Furthermore, different analysis procedures such as multivariate logistic regression (Vishwas et al., 2012; O'Sullivan et al., 2013; Byrne et al., 2011) or Spearman's' rho correlation coefficient (Ubeda et al., 2012) were used to determine prediction, which influences the results. Moreover, old versions of Beers' criteria were used (Vishwas et al., 2012; Ubeda et al., 2012) or used only STOPP criteria without Beers' criteria (Cahir et al., 2010; Bradley et al., 2012), affecting the number of PIMs identified. Cahir et al. (2010) indicated the presence of an age association, but this association declined when polypharmacy was adjusted. Numerous studies evaluating PIMs using different geriatric

assessments show variation in results. It is very important to consider the site of study or the health care setting where patients are enrolled because each health facility has different patient condition levels and this might affect patient clinical characteristics.

Having multiple illnesses does not necessarily mean that PIMs are among the patient's prescribed medications. In this study, there were no predictable or significant associations between the number of illnesses that a patient had and the probability of that patient having PIMs, under all sets of criteria. Only two articles discussing the number of diseases provided a positive link between using PIMs and the number of illnesses. In-patients who had more than three illnesses were found to be more likely to have PIMs than those with fewer illnesses in an Indian study (Undela et al., 2014), while a second Indian group found that patients with four or more illnesses were susceptible to PIMs (Vishwas et al., 2012).

Regardless of the number of illnesses, it is extremely important to know what types of diseases patients have, regardless of whether patients have multiple illnesses. Generally, patients who have neurological or urogenital diseases are more susceptible to using PIMs than patients with cardiovascular, gastrointestinal, respiratory, musculoskeletal, kidney, endocrine, immune system diseases, or cancer. Even though some of these diseases have associations with PIM usage, the associations are weak compared to those of neurological or urogenital diseases. Regardless of the criteria used, neurological and urogenital diseases had positive, significant associations, except that the significance of neurological diseases was reduced when using the Beers' criteria and combined criteria models.

One of the prominent predictors leading to the increased prevalence of PIMs is prescribing multiple medications to older adults, as all of the results for the different assessment models

agreed that the number of medications consumed had a statistically significant correlation with the occurrence of PIMs. In particular, patients who take fourteen or more drugs are much more likely to take PIMs compared to patents taking four or less medications. The number of medications used under both sets of criteria, whether used separately or combined, not only provides positive results but also has extremely significant associations. On the other hand, the three models differ between the two sub-categories of low and moderate number of medications consumed. STOPP criteria indicate insignificant associations for either of these medication categories, compared to the lowest category of medications used. While the occurrence of PIMs identified by combined criteria is significantly associated with patients who used ten to thirteen medications, the power of this association is reduced to borderline significance when patients used five to nine drugs.

This does not mean that PIMs are exclusive to patients who use multiple medications, because patients who receive fewer medications might still have PIMs. In the screened medications list, some patients with fewer medications still had PIMs because the identification of a PIM does not depend solely on drug–drug interactions or contradictions that do increase with the number of medications used. Thus, all patients' medications should be screened at the same level, but the focus should be on patients who use multiple medications. It is necessary to report patients who receive ten to thirteen medications (moderate use) as vulnerable to using PIMs, and patients who use 14 or more medications (high use) as having a strong probability of using PIM, regardless of the tools used. All articles discussing PIMs considered polypharmacy the chief predictor, with some finding that more than five or more than ten prescribed medications should be used to predict PIMs (Vishwas et al., 2012; Ubeda et al., 2012; Cahir et al., 2010; Byrne et al., 2011; Undela et al., 2014; O'Sullivan et al., 2013).

Finally, the occurrence of PIMs unrelated to detectable criteria is not associated with gender or the number of illnesses. However, age depends on the criteria used; it is positively associated with taking PIMs only under Beers' criteria, but not when using the remaining criteria models. However, when the age categories are scrutinized, patients aged 70–74 are the group most likely to have PIMs, regardless of the criteria used. Similarly, patients taking more than 14 medications are significantly more probable to take PIMs, compared to patients who take fewer medications. Furthermore, there was no significant association between PIM usage and particular diseases, excluding urogenital and neurological diseases. All of the criteria sets showed a significant association between taking PIMs and urogenital diseases; however, the significance of the associations differed for neurological illnesses, based on the criteria applied. In fact, some of these findings are consistent with previous studies, but variations might depend on the study design and analysis, type of assessment for PIMs, heath care departments, and study site. Also, the patient's health status may have enhanced risk of PIMs prediction when in a critically ill condition.

5.7 Limitations

Despite this study providing crucial findings to determine the extent of PIMs in older patients admitted to rural hospitals, some limitations may exist. Selecting sites that have never conducted such medication reviews among admitted older patients, and perhaps unfamiliar with geriatric medication use guidelines or tools, may have resulted in the high prevalence of this problem. However, the intention was to determine the extent of PIMs use in a rural population. In addition, reporting and disseminating the results to the prescribers will increase awareness of medications that are probably harmful to the elderly. Another limitation is seemed that sample size of the study population that resulted in a large range of confidence interval values. However,

this population represents the maximum total number of eligible patients (less those who declined to participate) that could be recruited over the three month period. In addition, a number of patients were readmitted multiple times, but were excluded from our study for their next hospital visits. Moreover, each of the rural areas has a small population and hospital capacity compared with urban hospitals. Therefore, we asked multiple rural southwestern hospitals to participate in the study to cover the largest number of rural older patients who were recently admitted to the hospital.

While the study aimed to explore factors associated with the increased use of PIMs, it did not evaluate all factors leading to the prescribing of PIMs. Some of the factors include the rationale behind the prescribing of these medications, socioeconomic issues, and the prescribing patterns of clinicians. In this study, the main focus was to evaluate the extent of PIMs in rural elders. Investigation of those factors would require different study designs and data collection resources.

The goal of this study was not to investigate discharge medications or the patterns of prescribing medications in hospitals. Rather, these hospitals were employed as capture points to determine the prevalence of the use of PIMs in older rural residents recently admitted to these hospitals. This kind of study also required a different study design and implementation.

Despite the study's challenges, this study has delivered some valuable information about use of PIMs used by older adults admitted to rural hospital, where data has been sparse. Enrolling patients from different four sites increased the generalizability of the results for rural older adults in rural southwestern Ontario. Sufficient medical information and details related to the patients' conditions were available to judge whether medications were PIMs. This study could be the first

step to establish future research projects, such as interventions to reduce the prescribing of PIMs and evaluation of other external factors that might contribute to the use of PIMs.

5.8 Conclusions

Despite massive research efforts, PIMs still appear to be a globally crucial issue that needs further efforts to be resolved. The study used two well-documented criteria to evaluate the performance of these criteria and investigate the prevalence of PIMs at a site that has never been evaluated for the appropriateness of medication prescribed for the elderly. More than 60% of the rural elderly in this study take at least one PIM, regardless of which criteria are used. STOPP criteria were more likely to detect PIMs than Beers' criteria because they differ in features, causing dissimilar results in terms of prevalence, number of PIMs, and most frequent therapeutic category prescribed. However, those discrepancies were negated by applying both criteria simultaneously, resulting in the detection of PIMs in over 70% of admitted patients. The most frequent PIMs are cardiac and benzodiazepine drugs that are essential to review before the patient receives them. Secondly, this research explored factors that predict the occurrence of PIMs based on criteria use. Patient age (only with Beers' criteria), number of medications, and presence of neurological/urogenital diseases were associated with an increased probability of taking PIMs. Although this study estimated the extent of PIMs and discussed important distinctions between two assessment tools, continued research is required to evaluate this problem and other contributing factors in various health care settings since PIMs represent a serious health threat to older adults.

5.9 Future concerns and recommendations

This research evaluated concerns about the appropriateness of medication prescribed for the rural elderly. This issue persists internationally despite considerable research effort that led to proposed solutions. Thus, study findings would not be clinically meaningful if some solutions were not taken into consideration. There is a gap between evidence-based guidelines/criteria and translation of this knowledge and employment into professional practices, particularly for geriatric patients. It is necessary to implement educational or computerized interventions to reduce the number of prescribed PIMs. These criteria could be converted to a computerized database and incorporated into pharmacist and physician entry order program, medication reconciliation program, or any other health care system. This would alert prescribers who are not specialists in geriatrics to potential problems (Monane et al., 1998); their decisions would then more likely be based on knowledge, even if their decision is not changed (Beers, 1997). This is because each decision is made based on individualized treatment and the criteria are not used for conclusively deciding for all patients. Concurrent use of both criteria identified more PIMs and eliminated conflicts between criteria. Ongoing studies should continue to evaluate this issue using the most recent versions of criteria. Further research is required to evaluate criteria performance in predicting adverse drug reactions. Moreover, a periodic medication review program should be applied in each health care setting to evaluate PIMs, drug omission, drug-drug interactions, drug regimen, and correct use of drugs. Prescription quality can be improved by decreasing risk factors leading to PIMs, reducing polypharmacy, and providing better specific disease management. Duplications in treatment from different therapeutic drug classes were detected, particularly with the treatment of insomnia, depression, and neuropathic pain. These inappropriate treatments are not identified by criteria, but should be tapered, replaced, or discontinued. When neurologic medications are prescribed, a neuro/psycho specialist should be

consulted to avoid misuse or abuse and to prescribing the right dose for the right indication. Identifying the most frequently used PIM classes will help prescribers to pay greater attention when prescribing for the elderly, and may facilitate research into creating treatment algorithms that address that group of medications. PIMs continue to be prescribed for frail older adults. Further research is required to eradicate the continuation of this problem.

References

Agashivala, N. & Wu, W. K. (2009). Effects of potentially inappropriate psychoactive medications on falls in US nursing home residents: Analysis of the 2004 national nursing home survey database. *Drugs & Aging, 26*(10), 853-860.

Bao, Y., Shao, H., Bishop, T. F., Schackman, B. R., & Bruce, M. L. (2012). Inappropriate medication in a national sample of U.S. elderly patients receiving home health care. *Journal of General Internal Medicine, 27*(3), 304-310.

Beers, M. H. (1997). Explicit criteria for determining potentially inappropriate medication use by the elderly: an update. *Archives of Internal Medicine, 157*(14), 1531-1536.

Beers, M. H., Ouslander, J. G., Rollingher, I., Reuben, D. B., Brooks, J., & Beck, J. C. (1991). Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. *Archives of Internal Medicine, 151*(9), 1825-1832.

Berdot, S., Bertrand, M., Dartigues, J. F., Fourrier, A., Tavernier, B., Ritchie, K., & Alpérovitch A. (2009). Inappropriate medication use and risk of falls-a prospective study in a large community-dwelling elderly cohort. *BioMed Central Geriatrics, 9*, 30-2318-9-30.Bergqvist, M., Ulfvarson, J., & Karlsson, E. A. (2009). Nurse-led medication reviews and the quality of drug treatment of elderly hospitalized patients. *European Journal of Clinical Pharmacology, 65*(11), 1089-1096. doi:10.1007/s00228-009-0728-2.

Bero, L. A., Lipton, H. L., & Bird, J. A. (1991). Characterization of geriatric drug-related hospital readmissions. *Medical Care, 29*(10), 989-1003.

Bonnet-Zamponi, D., d'Arailh, L., Konrat, C., Delpierre, S., Lieberherr, D., Lemaire, A. I., Tubach, F., Lacaille, S., & Legrain, S. (2013). Drug-related readmissions to medical units of older adults discharged from acute geriatric units: Results of the optimization of medication in AGEd multicenter randomized controlled trial. *Journal of the American Geriatrics Society, 61*(1), 113–121.

Bradley, M. C., Fahey, T., Cahir, C., Bennett, K., O'Reilly, D., Parsons, C., & Hughes, C. M. (2012). Potentially inappropriate prescribing and cost outcomes for older people: a cross-sectional study using the Northern Ireland enhanced prescribing database. *European Journal of Clinical Pharmacology, 68*(10), 1425-1433.

Bregnhoj, L., Thirstrup, S., Kristensen, M. B., Bjerrum, L., & Sonne, J. (2009) Combined intervention programme reduces inappropriate prescribing in elderly patients exposed to polypharmacy in primary care. *European Journal of Clinical Pharmacology, 65*(2), 199–207.

Brundisini, F., Giacomini, M., DeJean, D., Vanstone, M., Winsor, S., & Smith, A. (2013). Chronic disease patients' experiences with accessing health care in rural and remote areas: a

systematic review and qualitative meta-synthesis. *Ontario Health Technology Assessment Series, 13*(15), 1-33.

Bushardt, R. L., Massey, E. B., Simpson, T. W., Ariail, J. C., & Simpson, K. N. (2008). Polypharmacy: misleading, but manageable. *Clinical Interventions in Aging, 3*(2), 383-389.

Byrne, S., O'Sullivan, D., Hughes, C., O'Mahony, D., Parsons, C., Patterson, S., McCormack, B., & Finn, F. (2011). An evaluation of the inappropriate prescribing in older residents in long term care facilities in the greater Cork and Northern Ireland regions using the STOPP and Beers' criteria. *Dublin: Centre for Ageing Research and Development in Ireland*.

Cahir, C., Fahey, T., Teeling, M., Teljeur, C., Feely, J., & Bennett, K. (2010). Potentially inappropriate prescribing and cost outcomes for older people: a national population study. *British Journal of Clinical Pharmacology, 69*(5), 543-552.

Campanelli, C. M., Beers Criteria Update Expert Panel. (2012). American Geriatrics Society updated Beers' criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society, 60*(4), 616-631.

Canadian Institute for Health Information. *Drug Use among Seniors on Public Drug Programs in Canada*, 2012. Ottawa, ON: CIHI; 2014. Retrieved from https://secure.cihi.ca/free_products/ Drug_Use_in_Seniors_on_Public_Drug_Programs_2012_EN_web.pdf.

Chang, C. B. & Chan, D. C. (2010). Comparison of published explicit criteria for potentially inappropriate medications in older adults. *Drug Aging, 27*(12), 947-957.

Chen, L. L., Tangiisuran, B., Shafie, A. A., & Hassali, M. A. (2012). Evaluation of potentially inappropriate medications among older residents of Malaysian nursing homes. *International Journal of Clinical Pharmacy, 34*(4), 596-603.

Corsonello, A., Onder, G., Abbatecola, A. M., Guffanti, E. E., Gareri, P., & Lattanzio, F. (2012). Explicit criteria for potentially inappropriate medications to reduce the risk of adverse drug reactions in elderly people: From Beers' to STOPP/START criteria. *Drug Safety: An International Journal of Medical Toxicology and Drug Experience, 35(Suppl 1)*, 21-28.

Corsonello, A., Pedone, C., Lattanzio, F., Lucchetti, M., Garasto, S., Di Muzio, M., Giunta, S., Onder, G., Di Iorio, A., Volpato, S., Corica, F., Mussi, C., & Antonelli Incalzi R. (2009). Potentially inappropriate medications and functional decline in elderly hospitalized patients. *Journal of the American Geriatrics Society, 57*(6), 1007-1014.

Curtain, C. M., Bindoff, I. K., Westbury, J. L., & Peterson, G. M. (2013). A comparison of prescribing criteria when applied to older community-based patients. *Drugs & Aging, 30*(11), 935-943.

Dedhiya, S. D., Hancock, E., Craig, B. A., Doebbeling, C. C., & Thomas, J.,3rd. (2010). Incident use and outcomes associated with potentially inappropriate medication use in older adults. *The American Journal of Geriatric Pharmacotherapy, 8*(6), 562-570.

Dionne, P. A., Vasiliadis, H. M., Latimer, E., Berbiche, D., & Preville, M. (2013). Economic impact of inappropriate benzodiazepine prescribing and related drug interactions among elderly persons. *Psychiatric Services (Washington, D.C.), 64*(4), 331-338.

DiPiro, J. T., Talbert, R. L., Yee, G. C., Matzke, G. R., Wells, B. G., & Posey, L. (2014). eChapter 8. Geriatrics. In: DiPiro, J. T., Talbert, R. L., Yee, G. C., Matzke, G. R., Wells, B. G., & Posey L (Eds), *Pharmacotherapy: A Pathophysiologic Approach, 9e.* Retrieved September 27, 2014 from http://accesspharmacy.mhmedical.com.proxy.lib.uwaterloo.ca/content.aspx?bookid=689&Sectionid=48811433.

Dobson, A. J. & Barnett, A. G. (2008). *An Introduction to Generalized Linear Models.* Boca Raton (FL): CRC Press.

Fadare, J. O., Agboola, S. M., Opeke, O. A., & Alabi, R. A. (2013). Prescription pattern and prevalence of potentially inappropriate medications among elderly patients in a Nigerian rural tertiary hospital. *Therapeutics and Clinical Risk Management, 6*, 115-120.

Fick, D. M., Cooper, J. W., Wade, W. E., Waller, J. L., Maclean, J. R., & Beers, M. H. (2003). Updating the Beers' criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Archives of Internal Medicine, 163*(22), 2716-2724.

Fick, D. M. & Semla, T. P. (2012). 2012 American Geriatrics Society Beers' criteria: new year, new criteria, new perspective. *Journal of the American Geriatrics Society, 60*(4), 614-615.

Fillenbaum, G. G., Hanlon, J. T., Landerman, L. R., Artz, M. B., O'Connor, H., Dowd, B., Gross, C. R., Boult, C., Garrard, J., & Schmader, K. E. (2004) Impact of inappropriate drug use on health services utilization among representative older community-dwelling residents. *American Journal of Geriatric Pharmacotherapy 2*(2):92-101.

Forbes, D. A. & Edge, D. S. (2009). Canadian home care policy and practice in rural and remote settings: challenges and solutions. *Journal of Agromedicine, 14*(2), 119-124.

Forthofer, R. N., Lee, E. S., & Hernandez, M. (2007). *Biostatistics: a Guide to Design, Analysis, and Discovery.* Amsterdam Boston, MA: Elsevier Academic Press.

Fu, A. Z., Jiang, J. Z., Reeves, J. H., Fincham, J. E., Liu, G. G., & Perri, M., 3rd. (2007). Potentially inappropriate medication use and healthcare expenditures in the US community-dwelling elderly. *Medical Care, 45*(5), 472-476.

Fu, A. Z., Liu, G. G., & Christensen, D. B. (2004). Inappropriate medication use and health outcomes in the elderly. *Journal of the American Geriatrics Society, 52*(11), 1934-

1939.Gallagher, P., Barry, P., & O'Mahony, D. (2007). Inappropriate prescribing in the elderly. *Journal of Clinical Pharmacy and Therapeutics, 32*(2), 113-121.

Gallagher, P., Lang, P. O., Cherubini, A., Topinkova, E., Cruz-Jentoft, A., Montero Errasquin, B., Mádlová, P., Gasperini, B., Baeyens, H., Baeyens, J. P., Michel, J. P., & O'Mahony, D. (2011). Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. *European Journal of Clinical Pharmacology, 67*(11), 1175-1188.

Gallagher, P., & O'Mahony, D. (2008). STOPP (screening tool of older persons' potentially inappropriate prescriptions): Application to acutely ill elderly patients and comparison with Beers' criteria. *Age and Ageing, 37*(6), 673-679.

Gokula, M., & Holly, M. H. (2012). Tools to reduce polypharmacy. *Clinics in Geriatric Medicine, 28,* 323–341.

Goldberg, R. M., Mabee, J., Chan, L., & Wong, S. (1996). Drug-drug and drug-disease interactions in the ED: analysis of a high-risk population. *The American Journal of Emergency Medicine, 14*(5), 447-450.

Gordis, L. (2009). *Epidemiology.* Philadelphia (PA): *Elsevier/Saunders.*

Gurwitz, J. H., Field, T. S., Harrold, L. R., Rothschild, J., Debellis, K., Seger, A. C., Cadoret, C., Fish, L. S., Garber, L., Kelleher, M., & Bates, D. W. (2003). Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *The Journal of the American Medical Association, 289*(9), 1107-1116.

Hajjar, E. R., Cafiero, A. C., & Hanlon, J. T. (2007). Polypharmacy in elderly patients. *The American Journal of Geriatric Pharmacotherapy, 5*(4), 345-351.

Howard, M., Dolovich, L., Kaczorowski, J., Sellors, C., & Sellors, J. (2004). Prescribing of potentially inappropriate medications to elderly people. *Family Practice, 21*(3), 244-247.

Kaur, S., Mitchell, G., Vitetta, L., & Roberts, M. S. (2009). Interventions that can reduce inappropriate prescribing in the elderly: a systematic review. *Drugs & Aging, 26*(12), 1013-1028.

Keith, S. W., Maio, V., Dudash, K., Templin, M., & Canale, S. D. (2013). A physician-focused intervention to reduce potentially inappropriate medication prescribing in older people. *Drugs & Aging, 30*(2), 119–127.

Landi, F., Russo, A., Liperoti, R., Barillaro, C., Danese, P., Pahor, M., Bernabei, R., & Onder, G. (2007). Impact of inappropriate drug use on physical performance among a frail elderly population living in the community. *European Journal of Clinical Pharmacology, 63*(8), 791-799.

Lane, C. J., Bronskill, S. E., Sykora, K., Dhalla, I. A., Anderson, G. M., Mamdani, M. M., Gill, S.S., Gurwitz, J. H., & Rochon, P. A. (2004). Potentially inappropriate prescribing in Ontario community-dwelling older adults and nursing home residents. *Journal of the American Geriatrics Society,52*(6), 582-587.

Lau, D. T., Kasper, J. D., Potter D. E., & Lyles, A. (2004). Potentially inappropriate medication prescriptions among elderly nursing home residents: their scope and associated resident and facility characteristics. *Health Services Research, 39*(5):1257-1276.

Lau, D. T., Kasper, J. D., Potter, D. E., Lyles, A., & Bennett, R. G. (2005). Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. *Archives of Internal Medicine, 165*(1), 68-74.

Lin, Y. J., Peng, L. N., Chen, L. K., Lin, M. H., & Hwang, S. J. (2011). Risk factors of potentially inappropriate medications among older patients visiting the community health center in rural Taiwan. *Archives of Gerontology and Geriatrics, 53*(2), 225-228.

Lund, B. C., Charlton, M. E., Steinman, M. A., & Kaboli, P. J. (2013). Regional differences in prescribing quality among elder veterans and the impact of rural residence. *The Journal of Rural Health, 29*(2), 172-179.

Mangoni, A. A., & Jackson, S. H. D. (2003) Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *British Journal of Clinical Pharmacology, 57*(1), 6-14.

McLean, A. J., & Le Couteur, D. G. (2004) Aging biology and geriatrics clinical pharmacology. *Pharmacological Reviews 56*(2):163–184.

McMahon, C. G., Cahir, C. A., Kenny, R. A., & Bennett, K. (2014). Inappropriate prescribing in older fallers presenting to an Irish emergency department. *Age and Ageing, 43*(1), 44-50.

Meurer, W. J., Potti, T.A., Kerber, K. A., Sasson, C., Macy, M. L., West, B. T., & Losman, E.D. (2010). Potentially inappropriate medication utilization in the emergency department visits by older adults: analysis from a nationally representative sample. *Academic Emergency Medicine, 17*(3), 231-237.

Monane, M., Matthias, D. M., Nagle, B. A., & Kelly, M. A. (1998). Improving prescribing patterns for the elderly through an online drug utilization review intervention: A system linking the physician, pharmacist, and computer. *The Journal of the American Medical Association, 280*(14), 1249-1252.

Monroe, T., Carter, M., & Parish, A. (2011). A case study using the Beers' list criteria to compare prescribing by family practitioners and geriatric specialists in a rural nursing home. *Geriatric Nursing (New York, N.Y.), 32*(5), 350-356.

Nixdorff, N., Hustey, F. M., Brady, A. K., Vaji, K., Leonard, M., & Messinger-Rapport, B. J. (2008). Potentially inappropriate medications and adverse drug effects in elders in the ED. *The American Journal of Emergency Medicine, 26*(6), 697-700.

O'Mahony, D., Gallagher, P., Ryan, C., Byrne, S., Hamilton, H., Barry, P., O'Connor M., & Kennedy J. (2010). STOPP & START criteria: a new approach to detecting potentially inappropriate prescribing in old age. *European Geriatric Medicine, 1,* 45–51.

Onder, G., Petrovic, M., Tangiisuran, B., Meinardi, M. C., Markito-Notenboom, W. P., Somers, A., Rajkumar, C., Bernabei, R., & van der Cammen, T. J.. (2010). Development and validation of a score to assess risk of adverse drug reactions among in-hospital patients 65 years or older: The GerontoNet ADR risk score. *Archives of Internal Medicine, 170*(13), 1142-1148.

O'Sullivan, D. P., O'Mahony, D., Parsons, C., Hughes, C., Murphy, K., Patterson, S., & Byrne, S. (2013). A prevalence study of potentially inappropriate prescribing in Irish long-term care residents. *Drugs & Aging, 30*(1), 39-49.

Page, R. L.,2nd, Linnebur, S. A., Bryant, L. L., & Ruscin, J. M. (2010). Inappropriate prescribing in the hospitalized elderly patient: Defining the problem, evaluation tools, and possible solutions. *Clinical Interventions in Aging, 5,* 75-87.

Pitkala, K. H., Juola, A. L., Soini, H., Laakkonen, M. L., Kautiainen, H., Teramura-Gronblad, M., Finne-Soveri, H., & Bjorkman, M. (2012). Reducing inappropriate, anticholinergic and psychotropic drugs among older residents in assisted living facilities: Study protocol for a randomized controlled trial. *Trials, 13,* 85-6215-13-85.

PL Detail-Document, Potentially Harmful Drugs in the Elderly: Beers' List. Pharmacist's Letter/Prescriber's Letter. June 2012. Retrieved from http://canadianpharmacistsletter.therapeuticresearch.com/pl/ArticleDD.aspx?nidchk=1&cs=&s=PLC&pt=2&segment=4413&dd=280610&AspxAutoDetectCookieSupport=1

Pong, R. W., DesMeules, M., Heng, D., Lagace, C., Guernsey, J. R., Kazanjian, A., Manuel, D., Pitblado, J. R., Bollman, R., Koren, I., Dressler, M. P., Wang, F., & Luo, W. (2011). Patterns of health services utilization in rural Canada. *Chronic Diseases and Injuries in Canada, 31*(Suppl 1), 1-36.

Préville, M., Bossé, C., Vasiliadis, H. M., Voyer, P., Laurier, C., Berbiche, D., Pérodeau, G., Grenier, S., Béland, S. G., Dionne, P. A., Gentil, L., & Moride, Y. (2012). Correlates of potentially inappropriate prescriptions of benzodiazepines among older adults: results from the ESA study. *Canadian Journal on Aging 31*(3), 313-322.

Price, S. D., Holman, C. D., Sanfilippo, F. M., & Emery, J. D. (2014). Association between potentially inappropriate medications from the Beers' criteria and the risk of unplanned hospitalization in elderly patients. *The Annals of Pharmacotherapy, 48*(1), 6-16.

Rancourt, C., Moisan, J., Baillargeon, L., Verreault, R., Laurin, D., & Gregoire, J. P. (2004). Potentially inappropriate prescriptions for older patients in long-term care. *BioMedCentral Geriatrics, 4,* 9.

Schwartz JB and Abernethy, DR. (2009). Aging and medications: Past, present, future .*Clin Pharmacol Ther,1* (85), 3-10.

Sanborn, M. D., Manuel, D. G., Ciechanska, E., & Lee, D. S. (2005). Potential gaps in congestive heart failure management in a rural hospital. *Canadian Journal of Rural Medicine, 10*(3), 155-161.

Scott, I. A., Gray, L. C., Martin, J. H., & Mitchell, C. A. (2012). Effects of a drug minimization guide on prescribing intentions in elderly persons with polypharmacy. *Drugs & Aging 29*(8), 659-667.

Sibley, L. M. & Weiner, J. P. (2011). An evaluation of access to health care services along the rural-urban continuum in Canada. *BioMed Central Health Services Research, 11,* 20-6963-11-20.

Steinman, M. A., Seth Landefeld, C., Rosenthal, G. E., Berthenthal, D., Sen, S. and Kaboli, P. J. (2006), Polypharmacy and Prescribing Quality in Older People. *Journal of the American Geriatrics Society,* 54: 1516–1523. doi: 10.1111/j.1532-5415.2006.00889.x

Toguri, C., Jong, M., & Roger, J. (2012). Needs of specialists in rural and remote Canada. *Canadian Journal of Rural Medicine, 17*(2), 56-62.

Tosato, M., Landi, F., Martone, A. M., Cherubini, A., Corsonello, A., Volpato, S., Bernabei, R., & Onder, G. (2014). Potentially inappropriate drug use among hospitalised older adults: Results from the CRIME study. *Age and Ageing,* Epub ahead of print.

Tripp, D. A., VanDenKerkhof, E. G., & McAlister, M. (2006). Prevalence and determinants of pain and pain-related disability in urban and rural settings in southeastern Ontario. *Pain Research & Management, 11*(4), 225-233.

Turnheim, K. (2003). When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. *Experimental Gerontology 38*, 843-853.

Ubeda, A., Ferrandiz, L., Maicas, N., Gomez, C., Bonet, M., & Peris, J. E. (2012). Potentially inappropriate prescribing in institutionalised older patients in Spain: The STOPP-START criteria compared with the Beers' criteria. *Pharmacy Practice, 10*(2), 83-91.

Undela, K., Bansal, D., D'Cruz, S., Sachdev, A., & Tiwari, P. (2014). Prevalence and determinants of use of potentially inappropriate medications in elderly inpatients: A prospective study in a tertiary healthcare setting. *Geriatrics & Gerontology International, 14*(2), 251-258.

Vishwas, H. N., Harugeri, A., Parthasarathi, G., & Ramesh, M. (2012). Potentially inappropriate medication use in Indian elderly: comparison of Beers' criteria and screening tool of older persons' potentially inappropriate prescriptions. *Geriatrics & Gerontology International, 12*(3), 506-514.

Weston, A. L., Weinstein, A. M., Barton, C., & Yaffe, K. (2010). Potentially inappropriate medication use in older adults with mild cognitive impairment. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 65*(3), 318-321.

Wong, J., Marr, P., Kwan, D., Meiyappan, S., & Adcock, L. (2014). Identification of inappropriate medication use in elderly patients with frequent emergency department visits. *Canadian Pharmacists Journal / Revue des Pharmaciens du Canada,* 147(4), 248-256.

Zhan C, Sangl J, Bierman AS, et al.(2001). Potentially Inappropriate Medication Use in the Community-Dwelling Elderly: Findings From the 1996 Medical Expenditure Panel Survey. *JAMA,*286(22):2823-2829. doi:10.1001/jama.286.22.2823.

Appendix A: Criteria Lists

i Beers' Criteria

AGS BEERS CRITERIA
FOR POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER ADULTS

FROM THE AMERICAN GERIATRICS SOCIETY

This clinical tool, based on *The AGS 2012 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (AGS 2012 Beers Criteria)*, has been developed to assist healthcare providers in improving medication safety in older adults. Our purpose is to inform clinical decision-making concerning the prescribing of medications for older adults in order to improve safety and quality of care.

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the *Beers Criteria* catalogues medications that cause adverse drug events in older adults due to their pharmacologic properties and the physiologic changes of aging. In 2011, the AGS undertook an update of the criteria, assembling a team of experts and funding the development of the AGS 2012 *Beers Criteria* using an enhanced, evidence-based methodology. Each criterion is rated (quality of evidence and strength of evidence) using the American College of Physicians' Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al.

The full document together with accompanying resources can be viewed online at www.americangeriatrics.org.

INTENDED USE

The goal of this clinical tool is to improve care of older adults by reducing their exposure to Potentially Inappropriate Medications (PIMs).

- This should be viewed as a guide for identifying medications for which the risks of use in older adults outweigh the benefits.
- These criteria are not meant to be applied in a punitive manner.
- This list is not meant to supersede clinical judgment or an individual patient's values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making.
- These criteria also underscore the importance of using a team approach to prescribing and the use of non-pharmacological approaches and of having economic and organizational incentives for this type of model.
- Implicit criteria such as the STOPP/START criteria and Medication Appropriateness Index should be used in a complementary manner with the 2012 AGS *Beers Criteria* to guide clinicians in making decisions about safe medication use in older adults.

The criteria are not applicable in all circumstances (eg, patient's receiving palliative and hospice care). If a clinician is not able to find an alternative and chooses to continue to use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that the potential for an adverse drug effect can be incorporated into the medical record and prevented or detected early.

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	**Recommendation**, Rationale, *Quality of Evidence (QE) & Strength of Recommendation (SR)*
Anticholinergics (excludes TCAs)	
First-generation antihistamines (as single agent or as part of combination products) ■ Brompheniramine ■ Carbinoxamine ■ Chlorpheniramine ■ Clemastine ■ Cyproheptadine ■ Dexbrompheniramine ■ Dexchlorpheniramine ■ Diphenhydramine (oral) ■ Doxylamine ■ Hydroxyzine ■ Promethazine ■ Triprolidine	**Avoid.** Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/ toxicity. Use of diphenhydramine in special situations such as acute treatment of severe allergic reaction may be appropriate. *QE = High (Hydroxyzine and Promethazine), Moderate (All others); SR = Strong*
Antiparkinson agents ■ Benztropine (oral) ■ Trihexyphenidyl	**Avoid.** Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease. *QE = Moderate; SR = Strong*

Table 1 (continued on page 2)

Table 1 (continued from page 1)

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	**Recommendation**, Rationale, *Quality of Evidence (QE) & Strength of Recommendation (SR)*
Antispasmodics ■ Belladonna alkaloids ■ Clidinium-chlordiazepoxide ■ Dicyclomine ■ Hyoscyamine ■ Propantheline ■ Scopolamine	**Avoid except in short-term palliative care to decrease oral secretions.** Highly anticholinergic, uncertain effectiveness. *QE = Moderate; SR = Strong*
Antithrombotics	
Dipyridamole, oral short-acting* *(does not apply to the extended-release combination with aspirin)*	**Avoid.** May cause orthostatic hypotension; more effective alternatives available; IV form acceptable for use in cardiac stress testing. *QE = Moderate; SR = Strong*
Ticlopidine*	**Avoid.** Safer, effective alternatives available. *QE = Moderate; SR = Strong*
Anti-infective	
Nitrofurantoin	**Avoid for long-term suppression; avoid in patients with CrCl <60 mL/min.** Potential for pulmonary toxicity; safer alternatives available; lack of efficacy in patients with CrCl <60 mL/min due to inadequate drug concentration in the urine. *QE = Moderate; SR = Strong*
Cardiovascular	
Alpha$_1$ blockers ■ Doxazosin ■ Prazosin ■ Terazosin	**Avoid use as an antihypertensive.** High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk/ benefit profile. *QE = Moderate; SR = Strong*
Alpha agonists ■ Clonidine ■ Guanabenz* ■ Guanfacine* ■ Methyldopa* ■ Reserpine (>0.1 mg/day)*	**Avoid clonidine as a first-line antihypertensive. Avoid others as listed.** High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension. *QE = Low; SR = Strong*
Antiarrhythmic drugs (Class Ia, Ic, III) ■ Amiodarone ■ Dofetilide ■ Dronedarone ■ Flecainide ■ Ibutilide ■ Procainamide ■ Propafenone ■ Quinidine ■ Sotalol	**Avoid antiarrhythmic drugs as first-line treatment of atrial fibrillation.** Data suggest that rate control yields better balance of benefits and harms than rhythm control for most older adults. Amiodarone is associated with multiple toxicities, including thyroid disease, pulmonary disorders, and QT interval prolongation. *QE = High; SR = Strong*
Disopyramide*	**Avoid.** Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred. *QE = Low; SR = Strong*
Dronedarone	**Avoid in patients with permanent atrial fibrillation or heart failure.** Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or heart failure. In general, rate control is preferred over rhythm control for atrial fibrillation. *QE = Moderate; SR = Strong*
Digoxin >0.125 mg/day	**Avoid.** In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity; decreased renal clearance may increase risk of toxicity. *QE = Moderate; SR = Strong*

Table 1 (continued on page 3)

Table 1 (continued from page 2)

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Nifedipine, immediate release*	**Avoid.** Potential for hypotension; risk of precipitating myocardial ischemia. *QE = High; SR = Strong*
Spironolactone >25 mg/day	**Avoid in patients with heart failure or with a CrCl <30 mL/min.** In heart failure, the risk of hyperkalemia is higher in older adults if taking >25 mg/day. *QE = Moderate; SR = Strong*
Central Nervous System	
Tertiary TCAs, alone or in combination: ▪ Amitriptyline ▪ Chlordiazepoxide-amitriptyline ▪ Clomipramine ▪ Doxepin >6 mg/day ▪ Imipramine ▪ Perphenazine-amitriptyline ▪ Trimipramine	**Avoid.** Highly anticholinergic, sedating, and cause orthostatic hypotension; the safety profile of low-dose doxepin (≤6 mg/day) is comparable to that of placebo. *QE = High; SR = Strong*
Antipsychotics, first- (conventional) and second- (atypical) generation *(see online for full list)*	**Avoid use for behavioral problems of dementia unless non-pharmacologic options have failed and patient is threat to self or others.** Increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia. *QE = Moderate; SR = Strong*
Thioridazine Mesoridazine	**Avoid.** Highly anticholinergic and greater risk of QT-interval prolongation. *QE = Moderate; SR = Strong*
Barbiturates ▪ Amobarbital* ▪ Butabarbital* ▪ Butalbital ▪ Mephobarbital* ▪ Pentobarbital* ▪ Phenobarbital ▪ Secobarbital*	**Avoid.** High rate of physical dependence; tolerance to sleep benefits; greater risk of overdose at low dosages. *QE = High; SR = Strong*
Benzodiazepines *Short- and intermediate-acting:* ▪ Alprazolam ▪ Estazolam ▪ Lorazepam ▪ Oxazepam ▪ Temazepam ▪ Triazolam *Long-acting:* ▪ Chlorazepate ▪ Chlordiazepoxide ▪ Chlordiazepoxide-amitriptyline ▪ Clidinium-chlordiazepoxide ▪ Clonazepam ▪ Diazepam ▪ Flurazepam ▪ Quazepam	**Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium.** Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults. May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, periprocedural anesthesia, end-of-life care. *QE = High; SR = Strong*
Chloral hydrate*	**Avoid.** Tolerance occurs within 10 days and risk outweighs the benefits in light of overdose with doses only 3 times the recommended dose. *QE = Low; SR = Strong*
Meprobamate	**Avoid.** High rate of physical dependence; very sedating. *QE = Moderate; SR = Strong*

Table 1 (continued on page 4)

Table 1 (continued from page 3)

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Nonbenzodiazepine hypnotics ▪ Eszopiclone ▪ Zolpidem ▪ Zaleplon	**Avoid chronic use (>90 days)** Benzodiazepine-receptor agonists that have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); minimal improvement in sleep latency and duration. *QE = Moderate; SR = Strong*
Ergot mesylates* Isoxsuprine*	**Avoid.** Lack of efficacy. *QE = High; SR = Strong*
Endocrine	
Androgens ▪ Methyltestosterone* ▪ Testosterone	**Avoid unless indicated for moderate to severe hypogonadism.** Potential for cardiac problems and contraindicated in men with prostate cancer. *QE = Moderate; SR = Weak*
Desiccated thyroid	**Avoid.** Concerns about cardiac effects; safer alternatives available. *QE = Low; SR = Strong*
Estrogens with or without progestins	**Avoid oral and topical patch. Topical vaginal cream: Acceptable to use low-dose intravaginal estrogen for the management of dyspareunia, lower urinary tract infections, and other vaginal symptoms.** Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women. Evidence that vaginal estrogens for treatment of vaginal dryness is safe and effective in women with breast cancer, especially at dosages of estradiol <25 mcg twice weekly. *QE = High (Oral and Patch), Moderate (Topical); SR = Strong (Oral and Patch), Weak (Topical)*
Growth hormone	**Avoid, except as hormone replacement following pituitary gland removal.** Effect on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose. *QE = High; SR = Strong*
Insulin, sliding scale	**Avoid.** Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting. *QE = Moderate; SR = Strong*
Megestrol	**Avoid.** Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults. *QE = Moderate; SR = Strong*
Sulfonylureas, long-duration ▪ Chlorpropamide ▪ Glyburide	**Avoid.** Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes SIADH Glyburide: higher risk of severe prolonged hypoglycemia in older adults. *QE = High; SR = Strong*
Gastrointestinal	
Metoclopramide	**Avoid, unless for gastroparesis.** Can cause extrapyramidal effects including tardive dyskinesia; risk may be further increased in frail older adults. *QE = Moderate; SR = Strong*
Mineral oil, given orally	**Avoid.** Potential for aspiration and adverse effects; safer alternatives available. *QE = Moderate; SR = Strong*
Trimethobenzamide	**Avoid.** One of the least effective antiemetic drugs; can cause extrapyramidal adverse effects. *QE = Moderate; SR = Strong*

Table 1 (continued on page 5)

Table 1 (continued from page 4)

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Pain Medications	
Meperidine	**Avoid.** Not an effective oral analgesic in dosages commonly used; may cause neurotoxicity; safer alternatives available. *QE = High; SR = Strong*
Non-COX-selective NSAIDs, oral ■ Aspirin >325 mg/day ■ Diclofenac ■ Diflunisal ■ Etodolac ■ Fenoprofen ■ Ibuprofen ■ Ketoprofen ■ Meclofenamate ■ Mefenamic acid ■ Meloxicam ■ Nabumetone ■ Naproxen ■ Oxaprozin ■ Piroxicam ■ Sulindac ■ Tolmetin	**Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent (proton-pump inhibitor or misoprostol).** Increases risk of GI bleeding/peptic ulcer disease in high-risk groups, including those ≥75 years old or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. Use of proton pump inhibitor or misoprostol reduces but does not eliminate risk. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months, and in about 2%–4% of patients treated for 1 year. These trends continue with longer duration of use. *QE = Moderate; SR = Strong*
Indomethacin Ketorolac, includes parenteral	**Avoid.** Increases risk of GI bleeding/peptic ulcer disease in high-risk groups *(See Non-COX selective NSAIDs)* Of all the NSAIDs, indomethacin has most adverse effects. *QE = Moderate (Indomethacin), High (Ketorolac); SR = Strong*
Pentazocine*	**Avoid.** Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs; is also a mixed agonist and antagonist; safer alternatives available. *QE = Low; SR = Strong*
Skeletal muscle relaxants ■ Carisoprodol ■ Chlorzoxazone ■ Cyclobenzaprine ■ Metaxalone ■ Methocarbamol ■ Orphenadrine	**Avoid.** Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures; effectiveness at dosages tolerated by older adults is questionable. *QE = Moderate; SR = Strong*

*Infrequently used drugs. Table 1 Abbreviations: ACEI, angiotensin converting-enzyme inhibitors; ARB, angiotensin receptor blockers; CNS, central nervous system; COX, cyclooxygenase; CrCl, creatinine clearance; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SR, Strength of Recommendation; TCAs, tricyclic antidepressants; QE, Quality of Evidence

TABLE 2: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug-Disease or Drug-Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Cardiovascular		
Heart failure	NSAIDs and COX-2 inhibitors	**Avoid.** Potential to promote fluid retention and/or exacerbate heart failure. *QE = Moderate (NSAIDs, CCBs, Dronedarone), High (Thiazolidinediones (glitazones)), Low (Cilostazol); SR = Strong*
	Nondihydropyridine CCBs (avoid only for systolic heart failure) ■ Diltiazem ■ Verapamil	
	Pioglitazone, rosiglitazone	
	Cilostazol	
	Dronedarone	

Table 2 (continued on page 6)

Table 2 (continued from page 5)

TABLE 2: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug-Disease or Drug-Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Syncope	Acetylcholinesterase inhibitors (AChEIs) Peripheral alpha blockers ■ Doxazosin ■ Prazosin ■ Terazosin Tertiary TCAs Chlorpromazine, thioridazine, and olanzapine	**Avoid.** Increases risk of orthostatic hypotension or bradycardia. *QE = High (Alpha blockers), Moderate (AChEIs, TCAs and antipsychotics); SR = Strong (AChEIs and TCAs), Weak (Alpha blockers and antipsychotics)*
Central Nervous System		
Chronic seizures or epilepsy	Bupropion Chlorpromazine Clozapine Maprotiline Olanzapine Thioridazine Thiothixene Tramadol	**Avoid.** Lowers seizure threshold; may be acceptable in patients with well-controlled seizures in whom alternative agents have not been effective. *QE = Moderate; SR = Strong*
Delirium	All TCAs Anticholinergics *(see online for full list)* Benzodiazepines Chlorpromazine Corticosteroids H_2-receptor antagonist Meperidine Sedative hypnotics Thioridazine	**Avoid.** Avoid in older adults with or at high risk of delirium because of inducing or worsening delirium in older adults; if discontinuing drugs used chronically, taper to avoid withdrawal symptoms. *QE = Moderate; SR = Strong*
Dementia & cognitive impairment	Anticholinergics *(see online for full list)* Benzodiazepines H_2-receptor antagonists Zolpidem Antipsychotics, chronic and as-needed use	**Avoid.** Avoid due to adverse CNS effects. Avoid antipsychotics for behavioral problems of dementia unless non-pharmacologic options have failed and patient is a threat to themselves or others. Antipsychotics are associated with an increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia. *QE = High; SR = Strong*
History of falls or fractures	Anticonvulsants Antipsychotics Benzodiazepines Nonbenzodiazepine hypnotics ■ Eszopiclone ■ Zaleplon ■ Zolpidem TCAs/SSRIs	**Avoid unless safer alternatives are not available; avoid anticonvulsants except for seizure.** Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls; shorter-acting benzodiazepines are not safer than long-acting ones. *QE = High; SR = Strong*
Insomnia	Oral decongestants ■ Pseudoephedrine ■ Phenylephrine Stimulants ■ Amphetamine ■ Methylphenidate ■ Pemoline Theobromines ■ Theophylline ■ Caffeine	**Avoid.** CNS stimulant effects. *QE = Moderate; SR = Strong*
Parkinson's disease	All antipsychotics (see online publication for full list, except for quetiapine and clozapine) Antiemetics ■ Metoclopramide ■ Prochlorperazine ■ Promethazine	**Avoid.** Dopamine receptor antagonists with potential to worsen parkinsonian symptoms. Quetiapine and clozapine appear to be less likely to precipitate worsening of Parkinson disease. *QE = Moderate; SR = Strong*

Table 2 (continued on page 7)

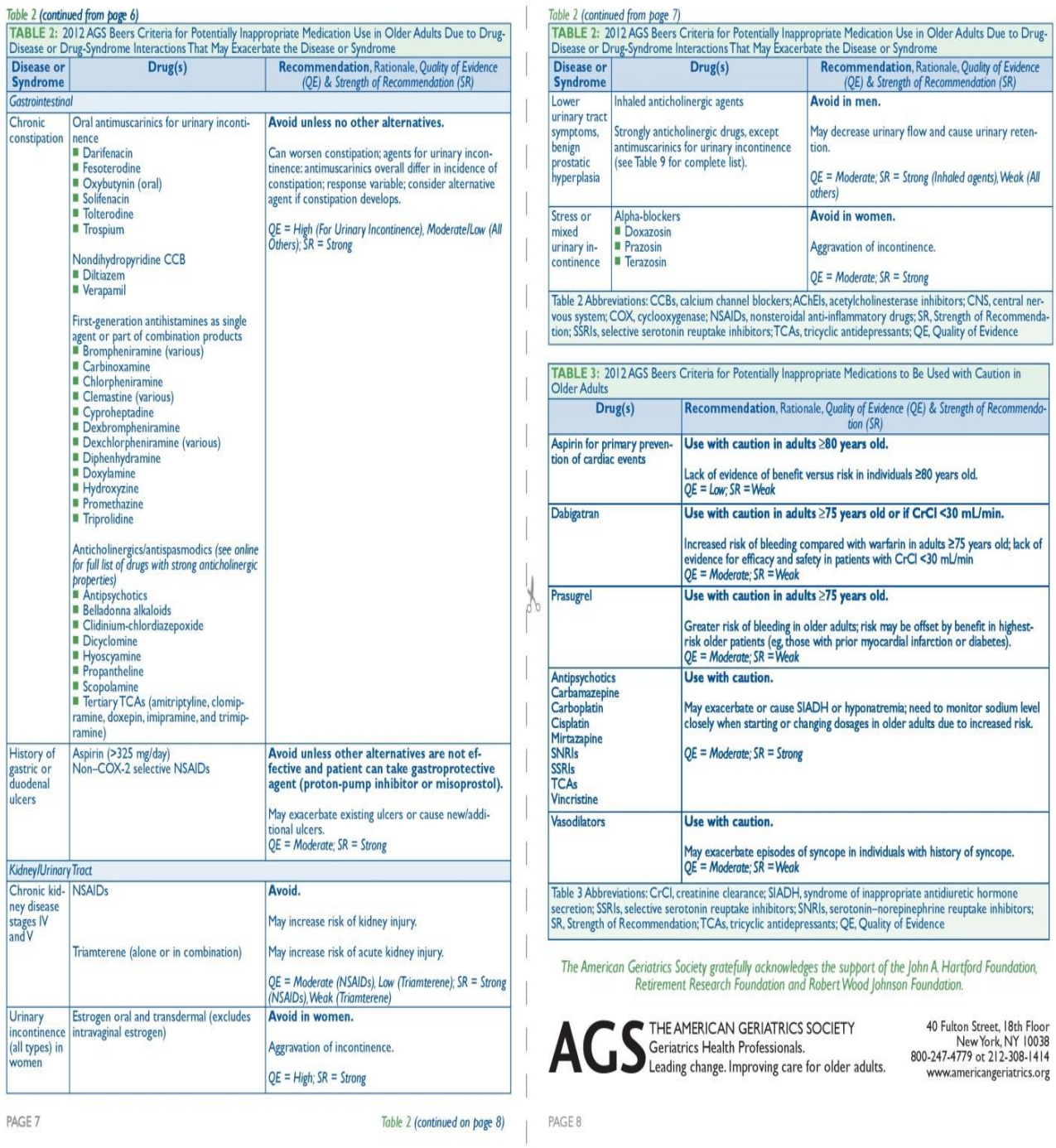


Table 2 (continued from page 6)

TABLE 2: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug-Disease or Drug-Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Recommendation, Rationale, *Quality of Evidence (QE) & Strength of Recommendation (SR)*
Gastrointestinal		
Chronic constipation	Oral antimuscarinics for urinary incontinence ■ Darifenacin ■ Fesoterodine ■ Oxybutynin (oral) ■ Solifenacin ■ Tolterodine ■ Trospium Nondihydropyridine CCB ■ Diltiazem ■ Verapamil First-generation antihistamines as single agent or part of combination products ■ Brompheniramine (various) ■ Carbinoxamine ■ Chlorpheniramine ■ Clemastine (various) ■ Cyproheptadine ■ Dexbrompheniramine ■ Dexchlorpheniramine (various) ■ Diphenhydramine ■ Doxylamine ■ Hydroxyzine ■ Promethazine ■ Triprolidine Anticholinergics/antispasmodics (*see online for full list of drugs with strong anticholinergic properties*) ■ Antipsychotics ■ Belladonna alkaloids ■ Clidinium-chlordiazepoxide ■ Dicyclomine ■ Hyoscyamine ■ Propantheline ■ Scopolamine ■ Tertiary TCAs (amitriptyline, clomipramine, doxepin, imipramine, and trimipramine)	**Avoid unless no other alternatives.** Can worsen constipation; agents for urinary incontinence: antimuscarinics overall differ in incidence of constipation; response variable; consider alternative agent if constipation develops. *QE = High (For Urinary Incontinence), Moderate/Low (All Others); SR = Strong*
History of gastric or duodenal ulcers	Aspirin (>325 mg/day) Non–COX-2 selective NSAIDs	**Avoid unless other alternatives are not effective and patient can take gastroprotective agent (proton-pump inhibitor or misoprostol).** May exacerbate existing ulcers or cause new/additional ulcers. *QE = Moderate; SR = Strong*
Kidney/Urinary Tract		
Chronic kidney disease stages IV and V	NSAIDs Triamterene (alone or in combination)	**Avoid.** May increase risk of kidney injury. May increase risk of acute kidney injury. *QE = Moderate (NSAIDs), Low (Triamterene); SR = Strong (NSAIDs), Weak (Triamterene)*
Urinary incontinence (all types) in women	Estrogen oral and transdermal (excludes intravaginal estrogen)	**Avoid in women.** Aggravation of incontinence. *QE = High; SR = Strong*

PAGE 7

Table 2 (continued on page 8)

Table 2 (continued from page 7)

TABLE 2: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug-Disease or Drug-Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Recommendation, Rationale, *Quality of Evidence (QE) & Strength of Recommendation (SR)*
Lower urinary tract symptoms, benign prostatic hyperplasia	Inhaled anticholinergic agents Strongly anticholinergic drugs, except antimuscarinics for urinary incontinence (see Table 9 for complete list).	**Avoid in men.** May decrease urinary flow and cause urinary retention. *QE = Moderate; SR = Strong (Inhaled agents), Weak (All others)*
Stress or mixed urinary incontinence	Alpha-blockers ■ Doxazosin ■ Prazosin ■ Terazosin	**Avoid in women.** Aggravation of incontinence. *QE = Moderate; SR = Strong*

Table 2 Abbreviations: CCBs, calcium channel blockers; AChEIs, acetylcholinesterase inhibitors; CNS, central nervous system; COX, cyclooxygenase; NSAIDs, nonsteroidal anti-inflammatory drugs; SR, Strength of Recommendation; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants; QE, Quality of Evidence

TABLE 3: 2012 AGS Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution in Older Adults

Drug(s)	Recommendation, Rationale, *Quality of Evidence (QE) & Strength of Recommendation (SR)*
Aspirin for primary prevention of cardiac events	**Use with caution in adults ≥80 years old.** Lack of evidence of benefit versus risk in individuals ≥80 years old. *QE = Low; SR = Weak*
Dabigatran	**Use with caution in adults ≥75 years old or if CrCl <30 mL/min.** Increased risk of bleeding compared with warfarin in adults ≥75 years old; lack of evidence for efficacy and safety in patients with CrCl <30 mL/min *QE = Moderate; SR = Weak*
Prasugrel	**Use with caution in adults ≥75 years old.** Greater risk of bleeding in older adults; risk may be offset by benefit in highest-risk older patients (eg, those with prior myocardial infarction or diabetes). *QE = Moderate; SR = Weak*
Antipsychotics Carbamazepine Carboplatin Cisplatin Mirtazapine SNRIs SSRIs TCAs Vincristine	**Use with caution.** May exacerbate or cause SIADH or hyponatremia; need to monitor sodium level closely when starting or changing dosages in older adults due to increased risk. *QE = Moderate; SR = Strong*
Vasodilators	**Use with caution.** May exacerbate episodes of syncope in individuals with history of syncope. *QE = Moderate; SR = Weak*

Table 3 Abbreviations: CrCl, creatinine clearance; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SSRIs, selective serotonin reuptake inhibitors; SNRIs, serotonin–norepinephrine reuptake inhibitors; SR, Strength of Recommendation; TCAs, tricyclic antidepressants; QE, Quality of Evidence

The American Geriatrics Society gratefully acknowledges the support of the John A. Hartford Foundation, Retirement Research Foundation and Robert Wood Johnson Foundation.

AGS THE AMERICAN GERIATRICS SOCIETY
Geriatrics Health Professionals.
Leading change. Improving care for older adults.

40 Fulton Street, 18th Floor
New York, NY 10038
800-247-4779 or 212-308-1414
www.americangeriatrics.org

PAGE 8

****Reference**

AGS 2012 Beers' Criteria Pocket Card. *The American Geriatrics Society.* Retrieved from http://www.americangeriatrics.org/files/documents/beers/PrintableBeersPocketCard.pdf.

Campanelli, C.M. (2012). American Geriatrics Society updated Beers' criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, *60*(4), 616-631.

ii STOPP Criteria

The following drug prescriptions are potentially inappropriate in persons aged ≥65years of age.
Cardiovascular System
1. Digoxin at a long-term dose >125 ag/day with impaired renal function
2. Loop diuretic for dependent ankle edema only; i.e. no clinical signs of heart failure (no evidence of efficacy, compression hosiery usually more appropriate).
3. Loop diuretic as first-line monotherapy for HTN (safer, more effective alternatives available).
4. Thiazide diuretic with a history of gout (may exacerbate gout).
5. Non-cardioselective Beta-blocker with Chronic Obstructive Pulmonary Disease (COPD) (risk of increased bronchospasm).
6. Beta-blocker in combination with verapamil (risk of symptomatic heart block).
7. Use of diltiazem or verapamil with NYHA Class III or IV heart failure (may worsen heart failure).
8. Calcium channel blockers with chronic constipation (may exacerbate constipation).
9. Use of aspirin and warfarin in combination without histamine H2 receptor antagonist (except cimetidine because of interaction with warfarin) or proton pump inhibitor (high risk of gastrointestinal bleeding).
10. Dipyridamole as monotherapy for cardiovascular secondary prevention (no evidence for efficacy).
11. Aspirin with a past history of peptic ulcer disease without histamine H2 receptor antagonist or Proton Pump Inhibitor (risk of bleeding).
12. Aspirin at dose >150 mg day (increased bleeding risk, no evidence for increased efficacy).
13. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event (not indicated).
14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease (not indicated).
15. Warfarin for first, uncomplicated deep venous thrombosis for longer than 6 months duration (no proven added benefit).
16. Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration (no proven benefit).
17. Aspirin, clopidogrel, dipyridamole, or warfarin with concurrent bleeding disorder (high risk of bleeding).
Central Nervous System and Psychotropic Drugs
18. Tricyclic antidepressants (TCA's) with dementia (risk of worsening cognitive impairment).
19. TCA's with glaucoma (likely to exacerbate glaucoma).
20. TCA's with cardiac conductive abnormalities (pro-arrhythmic effects).
21. TCA's with constipation (likely to worsen constipation).
22. TCA's with an opiate or calcium channel blocker (risk of severe constipation).
23. TCA's with prostatism or prior history of urinary retention (risk of urinary retention).
24. Long-term (i.e. >1 month), long-acting benzodiazepines e.g. chlordiazepoxide, flurazepam, nitrazepam, chlorazepate, and benzodiazepines with long-acting metabolites e.g. diazepam (risk of prolonged sedation, confusion, impaired balance, falls).
25. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics (risk of confusion, hypotension, extra-pyramidal side effects, falls).
26. Long-term neuroleptics (>1 month) in those with parkinsonism (likely to worsen extra-pyramidal symptoms)
27. Phenothiazines in patients with epilepsy (may lower seizure threshold).

28. Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity).
29. Selective serotonin re-uptake inhibitors (SSRI's) with a history of clinically significant hyponatremia (non-iatrogenic hyponatremia <130 mmol/L within the previous 2 months).
30. Prolonged use (>1 week) of first generation antihistamines i.e. diphenydramine, chlorpheniramine, cyclizine, promethazine (risk of sedation and anti-cholinergic side effects).
Gastrointestinal System
31. Diphenoxylate, loperamide, or codeine phosphate for treatment of diarrhea of unknown cause (risk of delayed diagnosis, may exacerbate constipation with overflow diarrhea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognized gastroenteritis).
32. Diphenoxylate, loperamide, or codeine phosphate for treatment of severe infective gastroenteritis i.e. bloody diarrhea, high fever, or severe systemic toxicity (risk of exacerbation or protraction of infection).
33. Prochlorperazine (Stemetil) or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonism).
34. PPI for peptic ulcer disease at full therapeutic dosage for >8 weeks (dose reduction or earlier discontinuation indicated).
35. Anticholinergic antispasmodic drugs with chronic constipation (risk of exacerbation of constipation).
Respiratory System
36. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).
37. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD (unnecessary exposure to long-term side-effects of systemic steroids).
38. Nebulized ipratropium with glaucoma (may exacerbate glaucoma).
Musculoskeletal System
39. Non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent histamine H2 receptor antagonist, PPI, or misoprostol (risk of peptic ulcer relapse).
40. NSAID with moderate-severe hypertension (risk of exacerbation of hypertension).
41. NSAID with heart failure (risk of exacerbation of heart failure).
42. Long-term use of NSAID (>3 months) for symptom relief of mild osteoarthritis (simple analgesics preferable and usually as effective for pain relief).
43. Warfarin and NSAID together (risk of gastrointestinal bleeding).
44. NSAID with chronic renal failure∗ (risk of deterioration in renal function).
45. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis or osteoarthritis (risk of major systemic corticosteroid side-effects).
46. Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol (allopurinol first choice prophylactic drug in gout)
Urogenital System
47. Bladder antimuscarinic drugs with dementia (risk of increased confusion, agitation).
48. Antimuscarinic drugs with chronic glaucoma (risk of acute exacerbation of glaucoma).
49. Antimuscarinic drugs with chronic constipation (risk of exacerbation of constipation).
50. Antimuscarinic drugs with chronic prostatism (risk of urinary retention).
51. Alpha-blockers in males with frequent incontinence i.e. one or more episodes of incontinence daily (risk of urinary frequency and worsening of incontinence).
52. Alpha-blockers with long-term urinary catheter in situ i.e. more than 2 months (drug not

indicated).
Endocrine System
53. Glibenclamide or chlorpropamide with type 2 diabetes mellitus (risk of prolonged hypoglycemia).
54. Beta-blockers in those with diabetes mellitus and frequent hypoglycemic episodes i.e. ≥1 episode per month (risk of masking hypoglycemic symptoms).
55. Estrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence)
56. Estrogens without progestogen in patients with intact uterus (risk of endometrial cancer).
Drugs that adversely affect fallers
57. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).
58. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).
59. First generation antihistamines (sedative, may impair sensorium).
60. Vasodilator drugs with persistent postural hypotension i.e. recurrent >20 mmHg drop in systolic blood pressure (risk of syncope, falls).
61. Long-term opiates in those with recurrent falls (risk of drowsiness, postural hypotension, vertigo).
Analgesic Drugs
62. Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain (WHO analgesic ladder not observed).
63. Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives (risk of severe constipation).
64. Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome (risk of exacerbation of cognitive impairment).
Duplicate Drug Classes
65. Any duplicate drug class prescription e.g. two concurrent opiates, NSAIDs, SSRIs, loop diuretics, ACE inhibitors (optimization of monotherapy within a single drug class should be observed prior to considering a new class of drug).

****Reference**

O'Mahony, D., Gallagher, P., Ryan, C., Byrne, S., Hamilton, H., Barry, P., O'Connor M., & Kennedy, J. (2010). STOPP & START criteria: A new approach to detecting potentially inappropriate prescribing in old age. *European Geriatric Medicine, 1*, 45–51.

Appendix B: Approval letters

i University of Waterloo

UNIVERSITY OF WATERLOO

OFFICE OF RESEARCH ETHICS

Notification of Ethics Clearance of Application to Conduct Research with Human Participants

---

Principal/Co-Investigator: Haya Al-Shamri	**Department:** pharmacy
Principal/Co-Investigator: Dr.Feng Chang	**Department:** pharmacy
Faculty Supervisor: Dr. Carlos Fernandez	**Department:** pharmacy
Faculty Supervisor: Dr. Leilei Zeng	**Department:** Statistics and Actuarial Science
Student Investigator: Haya Al-Shamri	**Department:** pharmacy

ORE File #: 19048

Project Title: Prevalence of Potentially Inappropriate Medications use in older patients admitted to Rural Hospitals.

This certificate provides confirmation the above project has been reviewed in accordance with the University of Waterloo's Guidelines for Research with Human Participants and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. This project has received ethics clearance through a University of Waterloo Research Ethics Committee.

***Note 1**: This ethics clearance is valid for one year from the date shown on the certificate and is renewable annually. Renewal is through completion and ethics clearance of the Annual Progress Report for Continuing Research (ORE Form 105).*

***Note 2**: This project must be conducted according to the application description and revised materials for which ethics clearance has been granted. All subsequent modifications to the project also must receive prior ethics clearance (i.e., Request for Ethics Clearance of a Modification, ORE Form 104) through a University of Waterloo Research Ethics Committee and must not begin until notification has been received by the investigators.*

***Note 3**: Researchers must submit a Progress Report on Continuing Human Research Projects (ORE Form 105) annually for all ongoing research projects or on the completion of the project. The Office of Research Ethics sends the ORE Form 105 for a project to the Principal Investigator or Faculty Supervisor for completion. If ethics clearance of an ongoing project is not renewed and consequently expires, the Office of Research Ethics may be obliged to notify Research Finance for their action in accordance with university and funding agency regulations.*

***Note 4**: Any unanticipated event involving a participant that adversely affected the participant(s) must be reported immediately (i.e., within 1 business day of becoming aware of the event) to the ORE using ORE Form 106. Any unanticipated or unintentional changes which may impact the research protocol must be reported within seven days of the deviation to the ORE using ORE form 107.*

[redacted]
Maureen Nummelin, PhD
Director, Office of Research Ethics

Sept 9/13
Date

OR
Susanne Santi, MMath
Senior Manager, Research Ethics

OR
Julie Joza, MPH
Manager, Research Ethics

ii South Bruce Grey Health Centre

South Bruce Grey Health Centre

"Your Health is the Centre of our Caring"

21 McGivern Street. Box 1300 **WALKERTON**. ON N0G 2V0 • Telephone: 519-881-1220 Fax 519-881-0452

December 20, 2013

Haya Mukhlef Al-Shamri
c/o Feng Chang
Assistant Professor
University of Waterloo School of Pharmacy
200 University Avenue West
Waterloo, Ontario
N2L 3G1

Dear Ms. Al-Shamri:

RE: Prevalence of Potentially Inappropriate Medication Use Among Admitted Geriatric Patients in Rural Hospitals

We are pleased to advise that your Application for Research noted above has been approved by our Ethics team.

A copy of the approved Application is attached for your records, and we look forward to meeting with you and seeing the results of your work.

Sincerely,

[redacted]

Paul Rosebush
President and CEO

Encl.

CHESLEY
39 – 2nd Street S.E.
Chesley, ON
N0G 1L0
Tel – 519-363-2340
Fax – 519-363-9871

DURHAM
320 College Street N.
P.O. Box 638
Durham, ON N0G 1R0
Tel – 519-369-2340
Fax – 519-369-6180

KINCARDINE
43 Queen Street
Kincardine, ON
N2Z 1G6
Tel – 519-396-3331
Fax – 519-396-3699

WALKERTON
21 McGivern Street
P.O. Box 1300
Walkerton, ON N0G 2V0
Tel – 519-881-1220
Fax – 519-881-0452

Appendix C: Consent Forms

i University of Waterloo

Information Consent Letter

University of Waterloo
Date: yy/mm/dd

Dear Sir/Madam:

This letter is an invitation to consider participating in a study that I am conducting as part of my Master's degree in Clinical Pharmacy at the University of Waterloo. I would like to provide you with more information about this project and what your involvement would entail if you decide to take part.

Certain medications that are prescribed to elderly patients can sometimes cause serious adverse effects, outweighing their benefits compared with other alternative treatments. Older adults tend to use multiple medications, and age-related physiological changes make some medications inappropriate. The purpose of this study, therefore, is to analyze the occurrence of inappropriate medication use among older patients.

The prevalence of the prescribing of these medications can be determined by reviewing patient profiles. In order to conduct this study, it will be necessary to review and analyze carefully your medical charts to find the required data such as: full name, age, medical diagnosis, home and admission medication lists. This information that has been collected upon admission for clinical purposes will be used again as research data in this study. Your permission to use your personal data will contribute to evaluating this problem and thus may then help to avoid any future predictable adverse drug reactions and medication problems for older adults.

All information you provide is considered completely confidential. Your name will not appear in any thesis or report resulting from this study. Data collected during this study will be stored in a secure place and only the principle investigator will have access to your data. There are no anticipated risks to you as a participant in this study.

If you have any further questions or require additional information regarding this study, please contact me at 519 -880-6191 or by email at halshamr@uwaterloo.ca. You can also contact my supervisor, Dr. Feng Chang at email feng.chang@uwaterloo.ca.

I would like to assure you that this study has been reviewed and has received ethics clearance through a University of Waterloo Research Ethics Committee. However, the final decision about participation is yours. If you have any comments or concerns resulting from your participation in this study, please contact Dr. Maureen Nummelin in the Office of Research Ethics at 1-519-888-4567, Ext. 36005 or maureen.nummelin@uwaterloo.ca.

I very much appreciate and thank you in advance for your assistance and participation in this project.

Yours Sincerely,
Haya Al-Shamri

Consent Form

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

I have read the information presented in the information letter about a study being conducted by Haya Al-Shamri of the Department of Clinical Pharmacy at the University of Waterloo. I have had the opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and any additional details I wanted.

I was informed that I may withdraw my consent at any time without penalty by advising the researcher.

This project has been reviewed by, and received ethics clearance through a University of Waterloo Research Ethics Committee. I was informed that if I have any comments or concerns resulting from my participation in this study, I may contact the Director, Office of Research Ethics at 519-888-4567 ext. 36005.

With full knowledge of all foregoing, I agree, of my own free will, to participate in this study.

☐YES ☐NO

Participant Name: _____ (Please print)

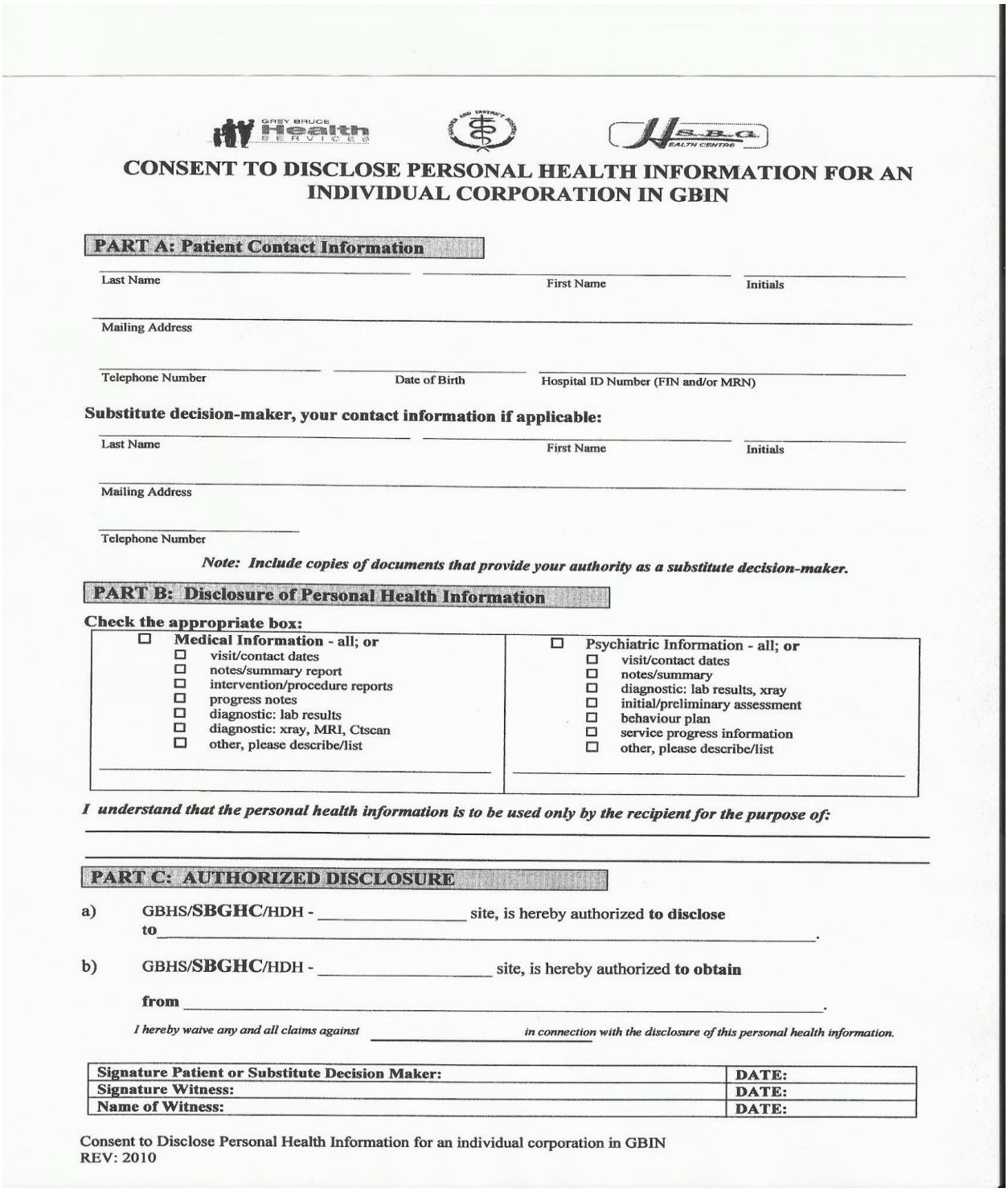
Participant Signature: _____

Witness Name: _____ (Please print)

Witness Signature: _____

Date: _____

ii South Bruce Grey Health Centre



CONSENT TO DISCLOSE PERSONAL HEALTH INFORMATION FOR AN INDIVIDUAL CORPORATION IN GBIN

PART A: Patient Contact Information

Last Name _____ First Name _____ Initials _____

Mailing Address _____

Telephone Number _____ Date of Birth _____ Hospital ID Number (FIN and/or MRN) _____

Substitute decision-maker, your contact information if applicable:

Last Name _____ First Name _____ Initials _____

Mailing Address _____

Telephone Number _____

Note: Include copies of documents that provide your authority as a substitute decision-maker.

PART B: Disclosure of Personal Health Information

Check the appropriate box:

☐ **Medical Information - all; or** ☐ visit/contact dates ☐ notes/summary report ☐ intervention/procedure reports ☐ progress notes ☐ diagnostic: lab results ☐ diagnostic: xray, MRI, Ctscan ☐ other, please describe/list _____	☐ **Psychiatric Information - all; or** ☐ visit/contact dates ☐ notes/summary ☐ diagnostic: lab results, xray ☐ initial/preliminary assessment ☐ behaviour plan ☐ service progress information ☐ other, please describe/list _____

I understand that the personal health information is to be used only by the recipient for the purpose of:

_____

_____

PART C: AUTHORIZED DISCLOSURE

a) GBHS/**SBGHC**/HDH - _____ site, is hereby authorized **to disclose to** _____.

b) GBHS/**SBGHC**/HDH - _____ site, is hereby authorized **to obtain from** _____.

I hereby waive any and all claims against _____ *in connection with the disclosure of this personal health information.*

Signature Patient or Substitute Decision Maker:	**DATE:**
Signature Witness:	**DATE:**
Name of Witness:	**DATE:**

Consent to Disclose Personal Health Information for an individual corporation in GBIN
REV: 2010

Appendix D: Feedback & Appreciation Letter

Feedback and Appreciation Letter

University of Waterloo
Date: yy/mm/dd

Dear Sir / Madam,

I would like to thank you for your participation in this study," Prevalence of Potentially Inappropriate Medications Prescribed for Geriatric Patients ".

This study is being conducted in the four hospitals of South Bruce Grey Health Centre in southwestern Ontario at Chesley, Durham, Kincardine, and Walkerton sites. The purpose of this study is to identify the use of potentially inappropriate medications. Data will be collected using patient medication chart review, and will contribute to measuring the prevalence of the use of these medications among older patients in rural areas. It is hoped that highlighting this problem will help to improve clinical services and reduce adverse drug events among older adults.

Please be assured that any data pertaining to you, personally will be kept confidential and private from the point of data collection. Also, you will not be identified in any way in any written reports coming out of this research. Once all the data are collected and analyzed for this project, I will provide you a summary of the results. Also, I am planning to share statistical information only with the research community through seminars, conferences, presentations, and journal articles.

It is anticipated that the study will be completed by April 30, 2014. In the meantime, if you have any questions about the study, please do not hesitate to contact me by email or telephone as noted below.

As with all University of Waterloo projects involving human participants, this project was reviewed by, and received ethics clearance through a University of Waterloo Research Ethics Committee. Should you have any comments or concerns resulting from your participation in this study, please contact Dr. Maureen Nummelin, the Director, Office of Research Ethics, at 1-519-888-4567, Ext. 36005 or maureen.nummelin@uwaterloo.ca.

Yours Sincerely,

Haya Al-Shamri
MSc. Pharmacy Candidate,
University of Waterloo
School of Pharmacy
Clinical Pharmacy Department
10 Victoria St. S., Kitchener, ON Ca. N2G1C5
519-880-6191
halshamr@uwaterloo.ca

Appendix E: Full Descriptive Data of Medications used by Patients

Drug Name	No. drugs	%	% of cases	No. of regular drug use	%
ASPIRIN	76	3.8%	43.2%	76	4.2%
ACHIS	10	0.5%	5.7%	10	0.5%
5-ARIS	7	0.3%	4.0%	7	0.4%
ANTICONVULSANT	26	1.3%	14.8%	26	1.4%
IMMUNOSUPPRESSANT	5	0.2%	2.8%	5	0.3%
ANTINEOPLASTIC 1	9	0.4%	5.1%	9	0.5%
ANTINEOPLASTIC 2	2	0.1%	1.1%	2	0.1%
ANTIPARKINSON	8	0.4%	4.5%	8	0.4%
ANTIMALARIAL	3	0.1%	1.7%	3	0.2%
ANTIGOUT	19	0.9%	10.8%	19	1.0%
ACEI	53	2.6%	30.1%	53	2.9%
ARBS	36	1.8%	20.5%	36	2.0%
PPI	79	3.9%	44.3%	79	4.3%
ANTIACID	10	0.5%	5.7%	7	0.4%
DIURETICS 1	95	4.7%	54.0%	158	8.7%
DIURETICS 2	27	1.3%	15.3%	26	1.4%
DIURETICS 3	5	0.2%	2.8%	5	0.3%
NSAIDS	37	1.8%	21.0%	24	1.3%
ACETAMINOPHEN	59	2.9%	33.5%	18	1.0%
OPIOIDS 1	53	2.6%	30.1%	26	1.4%
OPIOIDS 2	17	0.8%	9.7%	11	0.6%
OPIOIDS 3	2	0.1%	1.1%	1	0.1%
STATINS	83	4.1%	47.2%	84	4.6%
EZETIMIBE	14	0.7%	8.0%	13	0.7%
CHOLESTYRAMINE/FENOFIBRATE	4	0.2%	2.3%	4	0.2%
ANTIPSYCHOTIC 1	25	1.2%	14.2%	15	0.8%
ANTIPSYCHOTIC 2	2	0.1%	1.1%	2	0.1%
BENZODIAZEPINE 1	44	2.2%	25.0%	18	1.0%
BENZODIAZEPINE 2	6	0.3%	3.4%	4	0.2%
BENZODIAZEPINE 3	2	0.1%	1.1%	1	0.1%
SSRI	30	1.5%	17.0%	30	1.6%
SNRI	15	0.7%	8.5%	15	0.8%
TCA	11	0.5%	6.3%	10	0.5%
NON BENZODIAZEPINES	11	0.5%	6.3%	10	0.5%

TRAZODONE	20	1.0%	11.4%	19	1.0%
MIRTAZAPINE	9	0.4%	5.1%	9	0.5%
MUSCLE RELAXANTS	3	0.1%	1.7%	3	0.2%
CORTICOSTEROIDS	17	0.8%	9.7%	17	0.9%
BONE MODIFYING	3	0.1%	1.7%	3	0.2%
BETA BLOCKERS	60	3.0%	34.1%	60	3.3%
CCB 1	61	3.0%	34.7%	60	3.3%
CCB 2	1	0.0%	0.6%	1	0.1%
DIGOXIN	13	0.6%	7.4%	11	0.6%
ANTIHISTAMINE 1	28	1.4%	15.9%	6	0.3%
ANTIHISTAMINE 2	2	0.1%	1.1%	2	0.1%
ANTIMUSCURINIC	10	0.5%	5.7%	9	0.5%
ANTISPASMODIC	1	0.0%	0.6%	1	0.0%
ALPHA BLOCKER	14	0.7%	8.0%	13	0.7%
ANTIARRYTHMICS	2	0.1%	1.1%	2	0.1%
ONDASERTON	13	0.6%	7.4%	13	0.7%
INSULIN 1	15	0.7%	8.5%	15	0.8%
INSULIN 2	8	0.4%	4.5%	8	0.4%
METAFORMIN	36	1.8%	20.5%	35	1.9%
SULPHONYLUREA	13	0.6%	7.4%	13	0.7%
THIAZOLIDINEDIONE	3	0.1%	1.7%	3	0.2%
DPP-4 INHIBITORS	10	0.5%	5.7%	10	0.5%
GLUCAGON LIKE PEPTIDE	1	0.0%	0.6%	1	0.1%
FERROUS SUPPLEMENTS	25	1.2%	14.2%	25	1.4%
CALCIUM CARBONATE	27	1.3%	15.3%	26	1.4%
THIAMINE B1	4	0.2%	2.3%	4	0.2%
MAGNESIUM GLUCOHEPTONATE	15	0.7%	8.5%	15	0.8%
POTASSIUM CHLORIDE ER	20	1.0%	11.4%	20	1.1%
VITAMIN D3 & D2	76	3.8%	43.2%	76	4.2%
VITAMIN B 12	28	1.4%	15.9%	28	1.5%
VITAMIN C	13	0.6%	7.4%	13	0.7%
VITAMIN B6	1	0.0%	0.6%	1	0.1%
VITAMIN E	5	0.2%	2.8%	5	0.3%
VITAMINB COMPLEX	2	0.1%	1.1%	2	0.1%
MULTIVITAMIN	29	1.4%	16.5%	29	1.6%
FOLIC ACID	2	0.1%	1.1%	2	0.1%
BISPHOSPHONATE DERIVATIVE	18	0.9%	10.2%	18	1.0%
ANTIPLATELET	24	1.2%	13.6%	24	1.3%
ANTIBIOTIC	22	1.1%	12.5%	22	1.2%

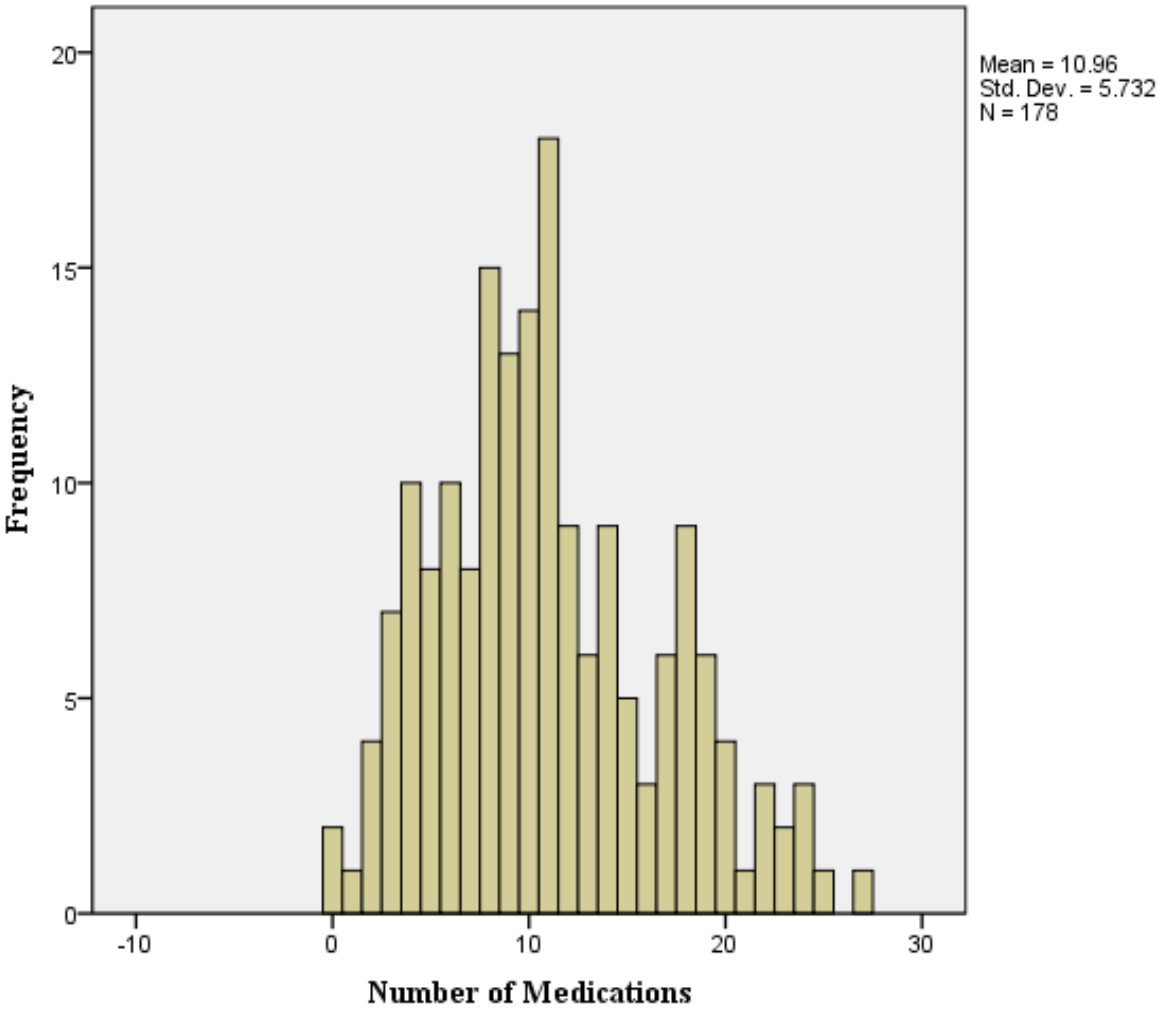
NITROGLYCERIN 1	31	1.5%	17.6%	17	0.9%
NITROGLYCERIN 2	7	0.3%	4.0%	3	0.2%
VASODILATOR	3	0.1%	1.7%	3	0.2%
LEVOTHYROXINE	45	2.2%	25.6%	45	2.5%
B2 AGONIST INH 1	38	1.9%	21.6%	18	1.0%
B2 AGONIST INH 2	11	0.5%	6.3%	1	0.1%
ANTICHOLENERGIC INH	22	1.1%	12.5%	22	1.2%
ANTICHOLENERGIC 2	1	0.0%	0.6%	1	0.1%
CORTICOSTEROID INH	29	1.4%	16.5%	29	1.6%
CORTICOSTEROID INH	1	0.0%	0.6%	1	0.1%
ESTROGEN CONJUGATED TOPICAL	2	0.1%	1.1%	2	0.1%
TOPICAL 1	24	1.2%	13.6%	24	1.3%
TOPICAL 2	6	0.3%	3.4%	5	0.3%
OPHTHALMIC 1	20	1.0%	11.4%	14	0.8%
OPHTHALMIC 2	5	0.2%	2.8%	5	0.3%
OPHTHALMIC 3	2	0.1%	1.1%	2	0.1%
LAXATIVE 1	65	3.2%	36.9%	60	3.3%
LAXATIVE 2	36	1.8%	20.5%	22	1.2%
LAXATIVE 3	9	0.4%	5.1%	5	0.3%
OTC 1	39	1.9%	22.2%	19	1.0%
OTC2	11	0.5%	6.3%	11	0.6%
OTC 3	2	0.1%	1.1%	2	0.1%
OTC 4	1	0.0%	0.6%	1	0.1%
ANTIDIARRHEAL	5	0.2%	2.8%	4	0.2%
SMOKING CESSATION AID	5	0.2%	2.8%	5	0.3%
ANTI-COAGULATION AGENTS	53	2.6%	30.1%	51	2.8%
OTHER	13	0.6%	7.4%	13	0.7%
TOTAL	2024	100.0%	1150.0%	1821	100.0%

AChIs; acetylcholinesterase inhibitors, CCB; calcium channel blocker, 5-ARIs s; 5α-reductase inhibitors, DPP-4Is; dipeptidyl peptidase 4 inhibitors, ACEI; angiotensin-converting enzyme inhibitors, ARBs; angiotensin II receptor blockers, PPI; proton-pump inhibitors, NSAIDs; nonsteroidal anti-inflammatory drugs, OTC; over the counter, SSRI; selective serotonin reuptake inhibitors, SNRI; serotonin and norepinephrine reuptake inhibitors

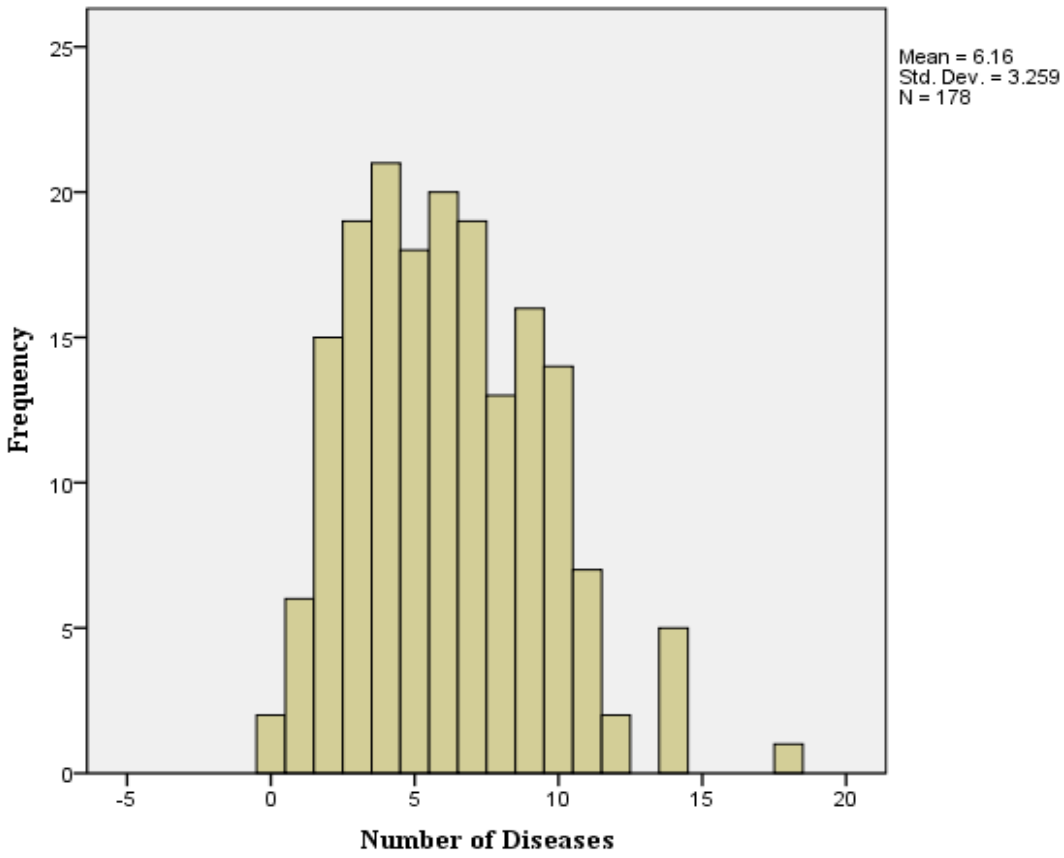
Number of medications per patient		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	2	1.1	1.1	1.1
	1	1	0.6	0.6	1.7
	2	4	2.2	2.2	3.9
	3	7	3.9	3.9	7.9
	4	10	5.6	5.6	13.5
	5	8	4.5	4.5	18.0
	6	10	5.6	5.6	23.6
	7	8	4.5	4.5	28.1
	8	15	8.4	8.4	36.5
	9	13	7.3	7.3	43.8
	10	14	7.9	7.9	51.7
	11	18	10.1	10.1	61.8
	12	9	5.1	5.1	66.9
	13	6	3.4	3.4	70.2
	14	9	5.1	5.1	75.3
	15	5	2.8	2.8	78.1
	16	3	1.7	1.7	79.8
	17	6	3.4	3.4	83.1
	18	9	5.1	5.1	88.2
	19	6	3.4	3.4	91.6
	20	4	2.2	2.2	93.8
	21	1	0.6	0.6	94.4
	22	3	1.7	1.7	96.1
	23	2	1.1	1.1	97.2
	24	3	1.7	1.7	98.9
	25	1	0.6	0.6	99.4
	27	1	0.6	0.6	100.0
	Total	178	100.0	100.0	

Appendix F: Histogram Charts

i Number of Medications



ii Number of Illnesses



Appendix G: Logistic Regression Outputs for "Enter Method"

i Beers' criteria

Case Processing Summary			
Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	178	100.0
	Missing Cases	0	0
	Total	178	100.0
Unselected Cases		0	0
Total		178	100.0

a. If weight is in effect, see classification table for the total number of cases.

- All cases were included in the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

- The table above gives the coding for the outcome variable.

Categorical Variables Codings

		Frequency	Parameter coding				
			(1)	(2)	(3)	(4)	(5)
Age	65-69	27	1.000	.000	.000	.000	.000
	70-74	31	.000	1.000	.000	.000	.000
	75-79	30	.000	.000	1.000	.000	.000
	80-84	35	.000	.000	.000	1.000	.000
	85-89	37	.000	.000	.000	.000	1.000
	90 and older	18	.000	.000	.000	.000	.000
Medications	1	24	.000	.000	.000		
	2	54	1.000	.000	.000		
	3	47	.000	1.000	.000		
	4	53	.000	.000	1.000		
Diseases	1	42	.000	.000	.000		
	2	39	1.000	.000	.000		
	3	52	.000	1.000	.000		
	4	45	.000	.000	1.000		
Gender	FEMALE	93	.000				
	MALE	85	1.000				

- The table above shows how the values of the categorical variable 'rank' were handled.

Block 0: Beginning Block

Classification Table[a,b]

Observed			Predicted		
			Beers		Percentage Correct
			0	1	
Step 0	Beers	0	0	66	.0
		1	0	112	100.0
	Overall Percentage				62.9

a. Constant is included in the model.

b. The cut value is 0.500.

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	0.529	0.155	11.614	1	0.001	1.697

Variables not in the Equation

Variables		Score	df	Sig.
Step 0	Male	0.611	1	0.434
	Overall age 90 and older as reference	12.694	5	0.026
	65-69	0.757	1	0.384
	70-74	2.044	1	0.153
	75-79	0.775	1	0.379
	80-84	0.000	1	0.993
	85-89	0.240	1	0.624
	Overall number of medications (0-4 medications as reference)	40.031	3	0.000
	5-9 medications	2.823	1	0.093
	10-13 medications	0.041	1	0.840
	≥14 medications	28.212	1	0.000
	Overall number of illnesses (0-3 illnesses as reference)	7.222	3	0.065
	4-5 illnesses	0.908	1	0.341
	6-8 illnesses	0.606	1	0.436
	≥9 illnesses	4.121	1	0.042
	Cardiovascular disease	0.466	1	0.495
	Neurological disease	9.231	1	0.002
	Gastrointestinal disease	0.631	1	0.427
	Respiratory disease	6.173	1	0.013
	Musculoskeletal disease	1.366	1	0.242
	Urogenital disease	6.802	1	0.009
	Kidney disease	1.099	1	0.294
	Endocrine disease	0.894	1	0.344
	Cancer and immune system diseases	0.823	1	0.364
	Overall Statistics	58.259	21	0.000

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	72.090	21	.000
	Block	72.090	21	.000
	Model	72.090	21	.000

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	6.126	8	0.633

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	162.646[a]	0.333	0.455

a. Estimation terminated at iteration number 6 because parameter estimates changed by less than 0.001.

Contingency Table for Hosmer and Lemeshow Test

		beers = 0		beers = 1		
		Observed	Expected	Observed	Expected	Total
Step 1	1	17	15.856	1	2.144	18
	2	12	13.310	6	4.690	18
	3	12	11.467	7	7.533	19
	4	9	8.237	9	9.763	18
	5	3	6.464	15	11.536	18
	6	7	5.022	11	12.978	18
	7	4	3.262	14	14.738	18
	8	1	1.564	17	16.436	18
	9	1	.661	17	17.339	18
	10	0	.158	15	14.842	15

Classification Table[a]

			Predicted		
			Beers		Percentage
	Observed		0	1	Correct
Step 1	beers	0	41	25	62.1
		1	16	96	85.7
	Overall Percentage				77.0

a. The cut value is 0.500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI EXP(B)	
Step 1[a]	Male	0.204	0.449	0.206	1	0.650	1.226	0.508	2.959
	Overall age 90 and older as reference			12.574	5	0.028			
	65-69	2.728	0.935	8.509	1	0.004	15.306	2.448	95.713
	70-74	2.812	0.892	9.928	1	0.002	16.638	2.894	95.648
	75-79	2.691	0.871	9.554	1	0.002	14.744	2.677	81.211
	80-84	1.634	0.808	4.090	1	0.043	5.124	1.052	24.963
	85-89	1.992	0.813	6.002	1	0.014	7.331	1.489	36.084
	Overall number of medications (0-4 medications as reference)			21.958	3	0.000			
	5-9 medications	1.218	0.646	3.552	1	0.059	3.382	0.952	12.006
	10-13 medications	1.703	0.689	6.113	1	0.013	5.493	1.423	21.195
	≥14 medications	3.959	0.869	20.741	1	0.000	52.384	9.535	287.785
	Overall number of illnesses (0-3 illnesses as reference)			0.954	3	0.812			
	4-5 illnesses	-0.533	0.644	0.683	1	0.408	0.587	0.166	2.075
	6-8 illnesses	-0.465	0.710	0.430	1	0.512	0.628	0.156	2.524
	≥9 illnesses	-0.805	0.914	0.776	1	0.378	0.447	0.074	2.682
	Cardiovascular disease	0.161	0.728	0.049	1	0.825	1.175	0.282	4.898
	Neurological disease	0.937	0.517	3.278	1	0.070	2.552	0.926	7.034
	Gastrointestinal disease	-0.689	0.499	1.909	1	0.167	0.502	0.189	1.334
	Respiratory disease	0.554	0.497	1.245	1	0.264	1.741	.657	4.610
	Musculoskeletal disease	0.043	0.469	0.008	1	0.927	1.044	0.417	2.616
	Urogenital disease	1.645	0.732	5.051	1	0.025	5.180	1.234	21.740
	Kidney disease	0.457	0.787	0.338	1	0.561	1.579	0.338	7.383
	Endocrine disease	0.066	0.452	0.022	1	0.883	1.069	0.440	2.593
	Cancer and immune system diseases	0.562	0.531	1.120	1	0.290	1.753	0.620	4.960
	Constant	-3.675	1.038	12.536	1	0.000	0.025		

ii STOPP criteria

Case Processing Summary			
Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	178	100.0
	Missing Cases	0	0
	Total	178	100.0
Unselected Cases		0	0
Total		178	100.0
a. If weight is in effect, see classification table for the total number of cases.			

- All cases were included in the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

- The table above gives the coding for the outcome variable.

Categorical Variables Codings

		Frequency	Parameter coding				
			(1)	(2)	(3)	(4)	(5)
Age	65-69	27	1.000	.000	.000	.000	.000
	70-74	31	.000	1.000	.000	.000	.000
	75-79	30	.000	.000	1.000	.000	.000
	80-84	35	.000	.000	.000	1.000	.000
	85-89	37	.000	.000	.000	.000	1.000
	90 and older	18	.000	.000	.000	.000	.000
Medications	1	24	.000	.000	.000		
	2	54	1.000	.000	.000		
	3	47	.000	1.000	.000		
	4	53	.000	.000	1.000		
Diseases	1	42	.000	.000	.000		
	2	39	1.000	.000	.000		
	3	52	.000	1.000	.000		
	4	45	.000	.000	1.000		
Gender	FEMALE	93	.000				
	MALE	85	1.000				

- The table above shows how the values of the categorical variable ‘rank’ were handled.

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			stopp		Percentage
	Observed		0	1	Correct
Step 0	STOPP	0	0	55	0
		1	0	123	100.0
	Overall Percentage				69.1

a. Constant is included in the model.

b. The cut value is 0.500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	0.805	0.162	24.619	1	0.000	2.236

Variables not in the Equation

Variables		Score	df	Sig.
Step 0	Male	0.541	1	0.462
	Overall age 90 and older as reference	5.650	5	0.342
	65-69	0.369	1	0.544
	70-74	2.343	1	0.126
	75-79	0.014	1	0.907
	80-84	0.006	1	0.940
	85-89	0.393	1	0.531
	Overall number of medications (0-4 medications as reference)	31.268	3	0.000
	5-9 medications	0.667	1	0.414
	10-13 medications	0.831	1	0.362
	≥14 medications	22.516	1	0.000
	Overall number of illnesses (0-3 illnesses as reference)	7.934	3	0.047
	4-5 illnesses	0.000	1	0.984
	6-8 illnesses	1.197	1	0.274
	≥9 illnesses	2.124	1	0.145
	Cardiovascular disease	0.599	1	0.439
	Neurological disease	7.004	1	0.008
	Gastrointestinal disease	1.299	1	0.254
	Respiratory disease	8.281	1	0.004
	Musculoskeletal disease	5.737	1	0.017
	Urogenital disease	12.319	1	0.000
	Kidney disease	1.215	1	0.270
	Endocrine disease	0.112	1	0.738
	Cancer and immune system diseases	1.349	1	0.245
	Overall Statistics	50.813	21	0.000

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	65.489	21	0.000
	Block	65.489	21	0.000
	Model	65.489	21	0.000

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	6.175	8	0.628

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	154.622[a]	0.308	0.434

a. Estimation terminated at iteration number 6 because parameter estimates changed by less than 0.001.

Contingency Table for Hosmer and Lemeshow Test

		STOPP = 0		STOPP = 1		
		Observed	Expected	Observed	Expected	Total
Step 1	1	14	14.367	4	3.633	18
	2	13	11.300	5	6.700	18
	3	8	9.665	10	8.335	18
	4	5	7.265	13	10.735	18
	5	8	5.389	10	12.611	18
	6	4	3.539	14	14.461	18
	7	2	2.081	16	15.919	18
	8	0	0.897	18	17.103	18
	9	1	0.436	17	17.564	18

Classification[a]

			Predicted		
			stopp		Percentage
	Observed		0	1	Correct
Step 1	stopp	0	35	20	63.6
		1	17	106	86.2
	Overall Percentage				79.2

a. The cut value is .500

	10	0	0.061	16	15.939	16

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI for EXP(B)	
								Lower	Upper
Step 1[a]	Male	0.131	0.452	0.084	1	0.772	1.140	0.470	2.765
	Overall age 90 and older as reference			7.646	5	0.177			
	65-69	2.128	0.919	5.362	1	0.021	8.395	1.387	50.828
	70-74	2.184	0.885	6.084	1	0.014	8.881	1.566	50.365
	75-79	1.734	0.850	4.160	1	0.041	5.662	1.070	29.960
	80-84	1.122	0.806	1.937	1	0.164	3.071	0.633	14.909
	85-89	1.209	0.795	2.314	1	0.128	3.352	0.706	15.920
	Overall number of medications (0-4 medications as reference)			12.909	3	0.005			
	5-9 medications	0.723	0.601	1.445	1	0.229	2.060	0.634	6.691
	10-13 medications	0.880	0.631	1.946	1	0.163	2.412	0.700	8.309
	≥14 medications	3.078	0.871	12.487	1	0.000	21.722	3.939	119.788
	Overall number of illnesses (0-3illnesses as reference)			2.782	3	0.426			
	4-5 illnesses	.105	0.636	0.027	1	0.868	1.111	0.319	3.868
	6-8 illnesses	-0.304	0.744	0.167	1	0.683	0.738	0.172	3.174
	≥9 illnesses	-1.314	1.006	1.706	1	0.192	0.269	0.037	1.931
	Cardiovascular disease	-0.013	0.719	0.000	1	0.985	0.987	0.241	4.036
	Neurological disease	1.104	0.554	3.974	1	0.046	3.016	1.019	8.928
	Gastrointestinal disease	-0.242	0.514	0.221	1	0.638	0.785	0.287	2.152
	Respiratory disease	0.897	0.561	2.554	1	0.110	2.451	0.816	7.360
	Musculoskeletal disease	0.732	0.499	2.148	1	0.143	2.079	0.781	5.530
	Urogenital disease	2.807	0.952	8.688	1	0.003	16.554	2.561	107.014
	Kidney disease	1.192	0.918	1.686	1	0.194	3.295	0.545	19.931
	Endocrine disease	-0.173	0.477	0.132	1	0.717	0.841	0.330	2.142
	Cancer and immune system diseases	-0.556	0.519	1.144	1	0.285	0.574	0.207	1.588
	Constant	-2.299	0.952	5.832	1	0.016	0.100		

iii Combined criteria

Case Processing Summary			
Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	178	100.0
	Missing Cases	0	0
	Total	178	100.0
Unselected Cases		0	0
Total		178	100.0
a. If weight is in effect, see classification table for the total number of cases.			

- All cases were included in the analysis.

Dependent Variable Encoding

Original Value	Internal Value
0	0
1	1

- The table above gives the coding for the outcome variable.

Categorical Variables Codings

		Frequency	Parameter coding				
			(1)	(2)	(3)	(4)	(5)
Age	65-69	27	1.000	.000	.000	.000	.000
	70-74	31	.000	1.000	.000	.000	.000
	75-79	30	.000	.000	1.000	.000	.000
	80-84	35	.000	.000	.000	1.000	.000
	85-89	37	.000	.000	.000	.000	1.000
	90 and older	18	.000	.000	.000	.000	.000
Medications	1	24	.000	.000	.000		
	2	54	1.000	.000	.000		
	3	47	.000	1.000	.000		
	4	53	.000	.000	1.000		
Diseases	1	42	.000	.000	.000		
	2	39	1.000	.000	.000		
	3	52	.000	1.000	.000		
	4	45	.000	.000	1.000		
Gender	FEMALE	93	.000				
	MALE	85	1.000				

- The table above shows how the values of the categorical variable ‘rank’ were handled.

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			beersstopp		Percentage
	Observed		0	1	Correct
Step 0	beersstopp	0	0	48	0
		1	0	130	100.0
	Overall Percentage				73.0

a. Constant is included in the model.

b. The cut value is 0.500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	0.996	0.169	34.800	1	000	2.708

Variables not in the Equation				
Variables		Score	df	Sig.
Step 0	Male	1.758	1	0.185
	Overall age 90 and older as reference	5.757	5	0.331
	65-69	0.364	1	0.546
	70-74	2.239	1	0.135
	75-79	0.242	1	0.623
	80-84	0.057	1	0.811
	85-89	0.709	1	0.400
	Overall number of medications (0-4 medications as reference)	31.629	3	0.000
	5-9 medications	0.279	1	0.597
	10-13 medications	0.016	1	0.901
	≥14 medications	17.396	1	0.000
	Overall number of illnesses (0-3illnesses as reference)	8.237	3	0.041
	4-5 illnesses	0.039	1	0.844
	6-8 illnesses	1.260	1	0.262
	≥9 illnesses	2.582	1	0.108
	Cardiovascular disease	0.412	1	0.521
	Neurological disease	7.119	1	0.008
	Gastrointestinal disease	2.814	1	0.093
	Respiratory disease	6.803	1	0.009
	Musculoskeletal disease	6.512	1	0.011
	Urogenital disease	9.486	1	0.002
	Kidney disease	0.603	1	0.438
	Endocrine disease	0.082	1	0.775
	Cancer and immune system diseases	0.015	1	0.902
	Overall Statistics	47.228	21	0.001

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	56.565	21	0.000
	Block	56.565	21	0.000
	Model	56.565	21	0.000

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	6.602	8	0.580

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	150.956[a]	0.272	0.395

a. Estimation terminated at iteration number 6 because parameter estimates changed by less than 0.001.

Contingency Table for Hosmer and Lemeshow Test

		beersstopp = 0		beersstopp = 1		
		Observed	Expected	Observed	Expected	Total
Step 1	1	16	13.503	2	4.497	18
	2	9	10.587	9	7.413	18
	3	5	7.709	13	10.291	18
	4	5	5.655	13	12.345	18
	5	6	4.336	12	13.664	18
	6	4	2.898	14	15.102	18
	7	1	1.756	17	16.244	18
	8	1	0.971	17	17.029	18
	9	1	0.477	17	17.523	18
	10	0	0.108	16	15.892	16

Classification Table[a]

			Predicted		
			beersstopp		Percentage
	Observed		0	1	Correct
Step 1	beersstopp	0	27	21	56.3
		1	13	117	90.0
	Overall Percentage				80.9

a. The cut value is 0.500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI EXP(B)	
								Lower	Upper
Step 1[a]	Male	0.411	0.461	0.796	1	0.372	1.508	0.612	3.719
	Overall age 90 and older as reference			5.984	5	0.308			
	65-69	1.736	0.910	3.638	1	0.056	5.674	0.953	33.771
	70-74	1.784	0.871	4.191	1	0.041	5.952	1.079	32.833
	75-79	1.490	0.835	3.184	1	0.074	4.438	0.864	22.807
	80-84	0.722	0.774	0.870	1	0.351	2.059	0.451	9.387
	85-89	0.855	0.762	1.260	1	0.262	2.352	0.528	10.477
	Overall # medications (0-4 medications as reference)			12.751	3	0.005			
	5-9 medications	1.101	0.603	3.332	1	0.068	3.007	0.922	9.807
	10-13 medications	1.361	0.636	4.574	1	0.032	3.899	1.120	13.571
	≥ 14 medications	3.031	0.851	12.679	1	0.000	20.728	3.907	109.964
	Overall number of illnesses (0-3 illnesses as reference)			1.646	3	0.649			
	4-5 illnesses	-0.153	0.649	0.055	1	0.814	0.859	0.241	3.063
	6-8 illnesses	-0.345	0.737	0.219	1	0.640	0.708	0.167	3.002
	≥9 illnesses	-1.135	0.981	1.341	1	0.247	0.321	0.047	2.196
	Cardiovascular disease	0.036	0.744	0.002	1	0.961	1.037	0.241	4.455
	Neurological disease	1.031	0.577	3.192	1	0.074	2.804	0.905	8.690
	Gastrointestinal disease	-0.002	0.519	0.000	1	0.997	0.998	0.361	2.758
	Respiratory disease	0.704	0.566	1.549	1	0.213	2.022	0.667	6.127
	Musculoskeletal disease	0.865	0.502	2.969	1	0.085	2.375	0.888	6.352
	Urogenital disease	2.273	0.936	5.894	1	0.015	9.712	1.550	60.870
	Kidney disease	0.507	0.869	0.340	1	0.560	1.660	0.302	9.119
	Endocrine disease	-0.096	0.484	0.040	1	0.842	0.908	0.352	2.344
	Cancer and immune system diseases	-0.074	0.536	0.019	1	0.890	0.929	0.325	2.657
	Constant	-2.256	0.960	5.520	1	0.019	0.105		