BEERS CRITERIA-BASED REVIEW OF MEDICATION APPROPRIATENESS IN BRITISH COLUMBIA SENIORS LIVING IN RESIDENTIAL CARE

by

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ABSTRACT

A study was conducted to explore the prevalence and predictors of inappropriate prescribing, as defined by the 2002 Beers criteria, in a sample of nursing home residents in British Columbia, Canada (n=449). Medication-related data were extracted from residents' medication review letters. The overall prevalence of inappropriate prescribing was 29.4 percent. The prevalence rates for the three sub-types of inappropriate prescribing, namely unconditionally inappropriate prescribing, inappropriate drug-disease combinations, and inappropriate doses or durations, were 16.9, 12.4, and 5.1 percent, respectively. The likelihood of inappropriate prescribing was increased with the total number of prescription medications and the number of prescribing physicians. The single most commonly prescribed inappropriate medication was anticholinergics for residents with cognitive impairment. Clinicians need to be extra vigilant to distinguish between the central nervous system effects of anticholinergic medications and the effects of the underlying disease.

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LIST OF ABBREVIATIONS

ADR	adverse drug reaction
CNS	central nervous system
GI	gastrointestinal
LTC	long-term care
MAOI	monoamine oxidase inhibitor
NSAID	non-steroidal anti-inflammatory drug
PRN	'pro re nata' or 'as needed'
SIADH	syndrome of inappropriate antidiuretic hormone secretion
SSRI	Selective Serotonin Reuptake Inhibitor
TCA	tricyclic antidepressant

DEFINITIONS

Beers criteria	A list of medications developed by a consensus panel led by geriatrician Dr. Mark Beers that serves as an explicit method for identifying inappropriate medications in the elderly population; there are three versions of the Beers criteria – the original criteria was developed in 1991, then later revised in 1997 and 2002
Explicit methods	Methods for assessing medication appropriateness based on applying standardized guidelines on medication use to a particular patient group
Implicit methods	Methods for assessing medication appropriateness based on an individual clinician's judgment applied to an individual patient
Resident	In this study, a person who lives in and receives care in a licensed residential care facility; the term resident will be used interchangeably with patient
Residential care facility [1]	A residence licensed under *The Community Care and Assisted Living Act* (British Columbia Ministry of Health Services, 2002) to provide care to seven or more persons
Unconditionally inappropriate medication	The subset of medications considered inappropriate for the elderly regardless of dose, frequency, or duration

[1] As defined by Bylaw 7 of the College of Pharmacists of British Columbia (2001)

CHAPTER 1: INTRODUCTION

Medication use amongst older adults

Older adults represent approximately 13 percent of the population (Statistics Canada, 2004), but consume 28-40 percent of all prescription medications (Chrischilles et al., 1992; Tamblyn & Perreault, 2000; British Columbia Ministry of Health Services, 2004b). In British Columbia, persons under the age of 65 fill an average of 10.4 prescriptions per year, while persons over the age of 65 who reside in the community setting fill an average of 15.98 prescriptions per year (British Columbia Ministry of Health Services, 2004b). One of the reasons seniors need to take multiple medications is that they are treating multiple chronic health conditions or comorbidities. In British Columbia, it is estimated that 36 percent of adults and 68 percent of adults aged 65 and older have at least one chronic condition. Approximately 30 percent of British Columbia adults aged 18 and over who have a chronic condition are said to have high or very high comorbidity because they have at least six or more additional chronic conditions (Centre for Health Services and Policy Research, 2005). The British Columbia Ministry of Health Services (2004a) reports that 45 percent of seniors take three to six medications for distinct health purposes, while 23 percent of seniors in British Columbia take seven to ten medications for distinct health purposes.

Approximately six percent of the B.C. population reside in a long-term care setting (British Columbia Ministry of Health Services, 2003). This subset of the population is often frail, has multiple chronic conditions, and is potentially more susceptible to the adverse effects of medications than their community-dwelling

counterparts. Medication use in the long-term care setting is high, where residents receive an average of seven to twelve different medications per day (Chutka, Takahashi, & Hoel, 2004; Dhalla et al., 2002). A number of studies have raised concerns over the appropriateness of prescribing amongst seniors living in residential care facilities. Researchers examining the use of medications in the residential care setting in both Canada and the United States over the past five years have found potentially inappropriate medication in 14.9 to 54.7 percent of residents (Dhalla et al., 2002; Gill, Misiaszek, & Brymer, 2001; Rancourt et al., 2004; Dhall, Larrat, & Lapane, 2002). Although methodological differences are likely responsible for these widely varying estimates, the above studies all highlight the potential to improve the use of medications in seniors living in long-term care.

To date, most studies on potentially inappropriate prescribing in older adults have been conducted on administrative claims databases. These databases do not contain information on the older adult's medical conditions. This study includes information on medical conditions in the analyses, and thereby expands previous research by examining the prevalence of inappropriate prescribing in older persons known to have specific medical conditions.

Significance of medication appropriateness in older adults

Adverse drug reactions

Every medication has benefits and risks associated with its use. On one hand, the potential benefits of medication use include curing a medical condition, eliminating or reducing the symptoms associated with a medical condition, and/or arresting or slowing disease processes. On the other hand, the potential risks of medication use include adverse drug reactions (ADRs). The World Health Organization (2002) defines an ADR

as "any response to a drug that is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis, or therapy of disease".[2] Edwards and Aronson (2000) build on this definition by suggesting that an ADR must be of sufficient severity to warrant "prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product".

ADRs are a significant cause of morbidity in the older adult population. Estimates of the incidence of ADRS in the older outpatient population range from 5 percent to 35 percent (Chrischilles, Segar, & Wallace, 1992; Gurwitz et al., 2003; Hanlon et al., 1997). An analysis of Health Canada's adverse drug reaction database in 2005 revealed that 3,300 seniors die every year due to adverse drug reactions (Canadian Broadcasting Centre, 2005). In the nursing home setting, Gurwitz et al. (2000) identified 546 adverse drug reactions in 2916 nursing home residents (18.7 percent) over a 12-month observation period. Studies have shown that ADRs are responsible for 18 percent to 24 percent of hospital admissions involving older adults (Mannesse, Derkx, de Ridder, Man in 't Veld AJ, & van der Cammen, 2000; Renteln-Kruse, Thiesemann, Thiesemann, & Meier-Baumgartner, 2000).

Among the community-dwelling elderly population, it has been estimated that 27.6 percent of ADRs are preventable (Gurwitz et al., 2003). Among the elderly nursing home population, it has been estimated that 51 percent are preventable; of these, 68 percent could have been avoided by ensuring that the medications ordered and the doses were appropriate for the elderly (Gurwitz et al., 2000). In other words, targeting medication appropriateness prevents significant medication-related morbidity in the older adult population.

[2] The WHO definition does not include error as a source of ADRs.

Factors leading to an increased risk of ADRs in the older adult population

Older adults are at greater risk for experiencing an ADR due to one or more of the following reasons. First, older adults experience physiological changes with aging that can impair the metabolism and excretion of medications. Second, older adults may experience increased sensitivity to certain medications. Third, older adults tend to be on multiple medications to treat multiple medical conditions. Therefore, the likelihood that they will experience a clinically significant drug-drug interaction is increased.

Pharmacokinetic changes associated with aging

Pharmacokinetics are the processes by which drug absorption, metabolism, distribution, and elimination occur in the body (Makoid, Vuchetich, & Banakar, 2000). Some of the physiological changes associated with aging that have pharmacokinetic consequences will be outlined below, as these should be taken into consideration when prescribing in the elderly. In general, the absorption of medications is minimally affected in the elderly. The distribution of drugs, however, is altered in the general population of older adults who experience a decrease in the relative amount of lean muscle mass and an increase in the relative proportion of body fat as they age. As a result of the altered muscle to fat ratio, the body stores of water-soluble drugs are diminished, while the body stores of lipid-soluble drugs are expanded. Lipid-soluble drugs such as benzodiazepines are more likely to accumulate in the body of older adults, resulting in ADRs such as falls, impaired alertness, drowsiness, and confusion (Pollock, 1998). One specific example is the long-acting benzodiazepine diazepam, which remains in the body four to five times longer in an older adult compared to a younger adult (Maletta, 1996), and is often considered inappropriate in the elderly (McLeod, Huang, Tamblyn, & Gayton, 1997).

The metabolism of drugs is dependent on liver function. Aged-related changes in liver function that occur in the general older adult population include a decrease in

functional liver volume and a decrease in hepatic blood flow (Cherry & Morton, 1989). In general, age-related changes in hepatic function do not significantly alter the metabolism of drugs (Linjakumpu, 2003). Instead, hepatic metabolism is most significantly affected in persons with hepatic diseases. However, the metabolism of drugs can be impaired if two or more concurrent medications overload the same metabolic pathway. For example, drugs known to inhibit or induce cytochrome P450 enzyme pathways in hepatic metabolism can lead to clinically significant drug-drug interactions.

The efficiency of the renal elimination of medications is diminished in the older adult because of a decreased rate of glomerular filtration in the kidneys. By the age of 65, the glomerular filtration rate has decreased on average by 30 percent (Correia & Castagnoli, 1989). This can affect the clearance of many drugs, including water-soluble antibiotics, diuretics, digoxin, water-soluble beta-blockers, lithium, and nonsteroidal anti-inflammatory drugs (Mangoni & Jackson, 2004). This pharmacokinetic change becomes particularly significant when the medication an older adult is taking has a narrow therapeutic window. Drugs with narrow therapeutic windows, such as aminoglycoside antibiotics, digoxin, and lithium, must be carefully administered and monitored in the elderly because of the narrow range between the dose that produces the intended therapeutic effect and the dose that produces ADRs. Serious ADRs are likely to occur if these drugs accumulate only marginally more than intended.

Pharmacodynamic changes associated with aging

Pharmacodynamics concern the manner in which drugs react with the body once they have been absorbed (Linjakumpu, 2003). Pharmacodynamic changes associated with aging are less well characterized than the pharmacokinetic changes. However, it is known that the cardiovascular system, the central nervous system, and homeostatic mechanisms (e.g. postural hypotension) are mainly affected. One example of a

pharmacodynamic change affecting older adults is the diminished function of beta-receptors. This leads to a muted response to both the beta-agonist salbutamol and the beta-blocker propranolol (Mangoni et al., 2004). Older adults also experience an increased sensitivity to the central nervous system side effects of benzodiazepines (Maletta, 1996). The exact mechanism responsible for this is unknown.

Polypharmacy

There are various definitions of polypharmacy. In the strictest sense, it is defined as the concurrent use of two or more medications. However, the use of multiple medications is often warranted because a patient has multiple medical conditions. Therefore, some researchers and clinicians have moved away from a numerical definition of polypharmacy to an alternative definition of polypharmacy as the administration or use of more medications than are clinically indicated (Jackson, Mangoni, & Batty, 2004). Polypharmacy is associated with an increased chance of interaction(s) between the drugs. There is a strong positive correlation between ADRs and the number of drugs prescribed (Field et al., 2001; Hajjar et al., 2003). The overuse of psychoactive medications in the elderly is of particular concern (Tamblyn et al., 1994; Pollock, 1998).

Defining medication appropriateness in the elderly

Criteria for determining medication appropriateness in older adults

The goal of pharmacological treatment is to maximize the therapeutic benefits of medications while minimising the risks or potential risks of an adverse drug reaction. Studies of medication appropriateness in the older adult population have focused on one or more of the following facets of appropriateness/inappropriateness:

1) Is the medication inappropriate for the older adult population in general?
2) Is the medication appropriate (i.e. indicated) for treating a particular patient's medical condition?
3) Is the medication appropriate (i.e. neither insufficient nor excessive) in dose, frequency (e.g. two times a day), and duration?
4) Is the medication inappropriate given a particular patient's other concurrent medical conditions (i.e. is there a drug-disease interaction)?
5) Is the medication inappropriate given a particular patient's other concurrent medications (i.e. is there a drug-drug interaction)?
6) Is the medication inappropriate given a particular patient's allergies?
7) Are there two or more medications intended to achieve the same therapeutic outcome (i.e. potential therapeutic duplication)? If so, are both medications necessary, or can one be eliminated while achieving the same desired effect?
8) Does the patient have a medical condition that is not being treated but could potentially be ameliorated with pharmacological treatment?
9) Is the medication cost-effective?

"Errors of commission'" occur when medications are prescribed that are inappropriate (e.g. numbers 4 and 5 above), while "errors of omission" occur when necessary drugs are not prescribed (e.g. number 8 above).

Determining medication appropriateness in older adults is particularly challenging due to a dearth of high-quality evidence for prescribing in the elderly. Clinical trials often exclude older adults, or only include those who are relatively young and healthy (Rochon, Berger, & Gordon, 1998). Therefore, their results cannot be generalized to the older adult population. One method of overcoming this problem is for clinicians to make judgments about the potential benefits versus risks of pharmacological treatment on an individual basis. Another method of overcoming this problem is for clinicians and/or researchers to make judgments about the potential benefits and risks of pharmacological treatment on a population basis, then generate and apply a standardized set of rules on medication use to a particular patient group. The former method has been labelled as 'implicit' while the latter has been labelled as 'explicit' (Shelton, Fritsch, & Scott, 2000). Medication assessment tools based on implicit methods, explicit methods, or a

combination of both may be employed by clinicians to facilitate optimal prescribing for the elderly.

Implicit methods

Implicit methods of determining medication appropriateness rely on clinicians to use their professional judgment to evaluate each patient's medications on an individual basis. Practitioners who conduct individualized medication reviews can take the patient's preferences, clinical history, and medical needs into consideration. Before dispensing a medication to a long-term care resident, the College of Pharmacists of British Columbia (2001) requires pharmacists to review the patient record to identify any drug interactions, allergies, therapeutic duplication, contraindicated medications, unintended dosage changes, inappropriate drug therapy, unusual dosages, or any other potential drug-related problems which may adversely affect the resident. Every six months, the pharmacist is required to review each resident's medication regimen with the prescribing doctor when available and a registered nurse if one is employed by the residential care facility. Where the resident's physician does not attend the resident's medication review, the pharmacist must communicate the review recommendations to the physician and receive authorization to continue dispensing the medications. Implicit reviews have been criticized as being unreliable since they rely too heavily on the expertise of the individual clinician. Although tools are available to assist clinicians in performing a thorough medication review, they are time-consuming and impractical in busy clinical settings (Shelton et al., 2000).

Explicit methods

Explicit methods have been used to develop a number of different criteria for appropriate prescribing in the elderly. A few of the most commonly cited ones are

outlined in this section. See Table 1 for a chart that facilitates comparison of the different explicit criteria.

Table 1: Comparison of explicit criteria

Facet of appropriateness/inappropriateness	1991 Beers	1997 Beers	1997 McLeod	2002 Beers
Inappropriate for the older adult population	•	•	•	•
Appropriate indication				
Inappropriate dose, duration, or frequency	•	•	•	•
Inappropriate drug-disease interaction		•	•	•
Inappropriate drug-drug interaction			•	
Inappropriate due to patient's allergy history				
Inappropriate therapeutic duplication				
"Errors of omission"				

Beers et al. (1991) were among the first to develop a set of explicit criteria for determining the appropriateness of medication use in older adults residing in nursing home settings. Mark Beers, a geriatrician, initiated the process by reviewing the literature on the use of medications in the elderly and constructing statements on which medications were inappropriate for this population. Then he convened a group of 13 experts in geriatric care, geriatric pharmacology, geriatric psychopharmacology, and nursing home care from the United States and Canada to review the statements. Using the Delphi technique, Beers achieved consensus amongst the expert panel so as to generate a list of medications considered potentially inappropriate for this patient population and the prescribing concern for each of the medications on the list. This consensus criteria, hereafter referred to as the 1991 Beers criteria, addressed two facets of medication (in)appropriateness: 1) individual drugs or drug classes generally considered inappropriate for all older nursing home residents, sometimes referred to as unconditionally inappropriate medications because the appropriateness of the

medication is not conditional on specific patient factors (e.g. other comorbid conditions) or medication-related factors; and 2) doses, durations, and frequencies of medication therapy that should not be exceeded in older nursing home residents. Medications included in this list were deemed 'inappropriate' because the expert panel concluded that they were either ineffective or that they posed unnecessarily high risk to the population of elderly nursing home residents as a whole. The list of medications included benzodiazepines, tricyclic antidepressants (TCAs), antipsychotics, antihypertensives, nonsteroidal anti-inflammatory drugs (NSAIDs), oral hypoglycemics, and opioid analgesics. The 1991 Beers criteria were designed to facilitate the evaluation of medication appropriateness with minimal additional clinical data.

In order to achieve its intended purpose, explicit criteria need to be regularly updated to reflect current evidence on medication appropriateness and to incorporate new medications introduced in the market. In 1997, Beers convened another expert panel to update the original criteria by considering newer drugs and incorporating new evidence on drug therapy. He also expanded the criteria to include all adults 65 years and older regardless of their level of frailty or their place of residence (Beers, 1997). The 1997 Beers criteria included three facets of medication (in)appropriateness: 1) medications or classes of medications considered inappropriate for all older patients; 2) doses, durations, and frequencies of therapies considered inappropriate in older adults; and 3) medications or classes of medications considered inappropriate because of a potential drug-disease interaction in older patients with 15 specific medical conditions. The 1997 Beers criteria offer greater specificity than the 1991 criteria because it lists medications considered inappropriate in patients with specific medical conditions. In addition, Beers asked his expert panel to assign either a high or low rating on the severity of ADRs that might arise if patients took any of the medications on the list.

Beers and colleagues conceptualized severity as a combination of both the likelihood that an adverse outcome would occur and the clinical significance of that outcome should it occur.

A similar list of inappropriate medications was developed by McLeod, Huang, Tamblyn, and Gayton (1997) in Canada. Seventy-one inappropriate medications or medication classes were categorized as follows: 1) medications generally considered inappropriate for the elderly because of an unacceptable risk-benefit ratio; 2) medications considered inappropriate because of potential drug-drug interactions; and 3) medications considered inappropriate because of potential drug-disease interactions. The 1991 Beers criteria served as a model for this list, but McLeod et al. (1997) excluded medications unavailable in Canada, medications which they felt had fallen into disuse and therefore did not merit inclusion, and medications for which they were unable to find supporting evidence of significant risk. Beside each inappropriate medication or class of medications, McLeod et al. list another medication or class of medications that they felt would be a suitable and safer alternative.

The 71 medications were grouped into four major pharmacological categories: cardiovascular, psychotropic (e.g. benzodiazepines, SSRIs), analgesic (e.g. NSAIDs, opioids), and miscellaneous medications. Previous studies have shown that cardiovascular drugs, psychotropic drugs, and NSAIDs are the classes of medications most commonly implicated in ADRs (Tamblyn et al., 1994). McLeod et al. (1997) also asked their expert panel to rate the clinical significance of all the medications on the list on a four-point scale ranging from 1 (not significant) to 4 (highly significant). The mean significance rating was greater than 3 for 38 of the 71 medications on the list.

Most recently, Fick et al. (2003) have updated the 1997 Beers criteria. This new version, known as the 2002 Beers criteria, was designed to include new products and

incorporate new information available from the scientific literature. It contains the following: a list of unconditionally inappropriate medications (see Table 2); a list of medications or medication classes considered inappropriate in older adults with specific medical conditions (see Table 3), and a list of doses and durations of medications that should not be exceeded in the older adult population (see Table 4)[3].

Table 2: Beers 2002 criteria for potentially inappropriate medication use in older adults independent of dose, duration, frequency, or diagnoses

Drug name or class	Concern	Severity
Sedative-hypnotics		
Long-acting benzodiazepines e.g. chlordiazepoxide, diazepam, flurazepam	These drugs have a long half-life in the elderly (often several days) producing prolonged sedation and increasing the risk of falls and facture. Short-and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.	High
Meprobamate	This is a highly addictive and sedating anxiolytic. Those using meprobamate for prolonged periods may become addicted and may need to be withdrawn slowly.	High
All barbiturates (except phenobarbital) except when used to control seizures	Are highly addictive and cause more adverse effects than most sedative or hypnotic drugs in elderly patients	High
Antidepressants		
Amitriptyline and combination drugs containing amitriptyline	Because of its strong anticholinergic and sedating properties, amitriptyline is rarely the antidepressant of choice for elderly patients	High
Doxepin	Because of its strong anticholinergic and sedating properties, doxepin is rarely the antidepressant of choice for elderly patients	High
Fluoxetine	Long half-life of drug and risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation. Safer alternatives exist.	High
Antipsychotics		
Thioridazine	Greater potential for CNS and extrapyramidal adverse effects	High
Mesoridazine	CNS and extrapyramidal adverse effects.	High

[3] For the purpose of this study, medications not available in Canada have been removed from these lists.

Drug name or class	Concern	Severity
Antihypertensives		
Methyldopa and methyldopa-hydrochlorothiazide	May cause bradycardia and exacerbate depression in elderly patients	High
Short-acting nifedipine	Potential for hypotension and constipation.	High
Clonidine	Potential for orthostatic hypotension and CNS adverse effects.	Low
Antiarrhythmics		
Disopyramide	Of all antiarrhythmic drugs, this is the most potent negative inotrope and therefore may induce heart failure in elderly patients. It is also strongly anticholinergic. Other antiarrhythmic drugs should be used.	High
Amiodarone	Associated with QT interval problems and risk of provoking torsades de pointes. Lack of efficacy in older adults.	High
Diuretics		
Ethacrynic acid	Potential for hypertension and fluid imbalances. Safer alternatives available.	Low
Oral hypoglycemics		
Chlorpropamide	Has a prolonged half-life in elderly patients and could cause prolonged hypoglycemia. Additionally, it is the only oral hypoglycemic agent that causes SIADH.	High
Analgesics		
Propoxyphene and combination products containing propoxyphene	Offers few analgesic advantages over acetaminophen, yet has the adverse effects of other narcotics	Low
Meperidine	Not an effective oral analgesic in doses commonly used. May cause confusion and has many disadvantages to other narcotic drugs.	High
Pentazocine	Narcotic analgesic that causes more CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs. Additionally, it is a mixed agonist and antagonist.	High
Histamine 2 blockers		
Cimetidine	CNS adverse effects including confusion.	Low

Drug name or class	Concern	Severity
Hormonal agents		
Estrogens only (oral)	Evidence of the carcinogenic (breast and endometrial cancer) potential of these agents and lack of cardioprotective effect in older women.	Low
Methytestosterone	Potential for prostatic hypertrophy and cardiac problems.	High
Treatment of benign prostatic hyperplasia		
Doxazosin	Potential for hypotension, dry mouth, and urinary problems.	Low
Antibiotics		
Nitrofurantoin	Potential for renal impairment. Safer alternatives available.	High
NSAIDs		
Indomethacin	Of all available NSAIDs, this drug produces the most CNS adverse effects.	High
Ketorolac	Intermediate and long-term use should be avoided in older persons, since a significant number have asymptomatic GI pathologic conditions.	High
Muscle relaxants and antispasmodics		
Methocarbamol, cyclobenzaprine, and oxybutynin. Do not consider the extended-release oxybutynin.	Most muscle relaxants and antispasmodic drugs are poorly tolerated by elderly patients since these cause anticholinergic adverse effects, sedation, and weakness. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.	High
Orphenadrine	Causes more sedation and anticholinergic adverse effects than safer alternatives.	High
Platelet inhibitors		
Short-acting dipyridamole. Do not consider the long-acting dipyridamole (which has better properties than the short-acting in older adults) except with patients with artificial heart valves.	May cause orthostatic hypotension.	Low
Ticlopidine	Has been shown to be no better than aspirin in preventing clotting and may be considerably more toxic. Safer, more effective alternatives exist.	High
GI antispasmodics		
Dicyclomine, hyoscyamine, propantheline, belladonna alkaloids, and clidinium-chlordiazepoxide	GI antispasmodic drugs are highly anticholinergic and have uncertain effectiveness. These drugs should be avoided (especially for long-term use).	High

Drug name or class	Concern	Severity
Dementia treatments		
Ergot mesyloids	Have not been shown to be effective in the doses studied.	Low
Amphetamines and anorexic agents	These drugs have potential for causing dependence, hypertension, angina, and myocardial infarction.	High
Amphetamines (excluding methylphenidate hydrochloride and anorexics)	CNS stimulant adverse effects.	High
Antiemetics		
Trimethobenzamide	One of the least effective antiemetic drugs, yet it can cause extrapyramidal adverse effects.	High
Anticholinergics and antihistamines		
Chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine, promethazine	All nonprescription and many prescription antihistamines may have potent anticholinergic properties. Nonanticholinergic antihistamines are preferred in elderly patients when treating allergic reactions.	High
Diphenhydramine	May cause confusion and sedation. Should not be used as a hypnotic, and when used to treat emergency allergic reactions, it should be used in the smallest possible dose.	High

Table 3: Beers 2002 criteria for potentially inappropriate medication use in older adults considering diagnoses or conditions

Disease or condition	Drug	Concern	Severity
Heart failure	Disopyramide	Negative inotropic effect. Potential to promote fluid retention and exacerbation of heart failure.	High
Hypertension	Pseudoephedrine, diet pills, and amphetamines	May produce elevation of blood pressure secondary to sympathomimetic activity	High
Gastric or duodenal ulcers	NSAIDS and aspirin (>325mg) (coxibs excluded)	May exacerbate existing ulcers or produce new/additional ulcers	High
Seizures or epilepsy	Clozapine, chlorpromazine, thioridazine, and thiothixene	May lower seizure thresholds	High
Blood clotting disorders or receiving anticoagulant therapy	Aspirin, NSAIDs, dipyridamole, ticlopidine, clopidogrel	May prolong clotting time and elevate INR values or inhibit platelet aggregation, resulting in an increased potential for bleeding	High
Bladder outflow obstruction	Anticholinergics and antihistamines, gastrointestinal antispasmodics, muscle relaxants, oxybutynin, flavoxate, antidepressants, decongestants, tolterodine	May decrease urinary flow, leading to urinary retention	High
Stress incontinence	α-blockers (doxazosin, prazosin, and terazosin), anticholinergics, tricyclic antidepressants (imipramine, doxepin, amitriptyline), and long-acting benzodiazepines	May produce polyuria and worsening of incontinence	High
Arrhythmias	Tricyclic antidepressants (imipramine, doxepin, amitriptyline)	Concern due to proarrhythmic effects and ability to produce QT interval changes	High
Insomnia	Decongestants, theophylline, methylphenidate, MAOIs, and amphetamines	Concern due to CNS stimulant effects	High
Parkinson disease	Metoclopramide, conventional antipsychotics	Concern due to their antidopaminergic/cholinergic effects	High

Disease or condition	Drug	Concern	Severity
Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, and muscle relaxants, CNS stimulants (dextroamphetamine, methylphenidate, methamphetamine, pemolin)	Concern due to CNS-altering effects	High
Depression	Long-term benzodiazepine use. Sympatholytic agents methyldopa, reserpine	May produce or exacerbate depression	High
Anorexia and malnutrition	CNS stimulants, dextroamphetamine, methylphenidate, methamphetamine, fluoxetine	Concern due to appetite-suppressing effects	High
Syncope or falls	Short- to intermediate-acting benzodiazepines and tricyclic antidepressants (imipramine, doxepin, amitriptyline)	May produce ataxia, impaired psychomotor function, syncope, and additional falls	High
SIADH/ hyponatremia	SSRIs: fluoxetine, citalopram, fluvoxamine, paroxetine, sertraline	May exacerbate or cause SIADH	Low
Seizure disorder	Bupropion	May lower seizure threshold	High
Obesity	Olanzapine	May stimulate appetite and increase weight gain	Low
COPD	Long-acting benzodiazepines: chlordiazepoxide, clidinium-chlordiazepoxide, diazepam, clorazepate; β-blocker: propranolol	CNS adverse effects. May induce respiratory depression. May exacerbate or cause respiratory depression.	High
Chronic constipation	Calcium channel blockers, anticholinergics, and tricyclic antidepressants (imipramine, doxepin, amitriptyline)	May exacerbate constipation.	Low

From "Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts." by Fick, D.M., Cooper, J.W., Wade, W.E., Waller, J.L., Maclean, J.R., & Beers, M.H., 2003, Archives of Internal Medicine, p. 2721.

Table 4: Beers 2002 criteria for doses and durations of medications that should not be exceeded in the older adult population

Drug name or class & dose/ duration not to be exceeded	Concern	Severity
Short-acting benzodiazepines: alprazolam 2mg, lorazepam 3mg, oxazepam 60mg, temazepam 15mg, triazolam 0.25mg	Because of increased sensitivity to benzodiazepines in elderly patients, smaller doses may be effective as well as safer. Total daily doses should rarely exceed the suggested maximums.	High
Digoxin 0.125mg	Digoxin 0.125mg should not be exceeded except when treating atrial arrhythmias. Decreased renal clearance may lead to increased risk of toxic effects.	Low
Ferrous sulfate 325mg	Doses > 325mg/day do not dramatically increase the amount absorbed but greatly increase the incidence of constipation.	Low
Long-term use of full-dosage, longer half-life non-COX selective NSAIDs: naproxen, oxaprozin, piroxicam	Have the potential to produce GI bleeding, renal failure, high blood pressure, and heart failure.	High
Long-term use of stimulant laxatives: bisacodyl and cascara sagrada except in the presence of opiate analgesic use	May exacerbate bowel dysfunction.	High

From "Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts." by Fick, D.M., Cooper, J.W., Wade, W.E., Waller, J.L., Maclean, J.R., & Beers, M.H., 2003, Archives of Internal Medicine, pp. 2719-2720.

According to Buetow, Sibbald, Cantrill, and Halliwell (1997), explicit consensus-based methods of defining medication appropriateness have two main advantages: 1) they provide guidance in health care decision-making by combining evidence-based medicine with professional opinion when the evidence base is incomplete; and 2) they link different elements of the evidence base (e.g. efficacy, cost-effectiveness) thereby overcoming some limitations associated with their individual use as indicators of health care quality. They are generally applied to larger databases such as administrative data sets or population health surveys in order to study medication appropriateness on a population level.

However, there are also limitations. For example, this method does not allow for the identification of drug-related problems associated with medications deemed appropriate for use in elderly people or in rare instances where benefits may outweigh risks for a particular patient (Shelton et al., 2000). Another limitation is the general absence of independent review. One exception to this is the review conducted by Chutka, Takahashi, and Hoel (2004) who searched the scientific literature to determine whether evidence existed to defend or refute the 1997 Beers criteria. Although they faced an imperfect body of evidence, they found case studies and controlled trials to support the majority of medications on the Beers list.

Another potential problem with consensus-based methods is the variation in group size, scope and composition. Discrepancies between what one group of experts considers inappropriate and what another group of experts considers inappropriate raise questions about which group is right. For example, McLeod et al. (1997) specifically state that they disagreed with Beers' designation of reserpine, chlorthalidone, chlorpropamide, and amitriptyline as inappropriate for the elderly, so they decided to exclude these from their list. However, they do not provide a detailed explanation of the reasons behind their decision. McLeod et al. also excluded isoxsuprine, cyclandelate and propoxyphene from their list because they felt that these medications had already fallen into disuse. In consensus studies of prescribing appropriateness, inter-rater reliability has seldom been reported (Buetow, Sibbald, Cantrill, & Halliwell, 1997), and no information is provided on how discrepancies are resolved within and between groups. Merrick (1987), however, suggests that the intent of consensus-based methods is not to force unanimity. Rather, areas of disagreement that are often controversial can serve as a starting point for discussion and future research.

One other limitation to the use of explicit methods, raised by Kahan et al. (1994), is the fact that appropriateness is an exclusionary criterion – an inappropriate medication should never be used but an appropriate one need not always be. In the past, researchers and clinicians who have examined medication use in the older adult population have focused their efforts on reducing or eliminating medications considered inappropriate for this population, rather than increasing the use of medications considered appropriate for this population. Only recently have researchers such as Ghosh, Ziesmer, and Aronow (2002) and Higashi et al. (2004) turned their attention to improving the use of appropriate medications in certain subgroups of the elderly population.

Prevalence and patterns of inappropriate prescribing

A number of empirical studies have been carried out using the Beers criteria to examine the prevalence and factors associated with potentially inappropriate prescribing in the elderly. Eight empirical studies based on the 1991 version of the Beers criteria were reviewed by Aparasu and Mort (2000). They found considerable variation in the setting, scope, sample size, study design, data source, and data collection period for the studies. For example, the 1991 Beers criteria were originally intended for the elderly nursing home population, but researchers such as Willcox, Himmelstein, and Woolhandler (1994) applied it to the community-dwelling elderly. Other researchers have also modified the Beers list to suit their needs. Study designs included retrospective cross-sectional, retrospective cohort, and prospective cohort designs. Data sources included prescription or administrative databases as well as individual patient surveys; the former focuses on the medications prescribed while the latter focuses on the medications prescribed and taken. Individual patient surveys can also offer more detailed information than large administrative databases (e.g. doses, frequency of

administration of medications prescribed on an 'as needed' basis). However, patient reports may not always be complete or accurate. Therefore, researchers such as Zhan et al. (2001) have attempted to address this shortcoming by verifying patient reports with pharmacy data.

Despite these studies' methodological differences, Aparasu and Mort were able to identify some consistent patterns of inappropriate prescribing based on the 1991 Beers criteria. Since seven out of the eight studies based their analyses on a subgroup of 20 unconditionally inappropriate medications from the 1991 Beers criteria and all but two of the studies used the patient as a unit of analysis, the studies provided sufficient data for Aparasu and Mort to conclude that the prevalence of inappropriate medication use ranged from 14.0 to 23.5 percent. However, when Beers et al. (1992) used the full list of medications on the explicit criteria as the basis for his analyses, he found that the prevalence of inappropriate prescribing in the nursing home setting was 40.3 percent.

Inappropriate use was generally limited to one medication per patient. The most commonly prescribed inappropriate medications were long-acting benzodiazepines (chlordiazepoxide, diazepam, flurazepam), dipyridamole, propoxyphene, and amitriptyline. The least commonly prescribed inappropriate medications included phenylbutazone, pentazocine, barbiturates, cyclandelate, and isoxsuprine. This provides partial support for removal of these medications from the 1997 McLeod criteria.

In Canada, Rancourt et al. (2004) conducted a study of inappropriate medication use amongst older adults living in long-term care in the Quebec City area. Their definition of appropriateness was based on an adaptation of the 1991 Beers, 1997 Beers and 1997 McLeod criteria. Drugs not available in Canada were excluded from the study. Rancourt et al. found that 54.7 percent of patients had a potentially inappropriate prescription. The most common types of inappropriate prescriptions were drug-drug

interactions (33.9 percent), followed by inappropriate durations (23.6 percent), unconditionally inappropriate medications (14.7 percent) and inappropriate dosages (9.6 percent). This study did not consider inappropriate drug-disease interactions. There are several possible reasons why the reported prevalence of inappropriate medication use is much higher in this study than in previous studies: 1) most studies in the past focused only on unconditionally inappropriate medications, while this study also examined inappropriate doses, durations, and drug-drug interactions; 2) these researchers combined three sets of explicit criteria, which produced a more extensive list of potentially inappropriate medications; 3) the duration of the study was 21 months, longer than for most other studies; and 4) it was assumed that all medications prescribed on an as-needed basis were taken, possibly inflating the prevalence estimates.

In another Canadian study, Dhalla et al. (2002) conducted a pre/post retrospective, cohort study to examine the prevalence of inappropriate prescribing in older adults before and after nursing home admission. Their analysis, based on the unconditionally inappropriate medications listed in the 1997 Beers criteria, along with the addition of three long-acting benzodiazepines (clorazepate, clonazepam, prazepam), showed that the prevalence of inappropriate prescribing fell from 25.4 to 20.8 percent after nursing home admission. They believe that the reason for this decrease may be the vigilant monitoring of patients by healthcare professionals in the long-term care setting.

Liu and Christensen (2002) reviewed 11 studies conducted in the United States on inappropriate prescribing in the elderly based on the 1997 Beers criteria. Of these, one study (Mort & Aparasu, 2000) focused only on psychotropic medications, so was of limited comparative value. Again, these studies varied widely in their setting, design, data sources, sample size, and time horizon. For example, the population studied varied from a nationally representative sample of community-dwelling elderly (Zhan et al.,

2001) to a sample of elderly patients admitted to a hospital emergency department (Chin et al., 1999) to elderly Medicaid recipients living in the nursing home setting (Piecoro, Browning, Prince, Ranz, & Scutchfield, 2000). Other researchers made modifications to the Beers list. For example, Zhan et al. (2001) classified the unconditionally inappropriate medications from the Beers list into 3 categories: drugs that 1) should always be avoided; 2) are rarely appropriate; 3) have some indications but are often misused.

The reported prevalence of inappropriate prescribing based on these ten studies varied from 17 to 28 percent in the community setting, to 33 percent in the nursing home setting. The fact that the prevalence of inappropriate prescribing was higher in studies based on the 1997 Beers criteria than in studies based on the 1991 Beers criteria could partly be due to the increased number of drugs in the 1997 criteria. Hanlon, Fillenbaum, Schmader, Kuchibhatla, and Horner (2000) did, however, show in their retrospective longitudinal study that the rate of inappropriate prescribing declined over time. In their study, it decreased from 27 percent in 1989-1990 to 23 percent in 1992-1993. Zhan et al. (2001) also observed a declining trend in the percentage of elderly receiving inappropriate prescriptions over the ten-year period, from 1987 to 1996.

Propoxyphene, amitriptyline, long-acting benzodiazepines, and dipyridamole were consistently cited as the most commonly prescribed inappropriate medications. This finding is identical to Aparasu and Mort's (2000) finding described above. So, although there is some evidence of a downward trend in the overall use of inappropriate medications in the elderly over time, the prescribing of a small number of inappropriate medications seems to have persisted over time.

A more recent study conducted in Saskatchewan showed that the prevalence of inappropriate prescribing was 33 percent in the long-term care population (Clatney et al.,

2004). These researchers based their analysis on the subgroup of unconditionally inappropriate medications and medications whose doses were not to be exceeded per the 2002 Beers criteria, but excluded medications not available in Canada and medications deemed to be used too infrequently in Saskatchewan's long-term care population to be meaningful. The most frequently prescribed inappropriate medications were digoxin (at a dose above that recommended by the Beers criteria), amitriptyline, temazepam (at a dose above that recommended by the Beers criteria), and hydroxyzine.

To date, most studies on potentially inappropriate prescribing in older adults have been conducted on administrative claims databases. These databases rarely contain information on a patient's medical condition(s). Due to this limitation in the data, the majority of researchers have not been able to examine inappropriate drug-disease interactions. One study that did examine inappropriate drug-disease interactions, as defined by the 1997 McLeod criteria, used prescription medications as surrogates for the disease state (Papaioannou et al., 2002). For example, chronic obstructive pulmonary disease was defined as any patient who was prescribed a beta-adrenergic agonist or a bronchial anti-inflammatory agent. However, this was based on the assumption that drugs were only used for the treatment of one specific disease, and this assumption is not necessarily correct. In addition, diseases that lacked distinct prescription drug markers (e.g. heart failure) had to be excluded from the analysis.

Another more recent study, conducted by Zhan et al. (2005) also focused specifically on inappropriate drug-disease interactions. These researchers combined 1997 Beers and the 1997 McLeod criteria in order to develop a comprehensive list of 50 inappropriate drug-disease interactions. Their unit of analysis was the outpatient visit and their sample included 70,203 visits by patients aged 65 and older to physicians' offices from 1995 to 2000. Overall, in 2.58 percent of visits, patients were prescribed a

medication that resulted in an inappropriate drug-disease combination. One of the limitations of this study is that it relied on patient surveys. Sixty-five percent of those surveyed reported taking only one prescription medication. The reported use of medications by this sample is much lower than in previous estimates, and may signify under-reporting.

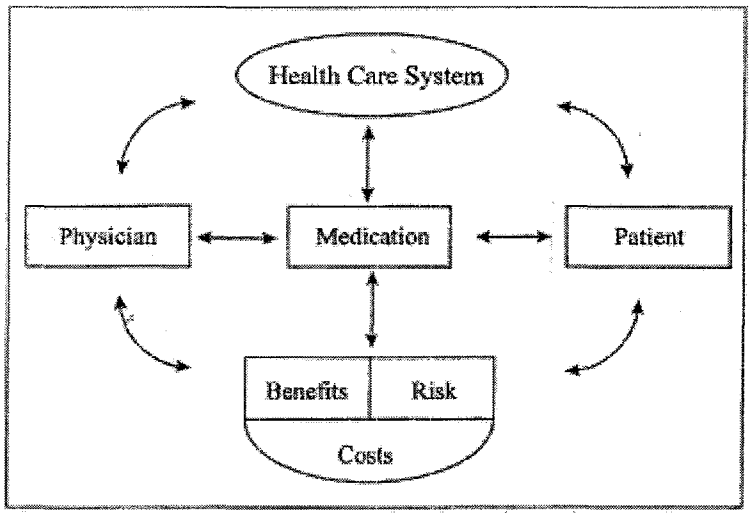
In summary, there have been some consistent patterns in the empirical studies of medication appropriateness in the elderly. The majority of researchers used the unconditional Beers criteria to define what is appropriate. Their studies showed that the prevalence of inappropriate prescribing in the elderly ranges from 14 to 28 percent in the community setting and 20 to 40 percent in the nursing home setting. Although there is some evidence of a downward trend in the overall use of inappropriate medications in the elderly over the last ten years, the prescribing of a small number of inappropriate medications such as propoxyphene, amitriptyline, long-acting benzodiazepines, and dipyridamole seems to have persisted over time.

Conceptual framework and correlates of inappropriate prescribing

A conceptual framework (Figure 1) was developed by Tamblyn, McLeod, Abrahamowicz, and Laprise (1996) to visualize the relationships amongst several factors that influence the risks versus benefits of prescription medication use. This framework can be used to guide studies of medication appropriateness in the elderly, as appropriateness is based on an evaluation of the risk-to-benefit ratio of a particular medication or class of medications in a particular patient population. When Beers created the Beers criteria, he asked a group of experts to reach a consensus about medications they feel have an unacceptable risk-to-benefit ratio in patients older than 65 years. Factors that influence the prescribing of a medication from the Beers criteria can

be grouped into one of four categories as suggested by Tamblyn's conceptual framework: 1) resident/patient characteristics; 2) physician-related variables; 3) the health care system; and 4) medication-related variables.

Figure 1 Tamblyn's conceptual framework for factors influencing the risks versus benefits of prescription medication use



From "Medication use in seniors: Challenges and solutions" by Tamblyn, R., 1996, Therapie, p. 276. Copyright © 1996, ADIS. With authorization of Therapie. All rights reserved. Reprinted with permission.

Resident/patient characteristics

As shown in Figure 1, the risks versus benefits of medication use can be affected by the characteristics of the resident or patient. In a previous section of this paper, I discussed three main reasons why older individuals are at increased risk ADRs: 1) they experience physiological changes with aging that can impair the metabolism and excretion of medications; 2) they may experience increased sensitivity to certain medications; and 3) they tend to be on multiple medications to treat multiple medical conditions, which increases the chances of experiencing a drug-drug interaction. Empirical studies have also shown that certain groups of older adults appear to receive

more inappropriate medication than others. Three studies based on the 1991 Beers criteria (Beers et al., 1992; Aparasu & Fliginger, 1997; Willcox et al., 1994) found that the rate of inappropriate prescribing was higher in women than in men. A number of studies based on the 1997 Beers criteria (Piecoro et al., 2000; Zhan et al., 2001; Meredith et al., 2001) also found the same. This could possibly be attributed to the fact that it is more socially acceptable for women to express feelings of depression and anxiety, and they are therefore more likely to be prescribed antidepressants and benzodiazepines.

The relationship between inappropriate prescribing and age is less certain. While Aparasu and Fliginger (1997) reported higher rates of inappropriate prescribing in patients above the age of 80, Beers et al. (1992) reported that inappropriate prescribing was higher in patients between the ages of 65 and 84. Nursing home elderly were also found to be at greater risk for receiving inappropriate prescriptions, compared with non-institutionalized elderly (Piecoro et al., 2000). Zhan et al. (2001) found that inappropriate prescribing was higher in those with poor health status, but Hanlon et al. (2000) did not find the same.

One study, conducted in board and care homes from 10 American states, found that the odds of being prescribed an inappropriate medication, as defined by a subset of the 1991 Beers criteria that only included unconditionally inappropriate medications, was increased by a factor of 1.63 for those with intact cognition versus those with moderate or severe cognitive impairment (Spore, Mor, Larrat, Hawes, & Hiris, 1997). A positive correlation between the presence of unconditionally inappropriate prescribing and intact cognition was replicated in a recent study by Perri et al. (2005). Other researchers have examined the correlation between inappropriate prescribing and various other factors, such as income, health status, and proportion of patients on Medicaid, but their results have been inconclusive.

Physician-related variables

Although there are only a limited number of studies examining the relationship between physician characteristics and inappropriate prescribing, there is evidence to suggest that general practitioners are more likely to prescribe inappropriately than specialists (Anderson, Beers, & Kerluke, 1997). Monette et al. (1997) found the same relationship in their study. They also found that physicians who were older were more likely to prescribe inappropriately. One possible explanation for this is that physicians who were trained more recently are better informed about newer medication alternatives, whereas physicians who were trained many years ago are more likely to prescribe older medications, and older medications are more likely to be captured in the Beers criteria. Two studies (Piecoro et al., 2000; Tamblyn, McLeod, Abrahamowicz, & Laprise, 1996) found that the rate of inappropriate prescribing was higher in physicians seeing a greater number of patients. Tamblyn et al. (1996) found that the rate of potentially inappropriate drug combinations is higher when there are multiple physicians prescribing for a patient, although these researchers did not use the Beers criteria for determining medication appropriateness.

Health care system

In the United States, nursing home care has been intensely criticized with respect to poor quality care (Institute of Medicine, 2001). One aspect of pharmaceutical care of particular concern was the use of psychotropic medications (antipsychotics, hypnotics, and anxiolytics) as 'chemical restraints' in the nursing home. In 1987, the federal government passed the Nursing Home Reform Act, embedded in the Omnibus Budget Reconciliation Act of 1987 (OBRA 1987), which stated that each resident's drug regimen must be free from unnecessary drugs (Hughes & Lapane, 2005). An unnecessary drug is defined as a drug that is used in excessive dose, for excessive

duration, without adequate monitoring or without adequate indications for its use, or in the presence of adverse consequences that indicate that the dose should be reduced or discontinued. Medical, environmental and psychosocial causes of behavioural problems must be ruled out, and nonpharmacologic management must be attempted before psychotropic drugs are prescribed to nursing home residents. Use of psychotropics must be justified and documented and periodic trials of medication withdrawal are encouraged.

For example, one regulation of this Act states that a resident with dementia who is exhibiting behavioural problems must not be treated with an antipsychotic unless the behaviour is documented, permanent, persistent, and causing psychotic symptoms or danger to the resident and others. Another regulation of this Act prohibits the use of barbiturates (e.g. amobarbital, aspirin-butalbital-caffeine, secobarbital) in the nursing home setting unless strict guidelines are adhered to (Gurvich & Cunningham, 2000). At the current time, no equivalent regulatory rules exist in Canada to control the use of psychotropics in nursing homes.

A study conducted by Cantrill, Dowell, and Roland (2000) suggests a positive correlation between continuity of care within the long-term care setting and medication appropriateness. When these researchers interviewed physicians about their prescribing practices in the long-term care setting, they found many expressed a reluctance in changing an inappropriate medication if it had been started a long time before or if it was initiated by another doctor. Long-term care residents who experience one or more changes in their family physician after they enter the long-term care facility experience a lack of continuity, and the new physician looking after them may make the assumption that their care is already optimised and that no changes are required in their medications.

One mechanism through which the health care system might act indirectly on the appropriateness of prescribing is through the reimbursement of physician services. Currently, physician visits to residential care facilities tend to be infrequent because they are penalized financially for leaving their office-based practice to see a patient in the residential care facility. British Columbia's current Residential Care Access Policy (2005), which assigns the first available bed to clients regardless of client preferences (e.g. for proximity to family) may have the unintended consequence of increasing the distance and travelling time between a physician's office and a residential care facility. This makes it even more difficult for long-term care residents to achieve good continuity in their care, and a significant number of residents are "orphaned" with no family physician.

Another mechanism through which the health care system might act indirectly on the appropriateness of prescribing is through the coverage of medications. Newer medications may demonstrate an improved safety profile over older medications but they may also be significantly more expensive, and they may not be covered on the provincial drug benefit plans if the government decides that their cost-to-benefit ratio is too high. For example, British Columbia Pharmacare initiated a Reference Drug Program (RDP) in 1995. Under the RDP, the least expensive drug within a class of drugs was identified as the 'reference drug' and was given full benefit status in the Pharmacare formulary. Any other drugs in the same therapeutic class that were more expensive than the reference drug were only covered up to the cost of the reference drug, and the difference in costs was passed on to the patient. Exceptions were made whereby physicians could request full reimbursement of non-reference drugs on medical grounds, although some physicians have protested against the RDP because they felt it restricted their

prescribing authority and added to their administrative costs (Maclure & Potashnik, 1997).

Medication-related variables

Three studies based on the 1991 Beers criteria (Spore et al., 1997; Aparasu & Sitzman, 1999; Aparasu & Mort, 2000) found that the strongest predictor of inappropriate prescribing is the number of prescribed medications. Seven out of eleven studies reviewed by Liu and Christensen (2002) examining inappropriate prescribing, based on the 1997 Beers criteria, also showed that the presence of inappropriate medications was correlated with the total number of prescribed medications. For example, Zhan et al. (2001) found that elderly patients who used more than the median number of prescriptions were three times as likely (OR = 2.9) to receive one of the inappropriate medications on the Beers list.

Summary

In summary, the rate of inappropriate prescribing tends to be higher in patients receiving a larger number of prescriptions and patients who are female. Inappropriate prescribing also tends to be correlated with older physicians and physicians who see a greater number of patients. One study found that the rate of inappropriate prescribing is higher when there are multiple physicians providing prescriptions for a patient. These findings suggest areas for targeted interventions for improving medication appropriateness in the elderly. Future studies need to consider organizational-level and system-level correlates of inappropriate prescribing.

Outcomes associated with inappropriate prescribing

Gupta, Rappaport, and Bennett (1996) were the first to examine the impact of inappropriate prescribing, based on the 1991 Beers criteria, on clinical and economic outcomes. Specifically, they examined how inappropriate prescribing was related to the mortality of elderly nursing home residents and the cost of pharmaceutical services. No relationship was found between inappropriate prescribing and mortality. Gupta et al. (1996) did, however, find a positive correlation between the number of inappropriate medications and the cost of pharmaceutical services. They attribute this finding to the possibility that inappropriate medications lead to ADRs, which, in turn, require more pharmaceutical services. Others have also raised the concern of a 'prescribing cascade' where ADRs are misidentified, particularly in the elderly population, and inappropriately treated as a new medical condition (Rochon & Gurwitz, 1997). One limitation of this study is that other factors influencing the cost of pharmaceuticals, including the substitution of older and cheaper medications with newer, more expensive alternatives, was not considered. Another limitation of this study is that the researchers studied the cost of pharmaceuticals in isolation, and did not consider any increased costs that might have resulted from outpatient visits, visits to the emergency department, or hospitalizations.

Chin et al. (1999) examined whether older persons presenting to the emergency department (ED) of a Chicago hospital who were taking inappropriate medications, as defined by the 1997 Beers criteria, would have worse health outcomes within one year from the ED visit than those who were not taking any inappropriate medications. No correlations were found between patients taking the Beers medications and revisits to the emergency department, hospitalization, or death, but correlations were found between patients taking the Beers medications and worse physical function and pain.

The results may have been influenced by the sociodemographic characteristics of the study sample, since 79 percent of the sample were African American and 43 percent of the sample had less than high school education. In addition, the generalizability of this study is limited.

Fick et al.'s (2001) study of Medicare managed care patients aged 65 and older found that those prescribed an inappropriate medication, based on the 1997 Beers criteria, had a significantly higher number of inpatient, outpatient, and emergency room visits compared with those not prescribed an inappropriate medication. However, when Fillenbaum et al. (2004) examined the impact of inappropriate drug use, also defined by the 1997 Beers criteria, on the utilization of health services amongst older community-dwelling residents in North Carolina, they found that the use of Beers medications was associated with reduced time to hospitalization but not to outpatient visits or nursing home entry. One unexpected finding of this study was that earlier hospitalization was more pronounced in those using Beers medications of low severity than in those using Beers medications of high severity.

Results from the Fillenbaum study are inconclusive since the study has several significant limitations. First, the data on medications relied on self-report. While the interviewers verified the information by asking to see the study participants' medications, the extent to which participants would fully disclose such information, particularly with medications that have a social stigma attached to them, is uncertain. Second, the information on medications was obtained at baseline only, and there was no follow-up to determine whether any medication changes had occurred over the three-year study. Therefore, it is uncertain whether a patient was on a Beers medication at the time of hospitalization. Third, the accuracy of patients' or their proxy's recall on the number of outpatient visits in year two of the study is questionable. Fourth, no explanation is

provided as to the reason these researchers chose time to hospitalization rather than hospitalization as an outcome measure, since there is no data to suggest that Beers medications would impact the former. Finally, given the unexpected finding that time to hospitalization is more strongly correlated with low severity medications, it is possible that other factors impacted the results without being accounted for.

A recent study by Perri et al. (2005) examined the relationship between the use of medications from two sub-types of the Beers criteria, namely unconditionally inappropriate medications and medications whose doses and durations were not to be exceeded, in elderly nursing home patients and the likelihood of hospitalizations, emergency department visits, and deaths. They found that the odds of experiencing at least one of the above adverse health outcomes increased by 2.3 times for those receiving Beers medications as opposed to those who were not receiving Beers medications. They also found that one particular inappropriate medication, propoxyphene, increased the risk of an adverse health outcome by more than twofold (odds ratio = 2.39).

Another recent study by Lau et al. (2005) also found that nursing home residents who received any medication from the 1997 Beers criteria were at increased risk of hospitalization (odds ratio = 1.27, $p<.005$) and death (odds ratio = 1.28, $p<.05$). One of the study's strengths is that it collected longitudinal data showing that residents who received a medication from the Beers criteria were at increased risk of hospitalization or death in the subsequent month. Another strength of this study is that it was based on a nationally representative nursing home resident population in the United States. Taken together, the studies conducted by Lau et al. and Perri et al. suggest that the nursing home population is susceptible to adverse health consequences due to inappropriate prescribing.

Limitations of existing research

Although the have been numerous studies on inappropriate prescribing, the majority of these focus only on one type of inappropriate prescribing, that is, medications that are considered unconditionally inappropriate for the geriatric population as a whole. These unconditional criteria have limitations in both sensitivity and specificity (Zhan et al., 2001). Explicit criteria cannot be relied upon to identify all cases of potentially inappropriate prescribing. On one hand, medications that do not appear on explicit criteria lists are not necessarily appropriate. For example, inappropriate prescribing occurs when a patient is prescribed a medication that is not clinically indicated or when a patient is prescribed a medication for a condition that can be treated just as effectively with non-pharmacological treatments. These types of inappropriate prescribing are less likely to be captured using explicit criteria. On the other hand, medications that do appear on the list are not always inappropriate. For example, the use of some drugs on the explicit criteria lists may be justified in a given circumstance because the benefits outweigh the risks for a particular patient.

The specificity of explicit criteria can be improved by taking a patient's diagnostic information into consideration. Hanlon et al. (2002) refer to inappropriate drug-disease interactions as an important but relatively unexplored category of suboptimal prescribing in the elderly. It is important to examine this type of inappropriate prescribing in the long-term care setting, where there are many patients with multiple chronic diseases, taking multiple medications. This is the contribution offered by this study, which includes inappropriate drug-disease combinations, as well as unconditionally inappropriate medications, and inappropriate doses, durations, and frequencies in the analysis so as to develop a more comprehensive picture of medication appropriateness in seniors living in the long-term care setting.

Research objectives

The purpose of this research was to conduct a study of medication appropriateness, as defined by the 2002 Beers criteria, in the nursing home setting. The research objectives were as follows:

1) To determine the overall prevalence of inappropriate prescribing in a sample of older adults living in the nursing home setting
2) To determine the prevalence of the following sub-types of inappropriate prescribing in older adults:
    a) Unconditionally inappropriate medications for the older adult population
    b) Inappropriate drug-disease combinations
    c) Inappropriate doses or durations
3) To examine whether a correlation exists between medication appropriateness and the following factors:
    a) Resident or patient attributes e.g. age, sex
    b) Diagnostic-related variables e.g. number and types of medical conditions
    c) Physician-related variables e.g. years since the resident's primary physician graduated, number of prescribers for each resident, continuity of care from a single physician, number of patients that each resident's physician has within the facility
    d) Medication-related variables e.g. number of prescription medications per resident
4) To determine the duration over which unconditionally inappropriate medications are used in the residential care setting

CHAPTER 2: METHODOLOGY

Sampling

The researcher, who is a licensed pharmacist, obtained the study sample from the pharmacy where she was employed. The pharmacy has three separate branches, located in Vancouver, Burnaby, and Surrey, British Columbia. The Vancouver and Burnaby branches are contracted to provide all pharmaceutical products and services to nine residential care facilities, including four licensed nursing homes for older adults, one facility for people with disabilities, two assisted living facilities, and two facilities for people facing mental health challenges.

A list of the residents living in the four nursing homes for older adults was generated in May 2005 (n=542). Residents under the age of 65 (n=38) were excluded from the analysis. Residents who had not lived in the facilities for at least six months (n=55) were also excluded from the analysis. This resulted in a final sample size of 449. Consideration was given to excluding residents who had not lived in the facilities for at least one year in order to extend the minimum length of time to study medication appropriateness. However, this would have resulted in a 21 percent reduction in sample size (n=114), and a significant reduction in statistical power. Therefore, a decision was made to retain the six-month residence inclusion criteria for this study.

Data sources

Data for each long-term care resident were collected from his/her file, which is stored securely at the pharmacy. Each file contains information on the resident's sex, date of birth, date of admission to the facility, and number and names of his/her chronic

medical conditions. Data pertaining to medication-related variables were taken from the medication review letters contained within each resident's file. According to Bylaw 7 of the Council of the College of Pharmacists of British Columbia (2001), which governs the provision of pharmacy services to residential care facilities and homes, a pharmacist and a registered nurse must review each resident's medication regimen at least once every six months. If the resident's physician does not attend the medication review, the pharmacist communicates the recommendations from the medication review to the physician in writing.[4] Physicians sign these letters and return them to the pharmacy to indicate their response to the recommendations outlined in the medication review letter and to authorize pharmacists to continue with the resident's current medications if no changes are required. One medication review letter for each resident was generated in the six-month period between November 2004 and April 2005. These letters served as the data source for the following medication-related variables: medication class; medication name; dose; frequency; and duration of treatment with a particular medication (where the latter three variables are pertinent to the study of medication appropriateness as outlined in Beers 2002 criteria).

Only information pertaining to orally administered medications was collected. Information pertaining to topical medications (e.g. creams, ointments), ophthalmic preparations, injections, and suppositories was not collected since the Beers criteria only pertain to medications that are orally administered or ingested. The most commonly prescribed medications, based on the researcher's experience as a pharmacist for the past 8 years, were coded according to the World Health Organization's Anatomic Therapeutic Chemical (ATC) Classification System. The ATC coding system assigns one code to each pharmacological entity, regardless of manufacturer.

[4] Since physicians did not attend the medication reviews at the residential care facilities where I provided pharmacy services, medication review letters were generated for all the residents and were sent to the physicians for their review.

Each medication that is filled for a resident, whether it is a prescription medication or an over-the-counter medication, must be entered into the resident's profile in the pharmacy software program. All medications on a resident's profile automatically appear on his/her medication review letter. However, since these letters are only generated every six months, there is a possibility that short-term orders, such as a ten-day course of antibiotics or a three-month course of a NSAID, are removed from the resident's profile before the medication review letter is printed. In order to address this shortcoming, reports were generated for each inappropriate medication filled between November 2004 and April 2005, and this information was also included in the study. Pharmacy records also served as the data source for all the physician-related variables, except the graduating year of the resident's primary physician, which was retrieved from the Physician Directory posted on the website of the College of Physicians and Surgeons of British Columbia (2005).

Measurement

Table 5 shows the independent and dependent variables that were tested in the bivariate analyses. Each dichotomous dependent variable was tested against each independent variable.

Table 5: Independent and dependent variables for the bivariate analyses

Independent variables	Dependent variables
• Age • Sex • Number of diagnoses • Presence of dementia or cognitive impairment • Facility • Years since the resident's primary physician graduated • Number of prescribers each resident had • Number of patients that each resident's primary physician had within the residential care facility • Number of changes of primary physician that a resident experienced after admission to the facility • Number of prescription medications each resident had	• Presence of any Beers medication • Presence of any unconditionally inappropriate medication • Presence of any inappropriate drug-disease combination

Dependent variables

The presence of any Beers medication, presence of any unconditionally inappropriate medication, and the presence of any inappropriate drug-disease interactions were the three dependent variables examined using bivariate and multivariate analyses. The sub-type of inappropriate prescribing that involved inappropriate doses or durations could not be included as a dependent variable due to the small number of cases (n=23).

Independent variables

Sociodemographic independent variables that were entered into this analysis included the resident's sex and age. The resident's age was calculated by subtracting the resident's date of birth from April 30, 2005, the last day of the study period. For the bivariate analyses, interval independent variables, such as the resident's age, were converted to categorical variables in order to obtain sufficient cell sizes to perform the

cross-tabulations. Based on the frequencies for the residents' ages, four groups of equal sizes were created: less than 81 years, 81 to 86 years, 87 to 91 years, and more than 91 years.

The number of diagnoses each resident had and the presence of cognitive impairment or dementia were chosen as two diagnostic-related independent variables. Each of the resident's diagnoses or medical conditions that were listed on his/her chart were coded according to the International Classification of Diseases (ICD-10) system developed by the World Health Organization (2003). For the bivariate analyses, the variable number of diagnoses was divided into thirds.

Since the study sample consisted of residents from four nursing homes, the facility was also chosen as an independent variable. By controlling for this variable in the analyses, one could rule out differences in inappropriate prescribing as a function of the facility where the resident lived.

Physician-related independent variables that were analyzed in this study included the number of years since the resident's primary physician graduated, the number of prescribers for each resident, the number of patients each resident's primary physician had within the same residential care facility, and the number of times a resident's primary physician changed after the resident was admitted to the residential care facility. For the bivariate analyses, the number of years since the resident's primary physician graduated was divided into quartiles: 8-23, 24-29, 30-33, 34 or more. This variable served as a proxy for the physician's training experience. It is, however, important to note that a physician's actual training experience can come from many different sources, including medical school, continuing education, and practical experience.

Data were only collected on the year of graduation for the resident's primary physician (i.e. general practitioner) and not for any specialists. The latter was not

collected because the Beers criteria are generalized criteria, and the medications listed by Beers are commonly prescribed by general practitioners. In addition, specialists often transfer the care of a patient back to the general practitioner once the patient is stabilized. It is also the resident's primary physician who signs the medication review letter and provides authorization to the pharmacists to continuing dispensing a medication.

Another physician-related independent variable that was entered into the analyses was the number of prescribers for each resident. For the bivariate analyses, this variable was divided into two groups – 1 and 2 or more – since it could be argued that residents who had two or more prescribers form a distinct group from residents who only had one prescriber. The variable number of patients that each resident's primary physician had in the facility also served as a independent variable for this study. For the bivariate analyses, this variable was divided into 4 equal groups – 1 to 2, 3 to 13, 14 to 36, and 37 or more – since it could be argued that physicians with only one or two patients in a facility (i.e. the lowest quartile) face a disincentive to leave their office, and may be less likely to conduct a thorough review of their medications. It was also postulated that residents whose family physicians had a large number of patients in the facility were less likely to receive an inappropriate medication because these physicians demonstrate an interest in geriatrics and are likely to possess greater clinical knowledge of medication appropriateness in the geriatric population.

The number of times a resident's primary physician changed after the resident was admitted to the residential care facility was also chosen as a independent variable. No specific hypotheses were developed with respect to the direction of the correlation because there was insufficient information available in the literature. For the bivariate analyses, this variable was divided into two groups – 0 and 1 or more – since it would

seem reasonable that residents without any changes in physicians had far greater continuity of care than those whose physicians had changed one or more times.

The number of prescription medications was also chosen as a independent variable. This variable was chosen rather than the total number of medications (prescription and over-the-counter) because nearly all the medications on the Beers criteria are prescription medications. For the bivariate analyses, this interval variable was converted into a categorical variable with three equal groups: 0-2, 3-4, and 5 or more.

Data cleaning

Data cleaning was achieved by selecting a random sample of five percent of the study sample (n=22) and comparing the data entered into the statistical software against the resident's profile in the pharmacy software. Data entered into the statistical software were also compared with reports on all inappropriate medications. In addition, frequencies were run on all variables, and outliers were checked to ensure that the data had been entered accurately. Out of a total of 449 cases, there were two missing values on the variable number of diagnoses, and these were replaced with the mean. There were also two missing values on the variable physician's year of graduation, and these were also replaced with the mean.

When frequencies were run for the diagnosis insomnia, it showed that only 9 out of 449 residents had this diagnosis recorded on their chart. Based on the researcher's experience as a pharmacist, this number seemed unusually low for the residential care population, leading the researcher to suspect that this diagnosis was underreported. Therefore, a decision was made to assign a diagnosis of insomnia to all other residents who were prescribed a hypnotic or agent that induces sleep (e.g. oxazepam, temazepam, zopiclone) (n=123). Another diagnosis that was likely underreported was

chronic constipation. When a frequency was run on this diagnosis, it showed that none of the residents had chronic constipation, leading the researcher to suspect that this diagnosis is generally not entered into the resident's medical records. Therefore, a decision was made to assign a diagnosis of chronic constipation to all residents who received laxatives on a regular basis (i.e. daily) (n=132), but not to those who received laxatives on a PRN basis. Other diagnostic information seemed fairly complete, and I was informed by a Director of Care at one of the residential care facilities that she regularly asks physicians to update the resident's medical information on their chart (T. Snow, personal communication, August 8, 2005)

Ethics

An ethics proposal was submitted and approved by the College of Pharmacists of British Columbia as well as the Office of Research Ethics at Simon Fraser University. The data that were abstracted from the pharmacy records contained no personal identifiers. This protected the anonymity of the research subjects.

Analysis

All statistical tests were computed with the SPSS 13.0 statistical software. Bivariate analyses were conducted to explore the direction and magnitude of the association between the three dependent variables and the 10 independent variables. Correlation coefficients can range from –1 to +1. As a general rule of thumb, correlations ranging from zero to r=.20 indicate a weak association, those between r=.20 and r=.40 indicate a moderate association, and those over r>.40 indicate a moderate to strong association. Dichotomous variables may be treated mathematically at any measurement level, and, generally speaking, the highest level is used in order to achieve the highest level of analysis. For example, in a cross-tabulation between the presence of any Beers

medication and sex, a Pearson's r could be used. However, for the nominal variable facility, Likelihood chi-square was used.

For the multivariate analyses, logistic regression was used to examine the effects of the independent variables on the presence of inappropriate prescribing. Logistic regression was chosen because the dependent variables were dichotomous, and logistic regression is considered the "standard method for regression analysis of dichotomous data in many fields, especially in the health sciences" (Hosmer & Lemeshow, 1989, p. vii). Logistic regression provides estimates of the likelihood of a specific event occurring, compared to not occurring, for each category of an independent variable while controlling for all other variables. Since the beta coefficients of logistic regression are in log form, they can be more easily interpreted if transformed into an odds ratio by taking its exponential. The resultant odds ratio can then be interpreted as the estimated factor change of a positive response for persons who are a unit apart on continuous variables, or compared to a reference category for categorical variables (DeMaris, 1995).

CHAPTER 3: RESULTS

Descriptive results

Out of the final sample of 449 residents, seventy-four percent (n=332) were female. The mean age of the residents was 85.9 years (SD 7.4). The old-old (i.e. 85 years and older) comprised 61.0 percent of the sample. In order to assess the generalizability of the sample to the B.C. population, the sex and age ranges for the study sample were broken down and compared with the population living in residential care facilities for the aged in British Columbia. Table 6 below shows that the sex distributions of the study sample and the B.C. residential care population are similar, but the study sample seems to be slightly older.

Table 6: Age and sex distribution for the study sample compared with population 65 years and older living in residential care facilities for the aged in British Columbia, 2001

	Study sample			Population living in BC residential care facilities for the aged		
Age range	**Males**	**Females**	**Total**	**Males**	**Females**	**Total**
65 – 69	0.9%	0.7%	1.6%	1.4%	1.5%	2.9%
70 – 74	3.3%	3.3%	6.6%	2.7%	3.4%	6.1%
75 – 79	4.0%	7.6%	11.6%	4.6%	8.3%	12.9%
80 – 84	5.8%	13.4%	19.2%	7.2%	15.9%	23.1%
85 and over	11.8%	49.2%	61.0%	12.1%	43.0%	55.0%
Total	25.8%	74.2%	100.0%	27.9%	72.1%	100.0%

Source: F. Markevicius, Data Dissemination Officer, Advisory Services, Statistics Canada, Western Region and Northern Territories, personal communication, November 24, 2005.

Each resident included in the study had, on average, 4.8 medical conditions (SD 1.9). Forty-three percent of the sample had dementia, 40.1 percent had hypertension, 19.6 percent had osteoporosis, 16.5 percent had osteoarthritis, 16.3 percent had depression, 13.8 percent had diabetes, 13.4 percent had cardiac dysrhythmias, and 13.1 percent had hypothyroidism. Each resident was prescribed an average of 7 medications per day, and an average of 5 prescription medications per day.

Table 7 summarizes the overall prevalence rate of inappropriate prescribing as well as the prevalence rates of the three sub-types of inappropriate prescribing: unconditionally inappropriate medications, inappropriate drug-disease combinations, and inappropriate doses or durations. The prevalence rates presented in the table below were calculated by dividing the number of residents who received one or more inappropriate medication by the total number of residents in the study sample (i.e. 449). Overall, 29.4 percent of the study sample (n=132) received one or more inappropriate medication as outlined in the 2002 Beers criteria. Of these, 21.4 percent of residents (n=96) received one inappropriate medication, 5.8 percent (n=26) received two inappropriate medications, and 2.2 percent (n=10) residents received three or more inappropriate medications.

Table 7: Prevalence rates of inappropriate prescribing in the study sample

Type of inappropriate prescribing	No. of residents	Prevalence (%)
Unconditionally inappropriate medication	76	16.9%
Inappropriate drug-disease combination	56	12.4%
Inappropriate dose or duration	23	5.1%
Overall [a]	132	29.4%

[a] The sum of the numbers of residents receiving each of the three sub-types of inappropriate medications exceeds the overall total number because some residents received inappropriate medications from more than one sub-category.

The most common sub-type of inappropriate prescribing was the unconditionally inappropriate medication. Approximately 17 percent (n=76) of the sample received one or more unconditionally inappropriate medications, that is, a medication considered inappropriate for any elderly person, regardless of dose, frequency, or duration. Of the 76 residents who received at least one unconditionally inappropriate medication, 61 (80.3 percent) received one unconditionally inappropriate medication, while 15 (19.7 percent) received two unconditionally inappropriate medications. All unconditionally inappropriate medications that were prescribed between November 2004 and April 2005 in the study sample are listed in Table 8. Out of the 46 unconditionally inappropriate medications and medication classes listed in the 2002 Beers criteria (see Table 2), only 19 were prescribed in the study sample. This could reflect the fact that many of the medications listed in the Beers criteria are rare, have fallen into disuse, and/or have been replaced with newer alternatives.

Table 8: Unconditionally inappropriate medication orders

Unconditionally inappropriate medication	No. of orders	Severity
Nitrofurantoin	18	High
Cimetidine	17	Low
Hydroxyzine	12	High
Diphenhydramine	8	High
Amitriptyline	7	High
Oxybutynin	6	High
Indomethacin	4	High
Dicyclomine	3	High
Cyclobenzaprine	3	High
Diazepam	2	High
Doxepin	2	High
Estrogen	2	Low
Amiodarone	1	High
Dexedrine	1	High
Dipyridamole	1	High
Fluoxetine	1	High
Methyldopa	1	High
Pentazocine	1	High
Ticlopidine	1	High
Total	91	

Out of the 91 orders of unconditionally inappropriate medications, 20 (including 18 orders for the antibiotic nitrofurantoin) were ordered on a short-term basis, while the remaining orders had no specified end date. Nineteen out of 91 orders were started before the resident was admitted to the facility, and 72 were started after the resident was admitted to the facility. For the 19 orders medications that were started before the residents were admitted to the facility, the average duration over which the inappropriate medication was being taken, calculated from the date they entered the facility to the end of the study period (April 30, 2005), was 1,153 days or approximately 38 months. This is a conservative estimate since the individual was most likely started on the medication before the time of nursing home admission. For the 72 orders of unconditionally inappropriate medications that were started after the residents entered the facility, the average duration over which the unconditionally inappropriate medication was being taken was 388 days, slightly over one year. These findings suggest that repeat prescribing and long-term use of unconditionally inappropriate medications is an issue that needs to be addressed.

The second most common subtype of inappropriate prescribing was the inappropriate drug-disease combination, affecting 12.4 percent of residents (n=56). Results showed that there were a total of 70 orders for medications or medication classes considered inappropriate in patients with specific diseases or diagnoses (see Table 9). Of the 56 residents affected, 45 (80.3 percent) received one inappropriate drug-disease combination, nine (16.1 percent) received two inappropriate drug-disease combinations, one received three inappropriate drug-disease combinations, and one received four inappropriate drug-disease combinations. The most common inappropriate drug-disease combination was the prescription of anticholinergic medications in

residents with cognitive impairment (n=31). This was also the single most commonly prescribed inappropriate medication found in the entire study.

Table 9: Inappropriate drug-disease combinations

Inappropriate medication	Disease/diagnosis	No. of combinations	Severity
Anticholinergics	Cognitive impairment	31	High
Anticholinergics	Chronic constipation	15	Low
Benzodiazepines (long-term use)	Depression	9	High
Calcium channel blocker	Chronic constipation	9	Low
Pseudoephedrine	Hypertension	2	High
Theophylline	Insomnia	1	High
Phenylzine	Insomnia	1	High
Dexedrine	Insomnia	1	High
Amitriptyline	Syncope	1	High
Total		70	

Anticholinergics, or medications with anticholinergic activity, can be found in many different therapeutic categories. Medications with moderate or strong anticholinergic activity are listed in Table 10 below. Side effects of these medications can include dry mouth, blurred vision, and tachycardia. These medications can also affect the central nervous system (CNS), resulting in drowsiness, fatigue, restlessness, irritability, disorientation, and delirium. Use of these medications in the nursing home setting can be problematic because this population already has a fairly high degree of cognitive impairment, and may therefore be more susceptible to these adverse CNS effects (Roe, Anderson, & Spivack, 2002). In addition, these CNS effects would be more difficult to detect in someone with cognitive impairment.

Table 10: Medications with moderate or strong anticholinergic activity

Antiarrhythmic	**Antihistamines (con't)**
Disopyramide	Doxylamine
Antiemetics	Hydroxyzine
Cyclizine	Promethazine
Dimenhydrinate	Triprolidine
Meclizine	**Gastrointestinal/urinary antispasmodics – single and combination products containing:**
Antiparkinsonian medications	
Benztropine	Belladonna alkaloids
Biperiden	Atropine
Procyclidine	Hyoscyamine
Trihexyphenidyl	Scopolamine
Antipsychotics	Dicyclomine
Chlorpromazine	Flavoxate
Clozapine	Oxybutynin
Mesoridazine	**Muscle relaxants**
Olanzapine	Cyclobenzaprine
Pimozide	Orphenadrine
Promazine	**Tricyclic antidepressants**
Thioridazine	Amitriptyline
Triflupromazine	Clomipramine
Antihistamines – single and combination products containing:	Doxepin
	Imipramine
Azatadine	Trimipramine
Brompheniramine	Clomipramine
Chlorpheniramine	
Cyproheptadine	
Dexbrompheniramine	
Dexchlorpheniramine	
Diphenhydramine	

From "Use of anticholinergic medications by older adults with dementia." by Roe, C.M., Anderson, M.J., & Spivack, B., 2002, Journal of the American Geriatrics Society, 50, p. 842. Copyright 2002 by Blackwell Publishing. Adapted with permission.

The third most common sub-type of inappropriate prescribing was the inappropriate dose or duration. In total, there were 23 cases of this sub-type of inappropriate prescribing affecting 23 residents, or 5.1 percent of the study sample. Nineteen residents each received one medication at a dose that exceeded the maximum

daily dose recommended by the 2002 Beers criteria, and four residents each received one medication at a duration that exceeded the maximum duration recommended by the 2002 Beers criteria (see Table 11).

Table 11: Medications with maximum dosage or duration exceeded

Medication	Maximum dose/duration	Total no. of orders for this medication	No. of orders exceeding maximum dose/duration [d]	% of orders exceeding maximum dose/duration	Severity
Alprazolam	2mg/day	8	0	0 %	High
Lorazepam	3mg/day	64	0	0 %	High
Oxazepam	60mg/day	55	0	0 %	High
Temazepam	15mg/day	10	5	50.0 %	High
Triazolam	0.25mg/day	1	0	0 %	High
Digoxin	0.125mg/day [a]	43	3	7.0 %	Low
Ferrous sulfate	325mg/day	25	11	44.0 %	Low
Naproxen	Long-term use [b]	5	2	40.0 %	High
Oxaprozin	Long-term use [b]	0	0	n/a	High
Piroxicam	Long-term use [b]	0	0	n/a	High
Bisacodyl [c]	Long-term use [b]	3	2	66.0 %	High
Cascara sagrada [c]	Long-term use [b]	1	0	0 %	High
Total		215	23	10.7 %	

[a] Except when treating atrial arrhythmias

[b] Duration not specified by Beers and colleagues; long-term equated with 3 months for this study

[c] Except in the presence of opiate analgesic use

[d] Doses and durations of medications were only examined for the medications listed in the Beers criteria (see Table 4).

Table 11 also shows that there was a total of 138 orders or prescriptions for benzodiazepines (alprazolam, lorazepam, oxazepam, temazepam, and triazolam) where an assessment of dose was required. Out of these 138 prescriptions, 66 were prescribed to residents on a regular basis, 61 were prescribed to residents on a PRN basis, and 12 were prescribed to residents on both a regular and PRN basis. When a benzodiazepine was ordered on a regular basis (e.g. oxazepam 30mg, one tablet daily at bedtime), it was possible to determine definitively whether the recommended maximum daily dose was exceeded. In this study sample, there were five prescriptions for temazepam 30mg, one capsule daily at bedtime, and all five of these prescriptions exceeded the

recommended maximum daily dose. However, when a benzodiazepine was ordered on a PRN basis (e.g. lorazepam 1mg, one to two tablets every four hours as needed for agitation), it was only possible to determine whether there was potential for the recommended maximum daily dose to be exceeded. Out of all the benzodiazepines ordered on a PRN basis, the potential to exceed the maximum daily dose only applied to three orders of Lorazepam. Since data were not collected on the frequency of administration of PRN orders, it was not possible to state definitively whether the maximum daily doses were exceeded, and therefore these three cases were not counted as cases of inappropriate prescribing.

Results of bivariate analyses

Presence of any Beers medication

The dependent variable chosen for the first set of bivariate analyses was the presence of any Beers medication, that is, any medication listed on the 2002 Beers criteria. In contrast to previous studies, there was no association between sex and the presence of any Beers medication. Nor was there any association between the age of the resident, divided into 4 equal groups, and the presence of any Beers medication.

Crosstabular analysis revealed a weak statistically significant positive association between the number of diagnoses and the presence of any Beers medication (Pearson's $r = 0.107$, $p<.05$; see Table 12). No association was shown between the presence of dementia/cognitive impairment and the presence of any Beers medication.

Table 12: Crosstabulation of the presence of any Beers medication and the number of diagnoses

		No. of diagnoses			Total
		1-3	**4-5**	**6+**	
Presence of any Beers medication	No	84	147	86	317
		74.3%	74.6%	61.9%	71.0%
	Yes	29	50	53	132
		25.7%	25.4%	38.1%	29.0%
Total		113	197	139	449
		100.0%	100.0%	100.0%	100.0%

Pearson's R = .107, p<.05

A weak statistically significant positive association was also found between the number of prescription medications and the presence of any Beers medication (Pearson's R = 0.186, p<.001; see Table 13).

Table 13: Crosstabulation of the presence of any Beers medication and the number of prescription (Rx) medications

		No. of Rx medications			Total
		0-2	**3-4**	**5+**	
Presence of any Beers medication	No	94	90	133	317
		85.5%	69.2%	63.6%	70.6%
	Yes	16	40	76	132
		14.5%	30.8%	36.4%	29.4%
Total		110	130	209	449
		100.0%	100.0%	100.0%	100.0%

Pearson's R = .186, p<.001

Neither the number of years since the resident's primary physician graduated nor the number of patients that each resident's primary physician had within the residential care facility showed any significant association with the presence of any Beers medications. However, there was a weak positive association between the number of prescribers each resident had and the presence of any Beers medication (Pearson's R = 0.137, p<.01; see Table 14). In other words, residents with more than one prescriber

were significantly more likely to receive a Beers medication than residents with only one prescriber.

Table 14: Crosstabulation of the presence of any Beers medication and the number of prescribers each resident had

		No. of prescribers each resident had		Total
		1	**2+**	
Presence of any Beers medication	No	248	69	317
		74.3%	60.0%	70.6%
	Yes	86	46	132
		25.7%	40.0%	29.4%
Total		334	115	449
		100.0%	100.0%	100.0%

Pearson's R = .137, p< .01

A crosstabular analysis was conducted to determine if there was a significant correlation between the presence of any Beers medication and the number of changes in physician each resident experienced. For this analysis, the number of months a resident had been living in the facility was introduced as a layer variable to account for the fact that there is an increased chance of the resident changing physician if s/he lives in the facility for a longer period of time. In order to conduct this analysis, the interval variable months since admission was recoded into three groups: 6 to 24, 25 to 48, and 49 or more. A frequency for this variable was run in order to create three groups of roughly equal size, whilst also grouping together residents who had lived in the facility for similar periods of time. Results showed that there were no significant associations with this measure of continuity of care.

The crosstabular analysis between number of diagnoses and the presence of any Beers medication was repeated, with the number of prescription medications introduced as a layer variable. The number of prescription medications was chosen as a layer variable because there is a possibility that the association between number of diagnoses and the presence of any Beers medication could be a result of the number of prescription medications. In general, the number of prescription medications increases as the number of diagnoses increase. However, it is not a perfectly linear relationship because certain diagnoses (e.g. congestive heart failure) require a large number of medications to manage, while others do not.

In order to conduct the crosstabular analysis with the layer variable, the variable number of prescription medications needed to be recoded into two groups in order to maintain a cell size over five. For crosstabular analyses, cells are required to have a minimum of five cases in order to detect the difference between the observed and predicted cases. With the inclusion of the layer variable, the positive association between the number of diagnoses and the presence of any Beers medications was lost when the number of prescriptions was between 0 and 3, but retained when the number of prescriptions was 4 or more (tau-b = .116, $p<.05$). Therefore, it appears that the number of prescriptions is an intervening variable that specifies the conditions under which the relationship between the presence of any Beers medication and the number of diagnoses holds true.

Presence of any unconditionally inappropriate medication

Within the Beers criteria, there is a subset of medications considered unconditionally inappropriate, that is, these medications are considered inappropriate for the elderly regardless of dose, duration, or the individual's medical condition. The

presence of unconditionally inappropriate medications was tested for associations with all the independent variables listed in Table 5 above.

Results differed somewhat from the previous set of analyses. The presence of unconditionally inappropriate medications was not correlated with any of the following variables: sex, age, number of diagnoses, facility, number of years since the resident's physician graduated, or the number of changes in primary physician that a resident experienced after admission to the facility (controlling for the number of months since the resident's admission into the facility). However, results did show a weak negative association between the presence of any unconditionally inappropriate medication and residents who had dementia or cognitive impairment (see Table 15) .

Table 15: Crosstabulation of the presence of any unconditionally inappropriate medication and the presence of cognitive impairment or dementia

		Presence of cognitive impairment or dementia		Total
		No	**Yes**	
Presence of any unconditionally inappropriate medication	No	191	182	373
		78.0%	89.2%	83.1%
	Yes	54	22	76
		22.0%	10.8%	16.9%
Total		245	204	449
		100.0%	100.0%	100.0%

Pearson's R = -.149, p< .01

One possible explanation for this is that those without dementia or cognitive impairment are better able to voice their requests for pharmacological treatment than those with cognitive impairment, and, in doing so, they are prescribed a greater number of medications, including medications that are considered unconditionally inappropriate. In order to test whether the data support this premise, a crosstabular analysis was

performed between the presence of dementia or cognitive impairment and the number of prescription medications, and this showed that those with dementia or cognitive impairment received significantly fewer prescriptions than those without dementia or cognitive impairment (Pearson's R = -.165, p<.001).

A weak positive association was found between the presence of any unconditionally inappropriate medication and residents with two or more prescribers (Pearson's R = .116, p<.05; see Table 16). This was also found in the bivariate analyses using any Beers medication as the dependent variable. Again, this supports the premise that inappropriate prescribing is more likely to occur when two or more physicians prescribe for a patient.

Table 16: Crosstabulation of the presence of any unconditionally inappropriate medication and the number of prescribers each resident had

		No. of prescribers each resident had		Total
		1	**2+**	
Presence of any unconditionally inappropriate medication	No	286	87	373
		85.6%	75.7%	83.1%
	Yes	48	28	76
		14.4%	24.3%	16.9%
Total		334	115	449
		100.0%	100.0%	100.0%

Pearson's R = .116, p< .05

The crosstabular analyses also revealed a weak negative association between the presence of any unconditionally inappropriate medication and the number of patients each resident's primary physician had in the facility (Pearson's R = -.097, p<.05; see Table 17). This correlation was in the anticipated direction since it was speculated that physicians who have a larger number of patients in one facility would be more knowledgeable in geriatric medication management and spend more time caring for the patients in the facilities than physicians who only have one or two patients in the facility.

Table 17: Crosstabulation of the presence of any unconditionally inappropriate medication and the number of patients each resident's primary physician had in the facility

		No. of patients each resident's primary physician has in the facility				Total
		1-2	**3-13**	**4-36**	**37+**	
Presence of any unconditionally inappropriate medication	No	77	95	91	110	373
		78.6%	81.9%	81.3%	89.4%	83.1%
	Yes	21	21	21	13	76
		21.4%	18.1%	18.8%	10.6%	16.9%
Total		98	116	112	123	449
		100.0%	100.0%	100.0%	100.0%	100.0%

Pearson's R = -.097, p< .05

As anticipated, there was a positive association between the presence of unconditionally inappropriate medications and the number of prescription medications (Pearson's R = .177, p<.001; see Table 18).

Table 18: Crosstabulation of the presence of any unconditionally inappropriate medication and the number of prescription medications of each resident

		No. of Rx medications			Total
		0-2	**3-4**	**5+**	
Presence of any unconditionally inappropriate medication	No	104	107	162	373
		94.5%	82.3%	77.5%	83.1%
	Yes	6	23	47	76
		5.5%	17.7%	22.5%	16.9%
Total		110	130	209	449
		100.0%	100.0%	100.0%	100.0%

Pearson's R = .177, p<.001

Presence of any inappropriate drug-disease combination

The final dependent variable tested in the bivariate analyses was the presence of one or more medications that were prescribed inappropriately given the patient's medical conditions or diagnoses. Results showed a weak positive correlation between the presence of an inappropriate drug-disease combination and the number of diagnoses recorded on the resident's chart (Pearson's R = .115, p<.05).

Table 19: Crosstabulation of the presence of any inappropriate drug-disease combination and the number of diagnoses

		No. of diagnoses			Total
		1-3	**4-5**	**6+**	
Presence of any inappropriate drug-disease combination	No	105	173	115	393
		92.9%	87.8%	82.7%	87.5%
	Yes	8	24	24	56
		7.1%	12.2%	17.3%	12.5%
Total		113	197	139	449
		100.0%	100.0%	100.0%	100.0%

Pearson's R = .115, p<.05

The presence of dementia or cognitive impairment was also positively correlated with the presence of an inappropriate drug-disease combination (Pearson's R = .102, p<.05; see Table 20).

Table 20: Crosstabulation of the presence of any inappropriate drug-disease combination and the presence of cognitive impairment or dementia

		Presence of cognitive impairment or dementia		Total
		No	**Yes**	
Presence of any unconditionally inappropriate medication	No	222 90.6%	171 83.8%	393 87.5%
	Yes	23 9.4%	33 16.2%	56 12.5%
Total		245 100.0%	204 100.0%	449 100.0%

Pearson's R = .102, p< .05

This is not surprising since the most commonly seen inappropriate drug-disease combination was when an anticholinergic medication was prescribed to a person with cognitive impairment. No other variables were significantly correlated with the presence of any inappropriate drug-disease combination.

Results of logistic regression analyses

Since the presence of Beers medications is a dichotomous dependent variable, logistic analyses can be conducted to examine the relative importance of each independent variable in predicting the presence of Beers medications. In table 21, the independent variables are listed in hierarchical blocks, based on the logical sequencing of groups of variables (i.e. sociodemographic variables precede the diagnostic variables, which precede the facility variable, etc.), and these blocks are entered sequentially into the logistic regression analyses. Hierarchical regression was used to determine the effect that each group of variables has in predicting the presence of inappropriate prescribing, and to determine whether the addition of a subsequent group of variables make a significant contribution to the model over and above the group(s) of variables preceding it in the hierarchy.

Table 21: Hierarchical blocks of independent variables for the logistic regression analyses

Socio-demographic variables	Diagnostic variables	Facility	Physician-related variables	Medication-related variables
• Age • Sex	• No. of diagnoses • Presence of dementia or cognitive impairment	• Facility	• Years since the resident's physician graduated • Number of prescribers • Number of patients that each resident's physician has within the residential care facility • Number of changes of physicians that a resident experienced after admission to the facility	• No. of prescription medications

Interval variables, such as age, number of diagnoses, years since the resident's physician graduated, number of prescribers, number of patients that each resident's physician has within the facility, number of changes of physicians that a resident experienced after admission to the facility, and number of prescription medications, could be entered directly into the logistic regression analysis. As before, dichotomous variables such as sex and the presence of dementia or cognitive impairment are treated as interval variables since they can be converted into percentages. At the bivariate level, no apparent differences in inappropriate prescribing was found amongst the four facilities, and therefore a decision was made to conduct only one set of facility contrasts at the multivariate level. Facility 1 was chosen as the reference category, thereby creating three separate facility contrasts (facility 2 versus facility 1, facility 3 versus facility 1, and facility 4 versus facility 1).

Presence of any Beers medication

As shown in Table 22 below, model one, with the sociodemographic variables, was not significant. Model two was statistically significant (model chi-square=10.75, $p<.05$), and a statistically significant positive association was found between the presence of any Beers medication and the number of diagnoses the resident had (ß=.17, odds ratio=1.17, $p<.05$). However, when the facility variable was introduced as the third block of variables, the overall model lost its significance. With the addition of the fourth block of variables, or physician-related variables, the overall model again became statistically significant (model chi-square = 20.76, $p<.05$). A statistically significant positive association was found between the presence of any Beers medication and the number of prescribers for each resident (ß=.47, odds ratio=1.60, $p<.01$).

With the inclusion of the medication-related variable in model 5, the correlation between the presence of any Beers medication and the number of diagnoses lost its significance. Based on the relative size of the increase in the model chi-square, it would seem that the majority of the variance in overall inappropriate prescribing is explained by the single medication-related variable. Results showed a statistically significant positive correlation between the presence of any Beers medication and the number of prescription medications (ß=.20, odds ratio=1.22, $p<.001$). In other words, for every prescription medication added, the odds of receiving a Beers medication increased by a factor of 1.22 or 22 percent. The statistically significant correlation between inappropriate prescribing and the number of prescribers was replicated in Model 5. The odds ratio for this variable indicated that the odds of receiving any Beers medication increase by a factor of 1.48 for each additional physician prescribing a medication for a resident.

Table 22: Beta coefficients (odds ratios) for the presence of any Beers medication

	Model				
Variable	**1**	**2**	**3**	**4**	**5**
Intercept	0.71	0.28	0.19	-0.70	-2.08
Age	-0.01	-0.02	-0.02	-0.02	-0.01
Sex	-0.22	-0.24	-0.23	-0.14	-0.14
No. of diagnoses		0.16 (1.17)**	0.17 (1.18)**	0.16 (1.18)**	0.09
Dementia/cognitive impairment		-0.14	-0.13	-0.15	0.05
Facility					
Facility 1 (reference)					
Facility 2 versus facility 1			0.11	0.25	0.15
Facility 3 versus facility 1			-0.14	-0.13	-0.05
Facility 4 versus facility 1			-0.22	-0.04	0.06
Years since the resident's primary physician graduated				0.01	0.01
No. of prescribers for each resident				0.47(1.60)**	0.39(1.48)*
No. of patients each resident's primary physician has				-0.01	-0.01
No. of changes in physician				0.01	0.02
No. of prescription medications					0.20(1.22)***
Model chi-square	2.30	10.75*	11.69	20.76*	38.85***

Note: odds ratios are shown only for statistically significant findings
* p<.05, ** p<.01, *** p<.001

To summarize, this study found two statistically significant predictors of the presence of any Beers medication: the number of prescribers for each resident and the number of prescription medications received by each resident.

Presence of any unconditionally inappropriate medication

Logistic regression analyses were repeated using the presence of any unconditionally inappropriate medication as the dependent variable. As shown in Table 23, model two became statistically significant when the block of diagnostic-related variables was entered (model chi-square=14.98, p<.05).

Table 23: Beta coefficients (odds ratio) for the presence of any unconditionally inappropriate medication

	Model				
Variable	**1**	**2**	**3**	**4**	**5**
Intercept	-0.41	-0.46	-0.82	-2.38	-4.25
Age	-0.01	-0.02	-0.01	-0.01	0
Sex	-0.07	-0.06	-0.05	0.09	0.12
No. of diagnoses		0.13(1.14)*	0.13	0.11	0.01
Dementia/cognitive impairment		-0.87(0.42)*	-0.87(0.42)**	-0.90(0.41)*	-0.69(0.50)*
Facility					
Facility 1 (reference)					
Facility 2 versus facility 1			-0.19	0.04	-0.16
Facility 3 versus facility 1			-0.42	-0.53	-0.49
Facility 4 versus facility 1			-0.58	-0.27	-0.09
Years since the resident's primary physician graduated				0.03	0.03(1.04)*
No. of prescribers for each resident				0.56(1.74)*	0.46(1.59)*
No. of patients each resident's primary physician has				-0.02	-0.02
No. of changes in physician				0.15	0.18
No. of prescription medications					0.23(1.26)***
Model chi-square	0.67	14.98*	17.00*	31.72**	49.00***

Note: odds ratios are shown only for statistically significant findings
* p<.05, **p<.01, *** p<.001

Results showed a positive correlation between the presence of any unconditionally inappropriate medication and the number of diagnoses (ß = .13, odds ratio = 1.14, p<.05). Results also showed a negative correlation between the presence of unconditionally inappropriate prescribing and the presence of dementia or cognitive impairment (ß = -.87, odds ratio = .42, p<.05). When the facility variable was introduced in model 3, the correlation between the presence of any unconditionally inappropriate medication and the number of diagnoses lost its significance. When physician-related variables were introduced in model 4, results showed that the number of prescribers makes a significant contribution to the prediction of any unconditionally inappropriate medication over and above the contribution of the diagnostic-related factors.

With the inclusion of the medication-related variable in Model 5, the statistically significant association between the presence of any unconditionally inappropriate medication and the presence of dementia or cognitive impairment was repeated. The odds ratio of 0.50 suggests that the presence of dementia or cognitive impairment effects a 50 percent reduction in the odds of receiving an unconditionally inappropriate medication.

The statistically significant association between the presence of any unconditionally inappropriate medication and the number of prescribers was also repeated. In addition, a statistically significant association was revealed between the presence of any unconditionally inappropriate medications and the number of years since the physician graduated (ß = .03, odds ratio = 1.04, $p<.05$). The resultant odds ratio of 1.04 suggests that the odds of a resident receiving an unconditionally inappropriate medication increase by four percent for each year since the resident's primary physician graduated. In other words, physicians that graduated 30 years go are 20 percent more likely to prescribe an unconditionally inappropriate medication than physicians that graduated 25 years ago. This is expected, since the medications listed on the Beers criteria tend to be older, and more likely to be prescribed by physicians who were trained at a time when these older medications were more commonly used.

A positive correlation was also demonstrated between the presence of any unconditionally inappropriate medication and the number of prescription medications (ß = .23, odds ratio = 1.26, $p<.001$). To summarize, this study found four statistically significant predictors of the presence of any unconditionally inappropriate medication: the absence of dementia or cognitive impairment, the number of prescribers for each resident, the number of years since the resident's primary physician graduated, and the number of prescription medications received by each resident.

Presence of any inappropriate drug-disease combination

When logistic regression analyses were performed with the presence of any inappropriate drug-disease combination as the dependent variable, the overall model only became statistically significant when the final block of variables was introduced (see table 24). Results showed that the presence of dementia or cognitive impairment (ß = .91, odds ratio = 2.47, p<.01) and the number of prescription medications (ß = .22, odds ratio = 1.25, p<.001) were the only two significant predictors of the presence of an inappropriate drug-disease combination.

Table 24: Beta coefficients (odds ratio) for the presence of any inappropriate drug-disease combination

	Model				
Variable	**1**	**2**	**3**	**4**	**5**
Intercept	-0.48	-1.25	-1.18	-2.01	-3.53
Age	-0.02	-0.02	-0.02	-0.02	-0.01
Sex	-0.11	-0.15	-0.14	-0.08	-0.07
No. of diagnoses		0.14	0.16	0.16(1.17)*	0.07
Dementia/cognitive impairment		0.62(1.86)*	0.66(1.93)*	0.65(1.91)*	0.91(2.47)**
Facility					
Facility 1 (reference)					
Facility 2 versus facility 1			0.36	0.22	0.07
Facility 3 versus facility 1			-0.43	-0.42	-0.33
Facility 4 versus facility 1			0.18	0.03	0.11
Years since the resident's primary physician graduated				0	0.01
No. of prescribers for each resident				0.28	0.19
No. of patients each resident's primary physician has				0.01	0.01
No. of changes in physician				0.01	0
No. of prescription medications					0.22(1.25)***
Model chi-square	0.84	9.15	11.34	13.28	26.33*

Note: odds ratios are shown only for statistically significant findings
* p<.05, **p<.01, *** p<.001

CHAPTER 4: DISCUSSION

Review of results and implications

Prevalence rate and patterns of inappropriate prescribing

This is one of the few studies, and the first known one in Canada, that has examined inappropriate prescribing using all three sub-types of the 2002 Beers criteria: 1) unconditionally inappropriate medications; 2) inappropriate drug-disease combinations; and 3) inappropriate doses or durations. The majority of studies conducted thus far using the Beers criteria have been limited to the first sub-type of inappropriate prescribing. This study was able to examine the other two sub-types of inappropriate prescribing because it was conducted in a nursing home setting, and detailed records were available with nursing home residents' diagnostic and medication-related information.

The overall prevalence of inappropriate prescribing found in this study was 29.4 percent. The prevalence rates for the three sub-types of inappropriate prescribing examined in this study, namely unconditionally inappropriate prescribing, inappropriate drug-disease combinations, and inappropriate doses or durations, were 16.9, 12.4, and 5.1 percent, respectively.

One study that also examined inappropriate prescribing using all three sub-types of the 2002 Beers criteria was the recent one conducted by van der Hooft et al. (2005) in the Netherlands. They found that the one-year prevalence rates of inappropriate prescribing between 1995 and 2000 ranged from 19.1 to 20.0 percent. The prevalence rate reported in the van der Hooft study is significantly lower than the prevalence rate

found in this study, possibly because physicians in the Netherlands prescribe fewer inappropriate medications. There is some support for this premise since the prevalence rate reported by van der Hooft's study is lower than the prevalence rates reported by most other published studies on inappropriate prescribing.

However, the lower prevalence rate found in the van der Hooft study might also be attributed to several other factors. First, Van de Hooft et al. conducted their study with an outpatient sample whereas this study was conducted in a nursing home sample. The former has, in the past, generally shown lower rates of inappropriate prescribing than the latter (Liu & Christensen, 2002). The difference between the two groups might be greatest with respect to inappropriate drug-disease combinations, since the nursing home resident tends to have multiple comorbidities, and is therefore more likely to be prescribed a drug that can potentially interact with one of their medical conditions. Second, there are several drugs from the 2002 Beers criteria that are not marketed in the Netherlands. These include meperidine, chlorpropamide, methocarbamol, diphenhydramine, dicyclomine, and cyclobenzaprine. Diphenhydramine, dicyclomine, and cyclobenzaprine were prescribed in the study sample, so this could also partly contribute to the difference in prevalence rates.

Another similar study was conducted by Clatney et al. in the long-term care setting in Saskatchewan (2004). The Clatney study examined two of the three sub-types of inappropriate prescribing outlined in the 2002 Beers criteria, namely, unconditionally inappropriate medications and inappropriate doses or durations. In this study, the combined prevalence rate of these two types of inappropriate prescribing was 21.6 percent, versus 33.0 percent in the Clatney study. One possible reason why Clatney's estimates were higher is that the time frame for their study was one year, while the time frame for this study was six months. It is also possible that the prescribing patterns of

physicians in Saskatchewan differ from the prescribing patterns of physicians in British Columbia. Another possible reason why the prevalence rate of inappropriate prescribing was higher in Clatney's study is that they conducted their analysis on prescriptions dispensed in the 2001 calendar year, whereas this study examined prescriptions dispensed in the six-month period from November 2004 to April 2005. Previous studies (Hanlon, Fillenbaum, Schmader, Kuchibhatla, & Horner, 2000; Zhan et al., 2001) have demonstrated a declining trend in the rate of inappropriate prescribing over time, as medications listed on the explicit criteria generally fall into disuse when replaced with newer medications. The three-year difference between the two studies could partially account for the difference in prevalence estimates.

The prevalence rate of the sub-type of unconditionally inappropriate medications in this study was 16.9 percent. This figure is lower than other prevalence estimates of unconditionally inappropriate prescribing in the nursing home setting. For example, Dhalla et al.'s (2002) study of nursing home patients in Ontario reported a prevalence rate of 20.8 percent, while Piecoro et al.'s (2000) study of Medicaid recipients in Kentucky reported a prevalence rate of 33 percent in the nursing home setting. A more recent study by Rigler, Jachna, Perera, Shireman, and Eng (2005) reported a 38 percent prevalence rate amongst Medicaid recipients in Kansas in the nursing home setting. The difference between the prevalence rate reported in this study and the prevalence rates reported in these three studies would be magnified even further if one considered the fact that the Dhalla, Piecoro, and Rigler studies were all based on the 1997 Beers criteria, while this study was based on the 2002 Beers criteria. Since 1997, only one medication (phenylbutazone) has been removed from Beers' list of unconditionally inappropriate medications, but 23 medications or medication classes have been added to this list. In other words, the prevalence rate reported in this study was lower than the

prevalence rates reported in three other studies conducted in the nursing home setting, despite the use of a more extensive list of unconditionally inappropriate medications for this study.

The single most commonly prescribed inappropriate medication, of which there were 31 cases, was anticholinergic medications prescribed to residents with cognitive impairment. As shown in Table 10 above, there is a fairly long list of medications with moderate or strong anticholinergic property. The concern with anticholinergic medications, as outlined in the 2002 Beers criteria, is that they can affect the central nervous system (CNS). This has important implications because the high prevalence of cognitive impairment found in the nursing home population makes it difficult to determine whether symptoms such as confusion, impaired cognition, anxiety, and restlessness are due to an adverse reaction of the medication or due to the underlying medical condition. If these symptoms are attributed to the anticholinergic medication, then the proper response would be to reduce the dose or remove the medication that might be causing these symptoms. However, if these symptoms are misinterpreted, then there is a chance that the resident might be administered an anxiolytic, or anti-anxiety medication such as a benzodiazepine, even though this would not resolve the underlying problem, and might even lead to additional adverse effects. This sequence of events which involves the misattribution of an ADR and subsequent addition of another medication to combat the adverse effects of the initial drug therapy is known as a 'prescribing cascade', and is of particular concern in patients with cognitive impairment (Gill et al., 2005).

Other inappropriate medications commonly prescribed in the study sample included, in descending order, nitrofurantoin, cimetidine, hydroxyzine, oxybutynin, and amitriptyline. These medications were found to be frequently prescribed by other researchers as well. For example, hydroxyzine was found to be one of the most

frequently prescribed inappropriate medications by Perri et al. (2005), while oxybutynin and amitriptyline were found to be amongst the most frequently prescribed by Dhalla et al. (2002). Amitriptyline and hydroxyzine were found to be among the most frequently prescribed inappropriate medications by Clatney et al. (2004). Nitrofurantoin and cimetidine were listed in the van der Hooft et al. (2005) study as two of the five most frequently prescribed inappropriate medications. These two medications have been found less frequently in studies on inappropriate prescribing, partly because they were only added to the Beers criteria in 2002, and the majority of studies published thus far were based on the 1997 Beers criteria.

Within the six-month study period of this study, there were 18 orders of nitrofurantoin, an antibiotic indicated for the treatment of urinary tract infections. Beers and colleagues' gave this medication a high severity rating and stated that their concern about this medication was its potential for renal impairment. Kunin (2004) reviewed the literature, but found no evidence to show that nitrofurantoin causes renal impairment. Instead, he found information stating that nitrofurantoin is contraindicated in patients who already have renal failure.[5] To my knowledge, Beers and colleagues have not yet responded to Kunin, so it is still debatable as to whether nitrofurantoin belongs on a list of unconditionally inappropriate medications.

The second most commonly prescribed unconditionally inappropriate medication was cimetidine. This medication is a histamine H2 receptor antagonist or H2 blocker that blocks the acid-secreting cells in the stomach, and is used in the treatment of gastric ulcers, duodenal ulcers, and reflux. Altogether, there are four H2 receptor antagonists, including cimetidine, ranitidine, famotidine, and nizatidine. One of the reasons why cimetidine might be more commonly prescribed than the other H2 blockers in this study

[5] My own findings, based on reviewing monographs of nitrofurantoin in current pharmacotherapy reference guides, cooincides with Kunin's.

sample is that this medication is listed by BC Pharmacare as a 'reference drug' under its Reference Drug Program. In other words, the government will pay for the cost of the cimetidine, and the difference in cost between all other H2 blockers and the cost of cimetidine would be passed on to the patient. The government based this decision on research showing that all four H2 blockers had similar efficacy and safety profiles (Therapeutics Initiative, 1994). Beers and colleagues, however, have argued that they were concerned about using cimetidine in the older adult population because it is more likely to cause CNS adverse effects including confusion. While it is beyond the scope of this paper to review the primary literature on cimetidine, one important question to consider is whether it is appropriate to apply the findings from randomized controlled trials mostly conducted in relatively healthy older adults with few comorbidities to a population of older adults with multiple comorbidities living in residential care? Given the challenges of conducting randomized controlled trials in the nursing home population, one practical course of action would be to ask nurses working in the nursing homes to monitor residents recently started on cimetidine for any CNS adverse effects.

Hydroxyzine and diphenhydramine, both antihistamines with anticholinergic properties, were also among the most commonly prescribed inappropriate medications in this study sample, and accounted for 20 out of 91 orders (22.0 percent) of unconditionally inappropriate medications over the six-month study period. Although Beers and colleagues designated these two medications as unconditionally inappropriate for the elderly, Zhan et al. (2001) considered them appropriate in the treatment of allergic reactions and urticaria. In other words, Zhan et al. suggested that it is not necessary for elderly patients to avoid these medications altogether, but rather limit the duration of their usage to the acute treatment of the allergic reaction or urticaria. Unfortunately, this and other studies have shown that inappropriate medications are

often administered to nursing home residents on an extended basis. In the study sample, residents who were prescribed an unconditionally inappropriate medication following their admission to the nursing home were continued on that medication for an average duration of 388 days, slightly over one year. In the Rigler et al. (2005) study, 46 percent of the nursing home residents who received an unconditionally inappropriate antihistamine received it on an extended (i.e. between one and nine months) or chronic (i.e. between nine and twelve months) basis. One practical strategy for addressing this problem might be to encourage physicians to prescribe these medications on a short-term basis, or else flag them for review/reassessment in a more timely manner (i.e. ten days to two weeks) than the regular six-month medication review. Research might also explore the reasons for long-term use of these medications.

Amitriptyline was also one of the more frequently prescribed unconditionally inappropriate medications in this study sample. When this medication was first included in the 1991 Beers criteria, it was prescribed as an antidepressant. Since that time, newer antidepressants (e.g. SSRIs) have been introduced in the market that have a better side effect profile. As a result, amitriptyline is much less frequently prescribed for depression. However, this medication is currently being prescribed in low doses for the treatment of neuropathic pain. Some clinicians (Chutka et al., 2004; Zhan et al., 2001) feel that this medication is safe in the elderly if prescribed in low doses, and therefore disagree with Beer and colleagues' decision to include this medication on their list of unconditionally inappropriate medications. One suggestion might be for those working on the next version of the Beers criteria to consider new evidence on the use of amitriptyline in the elderly in low doses for the treatment of neuropathic pain.

Predictors of inappropriate prescribing

Statistically significant predictors of inappropriate prescribing found in this study are summarized in Table 25 below. Logistic regression analyses could not be performed on the third sub-type of inappropriate prescribing (i.e. inappropriate doses or durations) due to the small number of cases.

Table 25: Predictors of inappropriate prescribing per the 2002 Beers criteria

Type of inappropriate prescribing	Correlates
Overall	Number of prescription medications Number of prescribers
Unconditionally inappropriate medications	Absence of cognitive impairment or dementia Number of prescribers Number of years since physician graduated Number of prescription medications
Inappropriate drug-disease combinations	Presence of cognitive impairment Number of prescription medications

This study found that the number of prescription medications taken by each resident is a significant predictor of all three dependent variables: 1) overall inappropriate prescribing, as defined by the presence of any medication from the 2002 Beers criteria (OR=1.22, $p<.001$); 2) the presence of unconditionally inappropriate medications (OR=1.26, $p<.001$); and 3) the presence of inappropriate drug-disease combinations (OR=1.25, $p<.001$). Other studies have also found this variable to be a strong predictor of inappropriate prescribing across various settings (Lau, Kasper, Potter, Lyles, & Bennett, 2005; Rancourt et al., 2004). These findings suggest that patients taking a large number of medications should be a target for intervention.

Another finding of this study is that the number of prescribers is associated with overall inappropriate prescribing as well as the presence of unconditionally inappropriate

medications. In addition, the number of years since the resident's primary physician graduated is predictive of the presence of unconditionally inappropriate medications. This finding was expected since the medications listed on the Beers criteria are mostly older medications, and one might expect older medications to be prescribed more frequently by physicians who graduated many years ago, as opposed to physicians who just recently graduated.

Residents who were cognitively intact were more likely to receive an unconditionally inappropriate medication than residents with dementia or cognitive impairment. This was also found in the Perri et al. (2005) study. One possible reason for this is that physicians are more careful in prescribing for patients with cognitive impairment. Another possible explanation is that those without dementia or cognitive impairment are better able to voice their requests for pharmacological treatment than those with cognitive impairment, and, in doing so, they are prescribed a greater number of medications, including medications that are considered unconditionally inappropriate. A third possible reason why cognitively impaired residents received fewer unconditionally inappropriate medications is that the presentation of their illness is affected by their condition, and this impacts the treatment that they receive.

On the other hand, those with cognitive impairment were more likely to receive an inappropriate drug-disease combination. The most common inappropriate drug-disease combination found in this sample was when anticholinergics were prescribed to those with cognitive impairment. The concern is that it is difficult to determine whether CNS symptoms are attributed to the adverse effect of medications or the underlying medical condition. Therefore, extra vigilance in monitoring the effects of medications is warranted, particularly when a new anticholinergic medication is started or when a resident is receiving more than one anticholinergic medication (Roe et al., 2002).

Currently, one of the more common approaches to treating dementia is through the use of cholinesterase inhibitors. Medications such as donepezil (Aricept), rivastigmine (Exelon), and galantamine (Reminyl) that are prescribed for the treatment of dementia, in essence, increase cholinergic activity. However, their effectiveness is questionable when the patient is also taking an anticholinergic medication, which has the opposite pharmacological effect. In this study, 10 residents were receiving medications that had both cholinergic and anticholinergic effects. This problem is not uncommon. For example, in the Roe et al. (2002) study, older patients with probable dementia were significantly more likely to use anticholinergics than a matched comparison group of patients (33.0 versus 23.4 percent, p=.001). This highlights the need to improve prescriber education about the potential for pharmacological antagonism in this particular sub-set of the nursing home population.

Unlike previous studies (Piecoro et al., 2000; Zhan et al., 2001; Meredith et al., 2001), females in this study were not more likely to receive inappropriate medications compared with males. This may be due to the pattern of inappropriate medications prescribed in this sample. In this study, the inappropriate medications most commonly prescribed were nitrofurantoin, cimetidine, hydroxyzine, oxybutynin, and amitriptyline. There may not be any sex differentials in the prescribing of these particular medications.

This study also showed that a change in physician does not result in more inappropriate prescribing. However, if a resident is already receiving an inappropriate medication, the new physician is not discontinuing that inappropriate medication either. As Cantrill et al. (2000) found, physicians expressed a reluctance in changing an inappropriate medication if it had been started by another physician. Further research into this is required.

In summary, this study adds to previous studies on inappropriate prescribing because it is one of the few that have included diagnostic data in the analysis. The key findings of this study are as follows. The prevalence rate of inappropriate drug-disease combinations is 12.4 percent, indicating that a significant number of residents are receiving inappropriate medications given their medical conditions. The most common inappropriate drug-disease combination was the prescription of anticholinergic medications in residents with cognitive impairment. This was also the single most commonly prescribed inappropriate medication found in the entire study. Overall, the odds of a resident receiving any inappropriate drug-disease combination is increased by a factor of 2.47 for those with dementia or cognitive impairment. Not only are those with cognitive impairment at increased risk because they are more likely to receive an inappropriate medication, but their ability to report the negative effects of medications is impaired. The results of this study suggest that clinicians should take extra precautions to distinguish between the central nervous system effects of anticholinergic medications and the effects of the underlying disease in those with cognitive impairment.

Linkages to Tamblyn's conceptual framework

This study was guided by Tamblyn's (1996) conceptual framework, which outlines the factors influencing the risks versus benefits of prescription medications (refer to Figure 1). Tamblyn's framework also helps us examine some of the interrelationships between the various factors. The risk-to-benefit ratio of a medication is not absolute; instead, it varies with the characteristics of the patient population. In this study, the patient group consists of nursing home residents who were, on average, 85.9 years old, had, on average, 4.8 medical conditions, and took, on average, 5 prescription medications each day. Increased age, the number of medical conditions, and the

number of prescription medications have all been shown to be predictive of adverse drug reactions in the elderly (Routledge, O'Mahony, & Woodhouse, 2004).

Special consideration needs to be given to the organizational environment within which the patient group for this study lives. In the nursing home setting, health professionals such as physicians, nurses, and pharmacists work together to manage medications for the residents. This is in contrast to the community setting, where patients manage their own medications. If a medication is prescribed to a nursing home resident on a regular basis, the nurse ensures that the resident takes the medication regularly. If a medication is prescribed on a PRN or 'as needed' basis, the nurse's discretion and professional judgment often play a role in determining how much medication a resident receives.

Nurses also impact the prescribing process in the long-term care setting. For example, if a nurse observes that a resident has an acute illness, s/he can contact the resident's physician to request pharmacological treatment. Nurses can be particularly instrumental in requesting pharmacological treatment for residents who are cognitively impaired. When residents are too sick or frail to go to the physician's office or when physicians are unable to leave their office to assess their patients in the nursing home, nurses play a pivotal role in guiding physicians' prescribing decisions.

Pharmacists are knowledgeable about the side effects of medications, and could work with nurses to identify parameters for monitoring both the positive and negative effects of medication. Pharmacists can also make prescribers aware of the Beers medications or other medications considered inappropriate in the elderly and offer suggestions for potentially safer alternatives. Since pharmacists are most familiar with provincial drug benefit plans, they can also help prescribers choose medications that residents can afford.

Tamblyn's conceptual framework also highlights the role of the health care system in medication management. One way in which the health care system affects medication management is through provincial regulations such as the B.C. Community Care and Assisted Living Act (British Columbia Ministry of Health Services, 2002) as well as the Pharmacists, Pharmacy Operations and Drug Scheduling Act (College of Pharmacists of British Columbia, 2004) that set standards for professional practice for nurses and pharmacists. The health care system also establishes remuneration schemes for professional services. In addition, provincial bodies such as B.C. Pharmacare decide which medications are covered under the publicly-funded drug benefits plan.

At times, different elements in Tamblyn's framework work in opposing directions. For example, newer medications are often touted as safer in the elderly, but are also more expensive and less likely to be covered by provincial drug plans. If two medications are shown to be equally safe and effective in a randomized clinical trial, then there is evidence to support the government's decision to cover the less expensive one. However, as previously discussed, these randomized clinical trials may be of limited generalizability to the nursing home residents. In these cases, other controlled studies may serve as the 'best available evidence' for helping us determine whether medications are equally safe and effective in the nursing home population.

In Canada, the health care system factors that affect prescribing patterns mostly operate on a provincial level. Hence, the prevalence rates and patterns of inappropriate prescribing found in this study would only be generalizable to other nursing homes within British Columbia. Nonetheless, other studies of inappropriate prescribing conducted in Canada, based on the Beers criteria, have reported similar prevalence rates. For example, the prevalence rate of inappropriate prescribing was found to be 33 percent

among elderly long-term care residents in Saskatchewan (Clatney et al., 2004) and 20.8 percent in nursing home residents in Ontario (Dhalla et al., 2002). A future research study that compares inappropriate prescribing across provinces might provide more details on how the health care system affects prescribing practices.

In the United States, there is federal legislation, namely the Nursing Home Reform Act, that governs the use of psychotropic medications in the nursing home (National Coalition for Nursing Home Reform, 1987). For example, barbiturate medications, which are listed as high-risk medications on the Beers criteria, are not to be used in the nursing home unless started before the resident was admitted to the home, or else given as a single dose for a medical or dental procedure. Another regulation of this Act states that a resident with dementia who is exhibiting behavioural problems must not be treated with an antipsychotic unless the behaviour is documented, permanent, persistent, and causing psychotic symptoms or danger to the resident and others. Research has shown that psychotropic drug use in nursing homes has declined significantly following the implementation of this legislation (Hughes et al., 2005). At the current time, no equivalent regulatory rules exist in Canada to control the use of psychotropics in nursing homes.

Overall, Tamblyn's conceptual framework suggests a number of important variables to consider when evaluating the risks versus benefits of medication use. The framework also identifies the health care system as important in shaping health care practitioner's decisions and behaviours around medication management. For this study, variables from three key elements of the conceptual framework (resident, physician, and medication) were analyzed in this study to determine whether they were predictive of the presence of inappropriate prescribing per the 2002 Beers criteria. Residents with a high number of prescription medications and residents with more than one prescriber were

more likely to receive Beers medications. While residents who were cognitively intact were more likely to receive an unconditionally inappropriate medication, residents with dementia or cognitive impairment were more likely to receive an inappropriate drug-disease combination. More work needs to be done to quantify the relationships between the variables suggested by Tamblyn's framework and the presence of inappropriate prescribing. Factors such as the physician's scope of practice, training experiences, and awareness of the Beers criteria could be examined in detail to determine whether they affect prescribing patterns. This information can then be used to modify the Tamblyn framework so as to increase its predictive capacity and usefulness.

Limitations

There are a number of limitations of this research. This study of medication appropriateness relied on explicit criteria as defined by Beers and colleagues in 2002. These authors emphasized that their explicit criteria were not meant to supersede the clinical judgment and assessment of a physician. The Beers criteria can only serve as a screening tool to identify some potential cases of inappropriate prescribing. Each patient's medical history and medications must be reviewed on a case-by-case basis to determine the risk-to-benefit ratio of that individual's pharmacological treatment.

Another limitation to studying medication appropriateness using explicit criteria is that the criteria can become outdated. The 2002 Beers criteria were based on the information available to the authors at that time. Since then, new medications have been introduced to the market and more information is available on the safety profile of medications. A number of medications, such as reserpine and cyclandelate, that appeared on the original Beers criteria in 1991 have largely fallen into disuse, and should perhaps be removed from the criteria. Overall, explicit criteria need to be updated regularly to remain useful.

A few limitations exist with respect to the quality of the data. Medication review letters were used as the source of medication-related data. These letters were generated by the same computer program that the pharmacists used to process the prescriptions, and therefore offer an accurate account of all medications taken by a nursing home resident at the time the letter is printed. However, only one medication review letter was printed for each resident over the six-month study period. If, for example, a short-term course of a Beers medication (e.g. nitrofurantoin for ten days for treatment of a urinary tract infection) was already completed before the medication review letter was printed, it would not be captured in the letter. In order to address this shortcoming, it was necessary to supplement the data from the medication letters with computer-generated reports on each of the Beers medications dispensed over the study period. Another potential limitation to this study is the accuracy with which data were transferred from the medication review letters to the statistical software. In order to check the accuracy of data entry, a random sample consisting of five percent of all cases was drawn from the statistical database and directly compared with the medication review letters.

Another potential data-related limitation pertains to the accuracy and completeness of the residents' diagnostic information as listed in the nursing homes' medical records and subsequently transferred to the pharmacy database where it was retrieved for this study. Although physicians are asked to check residents' medical records regularly, there is the possibility that certain medical conditions are under-reported. For example, a review of the medical records for the study sample showed that only nine out of 449 residents had a diagnosis of insomnia recorded on their medical records. However, 123 residents were prescribed a hypnotic or sleep-inducing agent. Therefore, a decision was made to assign a diagnosis of insomnia to all residents who

were receiving hypnotic medications. A similar situation was found for the diagnosis of chronic constipation. Hypothetically, this potential problem might affect the conclusions of this study if the diagnosis of cognitive impairment is under-reported. In order to be more confident about the quality of residents' diagnostic information, I could have compared the information on the pharmacy records against the patient's medical records stored at the physician's office, which are likely to be the most accurate and complete. However, this was beyond the scope of the study.

Another data-related limitation in this study is that data were not collected on the frequency of PRN medication use. As a result, it was not possible to state, definitively, whether the doses of medications administered on a PRN basis exceeded the maximum doses recommended in the Beers criteria. Fortunately, there were only three cases in this study where a PRN order had the potential to exceed the maximum recommended doses. This small number of cases is unlikely to have a significant effect on the overall conclusions of the study.

Other data limitations pertain to the physician-related variable years since graduation. This variable is only a proxy for the physician's training experience. A physician's actual training experience can come from many different sources, including medical school, continuing education, self-study, and practical experience. In addition, data on the years since graduation was only collected for the resident's primary physician, and not on for specialists that might have prescribed for the resident. Finally, the resident's primary physician was not necessarily the one who originally ordered the Beers medications, although physicians were presented with opportunities review all the residents' medications every six months.

Future directions

This study suggests ways in which medication appropriateness in the nursing home setting can be addressed using an applied or practical approach as well as a research-based approach. From an applied perspective, pharmacists should familiarize themselves with the Beers criteria, and the reasons why these medications are considered high risk for older adults. In doing so, they can assist physicians with their prescribing decisions, incorporate the Beers criteria for medication appropriateness into the medication review letters, and/or possibly suggest safer medications for use in nursing home residents. This study suggests that residents who receive a large number of prescription medications are more likely to receive an inappropriate medication. Therefore, these residents' files should be flagged, and their medications reviewed more frequently than the currently scheduled biannual review.

Since the medications listed on the Beers criteria are generally older medications, some have fallen into disuse, while others, such as nitrofurantoin, cimetidine, hydroxyzine, oxybutynin, and amitriptyline are still commonly prescribed. In this study, 72 out of the 91 orders of unconditionally inappropriate medications were initiated after the older adult was admitted to the residential care facility. This has two implications: 1) it shows that Beers medications are still being prescribed fpr nursing home residents; and 2) it identifies opportunities in the nursing home setting where nurses can monitor the effects of Beers medications. If adverse drug reactions are detected for residents taking a medication from the Beers criteria, there needs to be a concerted effort to report these to Health Canada's adverse drug reaction database. Currently, it is estimated that only 10 percent of adverse drug reactions are reported to Health Canada (Canadian Broadcasting Centre, 2005). If the rate of reporting adverse

drug reactions is increased, prescribers will be more aware of which medications cause adverse outcomes in the elderly.

From a research perspective, there is a need to conduct further research to strengthen the validity of the Beers criteria. Although Beers and colleagues review the existing literature on medication use in the elderly as the first step in developing their consensus criteria, the strength of the evidence on which they base their criteria is not reported. That a particular medication is listed on the Beers criteria speaks more to the consensus of the expert panel that Beers convenes than the evidence base supporting the decision to include a particular medication in the list of inappropriate medications. Chutka, Takahashi, and Hoel (2004) have tried to address this by searching the scientific literature for evidence supporting the inclusion of particular medications or medication classes in the 1997 Beers criteria. For example, they state that fairly strong evidence (i.e. case studies and controlled trials) supports the inclusion of tricyclic antidepressants in the Beers criteria, but that the level of evidence supporting the inclusion of meprobamate in the Beers criteria is not as strong. This type of validation study should be repeated for the 2002 version of the Beers criteria, and repeated periodically as new evidence on the adverse effects of medications in the elderly arises. Research studies can be also designed to target areas where the level of evidence is not as strong.

More research is needed to examine the relationship between Beers medications and adverse health outcomes. To date, the health outcomes most commonly studied are hospitalizations and deaths. These measures may not be sensitive enough to detect all the adverse effects associated with the use of the Beers medications in the elderly. Research can also help us identify individuals most at risk of experiencing other negative health outcomes, such as falls and fractures, while receiving medications listed on the Beers criteria.

One finding of this study worth further investigation is the higher rate of use of inappropriate medications in residents who are cognitively intact. Future research could examine the differences in prescribing patterns between cognitively intact residents and cognitively impaired residents to examine whether there are differentials in the prescribing of certain medication classes. One could also test the premise that cognitively intact residents receive more medications, and more unconditionally inappropriate medications, because they initiate more requests for medications from their physicians and/or resist the discontinuation of medications. Future research could also examine the presentation of illness or symptoms in the cognitively impaired and how this affects what medications they receive.

Another finding of this study worth further study is the long-term use of unconditionally inappropriate medications. Some preliminary work has been done by Dhalla et al. (2002) tracking the initiation and discontinuation rates of inappropriate medications in the nursing home setting. Cantrill, Dowell, and Roland (2000) have shown that physicians express reluctance in changing an inappropriate medication if it had been started by another physician. More research is needed to explore the reasons why potentially inappropriate medications are continued for extended periods and the barriers that physicians face in discontinuing these medications. Surveys can also be conducted to determine physicians' awareness of the Beers criteria, their opinions on whether they feel the criteria are valid and useful, whether they are aware that they are prescribing a Beers medication, and how they perceive the benefits versus risks of Beers medications when prescribing for the elderly.

Finally, more studies using the full Beers criteria need to be conducted, in representative samples of nursing home residents as well as patients from other settings. The inappropriate drug-disease combination still remains an important but

relatively unexplored category of suboptimal prescribing in the elderly, especially in subpopulations of the elderly with multiple comorbidities, such as the nursing home population. Previous studies conducted on administrative data did not have access to patients' diagnostic information, but this is likely to change with the widespread adoption of electronic medical records.

Conclusion

This study is unique in that it examined all three sub-types of inappropriate prescribing outlined in the 2002 Beers criteria in a nursing home setting. This is also the first known study in Canada to examine inappropriate drug-disease combinations. This is an important contribution to the literature because nursing home residents tend to have multiple comorbidities and take multiple medications, and are therefore more likely to experience this sub-type of inappropriate prescribing. In addition, the effects of inappropriate drug-disease combinations may be more difficult to detect in residents with cognitive impairment.

In this study, the overall prevalence rate of inappropriate prescribing, as defined by the 2002 Beers criteria, was 29.4 percent. This prevalence rate suggests that there is room for improvement with respect to prescribing in the nursing home elderly. Although the Beers criteria cannot definitively state whether a medication is inappropriate for a single nursing home resident, given that individual's unique circumstances, it can serve as an efficient screening tool for inappropriate prescribing in the nursing home setting.

The nursing home setting provides an opportunity for different health professionals to work together to optimize the management of medications for the residents. From an applied perspective, clinicians need to be more aware of the risks associated with the medications listed on the Beers criteria and establish clearer

guidelines for monitoring the effects of these medications. From a research perspective, more studies are required to examine the health outcomes associated with the use of Beers medications.

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