

High Risk Medication Regimens and Medication Related Predictors of Hospital
Readmission in Elderly Home Care Patients

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ABSTRACT

Adverse drug events are a primary cause of hospitalization in the elderly. Nearly 70% of the \$177.4 billion dollars spent on drug related morbidity and mortality in the U.S. is due to hospitalizations. Polypharmacy, inappropriate medications or medication regimen complexity have all been implicated as precursors to adverse drug events and as indicators of high risk medication regimens. Understanding the relationship between medication regimens and readmission is important when evaluating potential errors in administration, risk-benefit ratios, and readmission risk. However, due to definitional and measurement issues, the high risk medication regimen remains an elusive concept.

This study characterizes medication regimens, defines high risk medication regimens, and determines if high risk medication regimens predict re-hospitalization in home healthcare clients over age 65. An exploratory, secondary analysis of OASIS data and medication records from 15 home care agencies was used to characterize medication use in 911 older adults discharged from the hospital to their first episode of home care in 2004. Conceptual and operational definitions of polypharmacy, potentially inappropriate medications, medication regimen complexity, and high risk medication regimens were developed. Logistic regression and structural equation modeling were used to examine the relationship between comorbidity, a variety of risk factors supported by the literature, high risk medication regimens (defined by polypharmacy, potentially inappropriate medication regimens, and medication regimen complexity) and re-hospitalization to determine if high risk medication regimens predicted re-hospitalization in these subjects.

Factor analysis revealed that high risk medication regimens are composed of polypharmacy, potentially inappropriate medication regimens, and medication regimen complexity, and that a model using this concept rather than individual medication variables proved to be the most predictive and parsimonious model. The model accounted for 10% of variance in re-hospitalization in this sample. Additionally, high risk medication regimens appear to have as much influence as comorbidity on hospital readmission.

Future research should include high risk medication regimens as a predictor of readmission and previously completed studies may need to be re-evaluated in light of these findings. Both the findings and the methodology will be useful in examining predictive potential of high risk medications regimens in other settings.

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CHAPTER I

INTRODUCTION

Health care is a risky business. Everyday, millions of older adults ingest chemicals which can be hazardous to their health. Nevertheless, these chemicals are also the fabled fountain of youth, replacing compounds our bodies no longer make (insulin, thyroid hormone), preventing the aging process (statins, estrogen), and forestalling death (digoxin, chemotherapy). These chemical compounds, known as medications, are the miracles of modern medicine. Any medication consumed in too great an amount can disable or kill an individual, and if taken in too small an amount, allows the disease to disable or kill the individual. Not unlike the alchemists of old, the job of the modern health care provider is to find the right balance of these chemicals to improve an individual's health, while preventing further harm to the individual. Indeed, the Hippocratic principle, "first do no harm", places health providers squarely in the business of risk assessment. A primary area of risk assessment and management is the medication regimen.

Balancing the risks and benefits of a medication regimen is a familiar problem to providers caring for home health care (HHC) patients. Without the structure and supervision imposed by the inpatient setting, home health care patients also use over-the-counter (OTC) remedies and herbals besides their prescribed medication regimen. In addition, many patients have multiple diseases (comorbidity or multimorbidity) requiring treatment with multiple drugs used concurrently (polypharmacy).

Unfortunately, medications used concurrently may also increase risk due to

1) potential drug-to-drug or drug-to-disease interactions, 2) decreased metabolism and clearance of drugs, and 3) changes in the storage of medications within the body (Salazar, Poon, & Nair, 2007). However, changes in metabolism, clearance, and storage of medications in the body especially predispose older adults to these drug-drug or drug-disease interactions and are associated with an increased risk of adverse drug reactions which in turn, can increase the likelihood of being hospitalized (Fu et al., 2007; Fu, Liu, & Christensen, 2004; MacLaughlin et al., 2005; Meredith et al., 2002; Salazar et al., 2007; Simonson & Feinberg, 2005). Due to changes in drug metabolism and clearance, many medications are classified as potentially inappropriate medications when prescribed for older adults (Beers, 1997; Beers et al., 1991; Fick et al., 2003; Hanlon, Schmader et al., 1992; Hanlon, et al., 1997). These changes in metabolism and clearance permit the active metabolites in the drug to persist in an older adult's body at higher doses than therapeutically necessary (Nebeker, Barach, & Samore 2004). The combination of diseases, drugs, and medication regimens which are unfamiliar to the individual, increase the inherent risk of a medication regimen. This may be especially true if older adults have very complex regimens that are difficult to set up or have fluctuating dosing schedules, a concept referred to in the literature as medication regimen complexity (Conn, Taylor, & Kelley, 1991; Field, Mazor, Briesacher, DeBellis, & Gurwitz, 2007; George, Phun, Bailey, Kong, & Stewart, 2004; George et al., 2006).

Comorbidity increases both the risk of hospitalization and re-hospitalization (Coleman, Min, Chomiak, & Kramer, 2004; Hasan et al., 2010; Hastings et al., 2008; Madigan, Schott, & Mathews, 2001; Parker, McCoombs, & Graddy, 2003; Rosati & Huang, 2007), and is often the reason that older adults are thrust into medication

regimens that include polypharmacy, inappropriate medications, and medication regimen complexity. Any one of these three factors alone increases the risk for drug-to-drug interactions and drug-to-disease interactions, but when combined, may possess a synergy that increases the risk of hospitalization and readmission far beyond the risk conferred by comorbidity alone. The negative effect of the combination of polypharmacy, inappropriate medications, and medication regimen complexity have been conceptualized as a high risk medication regimen (George et al., 2004; Williams, 2002).

High risk medication regimens frequently result in an adverse drug reaction, a deleterious response to medications which is not foreseen and occurs at “normally therapeutic dosing” (Nebeker et al., 2004, p. 795). With high risk medication regimens, a potential chain of undesirable problems can be set into motion: adverse drug reactions lead to an adverse drug event (an untoward medical occurrence such as a fall, dizziness or cognitive changes) which can result in an adverse outcome such as hospitalization or readmission to the hospital (Fu et al., 2007; Meredith et al., 2002; Simonson & Feinberg, 2005; Sorensen, Stokes, Purdie, Woodward, & Roberts, 2005).

Significance of Problem

Death, Hospitalization and Re-hospitalization Related to Adverse Drug Events

As the wave of baby boomers begins to impact our health care institutions, medication regimen management will become an increasingly important aspect of health care quality, both in the inpatient and outpatient settings. In the United States, during 2006 (latest figures available), there were 34.9 million discharges from non-federally funded hospitals (DeFrances, Lucas, Buie, & Golosinskiy, 2008). Those age 65 and over comprised 38% of the inpatient discharges and consumed 43% of the inpatient days of

care (DeFrances et al., 2008). Among Medicare beneficiaries, 63% are re-hospitalized within one year of discharge, with 20% of beneficiaries readmitted within 30 days of discharge (Jencks, Williams, & Coleman, 2009). Zook, Savickes, and Moore (1980) noted that a second hospitalization is significantly more costly in terms of length of stay and subsequent cost, with the readmission ranging from 24-53% more expensive than the first admission.

In a meta-analysis of the existing literature on adverse drug events in hospitalized patients, Lazarou, Pomeranz, and Corey (1998) estimated that 4.7% of all hospitalizations in all age groups in the United States are due to adverse drug events. However, for older adults these numbers change dramatically; 28% of the hospitalizations, 2 million serious adverse drug reactions and 106,000 deaths annually are attributed directly to prescribed drug use (ASCP Update, 2000; Aspden, Wolcott, Bootman, & Cronenwett, 2007). In 2006, there were 141 deaths/100,000 older adults over age 65 attributed to adverse drug effects (both prescribed and non-prescribed drug use) in the United States (Centers for Disease Control [CDC], 2009g). Yet, the death rate attributed to adverse drug events is just a small portion of the overall problem leading to consequences of high risk medication regimens.

Cost of Medication Related Morbidity and Mortality

The cost associated with drug related morbidity and mortality is staggering. Ernst and Grizzle (2001) modeled the overall cost of drug-related morbidity and mortality and found the cost exceeded \$177.4 billion in 2000, with hospital admissions accounting for nearly 70% of these costs. Fu et al. (2007), citing Sellers' 1999 research, suggest that for every dollar spent on drugs in the United States, an additional dollar is spent to correct

problems caused by consumption of potentially inappropriate medications. It is believed that 25-66% of adverse events are preventable (Dennehy, Kishi, & Louie, 1996; Kallenbach, 2008). Field, Gilman, Subramanian, Fuller, Bates, and Gurwitz, (2005) estimated that the cost of preventable adverse drug events for Medicare beneficiaries in 2000 to be \$887 million (\$1983 per incident). However, the dollar amount in dealing with the aftermath of high risk medication regimens is only a portion of the adverse outcomes older adults suffer as a result of this problem.

Consequences of Hospitalization in Older Adults

For older adults, the consequences resulting from hospitalization or re-hospitalization can be devastating. Rapid transitions from home to hospital can lead to confusion, while catheter use can result in sepsis, and immobility in decubitus formation, aspiration pneumonia, and increasing frailty (Creditor, 1993; Naylor, et al., 1999). This downward spiral is difficult to reverse and all too often leads to increased length of stay, institutionalization, or death.

Directly after hospitalization seems to be a particularly dangerous period for an older adult due to higher numbers of medications being prescribed, unfamiliarity with the medications being prescribed, and likely, a higher degree of complexity in medication regimen management (Field et al., 2007). New medication regimens are prescribed by hospitalists unfamiliar with the patient's support system or home setting. These medication regimen changes occur when an older adult is most vulnerable, physically and mentally, from their hospitalization, and family members have a high level of stress arranging for transfer and also for care of the patient in the home (Field et al., 2007). Therefore, each time an older adult is hospitalized, a transition in care occurs, with an

increased risk of a medication problem potentially leading to subsequent re-hospitalization (Greenwald & Jack, 2009).

Adverse Drug Events after Hospitalization

Hanlon et al. (2006) found that 16% of subjects discharged from the hospital had preventable adverse drug reactions with most adverse drug reactions occurring within 4 months of discharge from the hospital. Gray, Mahoney, and Blough (1999) found the adverse drug event incidence during the month following discharge to be 20% with 53% of patients having an adverse event serious enough to consult a physician as a result of the event. Coleman, Smith, Raha, and Min (2005) found that 14.1% of elderly patients reported one or more medication discrepancies, compared to what the discharging physician ordered, when assessed 24-72 hours after hospital discharge. Fifty-one percent of the discrepancies were patient errors, but 49% of the discrepancies were attributed to system problems. Those with discrepancies had a 14% readmission rate compared to a 6% readmission rate for those without discrepancies. Bates et al. (1995) contended that 56% of all medication errors occur during the prescribing process; medications are prescribed that should not be prescribed.

Gray et al. (1999) also found older adults, on average, were prescribed 8.1 medications at hospital discharge, with 53% taking two new medications in their regimen at discharge. This figure does not include medications that older adults take without a prescription, including over-the-counter drugs, herbals, or drugs “borrowed” from friends or relatives. This can present serious problems as the incidence of drug interactions is estimated to be 50% in older adults who take five drugs, while in an older adult taking eight medications, the risk of having an adverse drug event (falls, cognitive changes)

increased to 100% (Lin, 2004). Clearly the prescribing of inappropriate medications, and subsequent adverse drug events, occur with regularity in this population despite providers' awareness of the dangers of high risk medication regimens.

Falls

One adverse event frequently leading to hospitalization in the older adult is falls. Unintentional falls are the leading cause of hospitalizations in this age group (CDC, 2009e). Stevens, Corso, Finkelstein, and Miller (2006), combining data from the 1) National Vital Statistics System, 2) the National Electronic Injury Surveillance System-All Injury Program, Health Care Utilization Program-National Inpatient Sample, and 3) the Medical Expenditure Panel Survey (MEPS), calculated that in the United States, for those age 65 and over, there were 10,300 fatal falls at an estimated cost of \$179 million dollars. The researchers estimated there were 2.6 million *non-fatal* fall injuries costing approximately \$19 billion dollars per year.

Most fall prevention programs recognize that medications are an important risk factor for falls; yet data supporting medications as a causal factor for falls is sparse. In 2004, researchers at Johns Hopkins University found a three times greater risk of falling in the two days following a medication change (CDC, 2009e).

Accidental Poisoning

A second adverse event resulting in hospitalization is accidental poisoning. Presumably, drugs used for recreational purposes are a rare phenomenon in the present cohort of older adults. Therefore, assuming that most of unintentional poisoning is due to drug overuse, examining the unintentional poisoning in this age group could shed some light on the prevalence of this outcome. The CDC (2009f) defines a poison as “any

substance that is harmful to your body when ingested (eaten), inhaled (breathed), injected, or absorbed through the skin. Any substance can be poisonous if enough is taken. This definition does not include “adverse reactions to medications taken correctly” (CDC, 2009f; CDC, 2009b). However, the CDC does count excessive use of drugs for non-recreational purposes in the definition of unintentional poisoning (CDC, 2009f).

About 95% of unintentional poisonings were caused by drugs (CDC, 2009d). For those age 65 and over, unintentional poisoning is the seventh leading cause (71,536 patients in 2007) of non-fatal injuries treated in emergency departments in the United States, the eighth leading cause of accidental death (1,025 deaths in 2006) (CDC, 2009b; CDC, 2009a; CDC, 2009d), and the second leading cause of hospitalizations (4.9%) for unintentional injuries in this age group (CDC, 2009a). Shamliyan (2010), using the National Inpatient Sample of the Healthcare Cost and Utilization Project for years 2000-2007, estimated the hospital costs associated with accidental poisoning were \$5,329,276,300 over those years or \$666,159, 527 per year. Additionally, in 2007, the hospital charges were \$905,776,509 for the 42,057 patients age 65 and over who suffered adverse drug effects from their medications. The study did not include post-hospitalization costs. Given that falls and unintentional poisonings account for many hospitalizations and can be presumed to be highly related to medication use, when the cost of these adverse outcomes are added to the morbidity and mortality figures for adverse events directly attributed to medication use, the cost of medication related morbidity and mortality increases substantially.

Current Management of High Risk Medication Regimens

Two common approaches to manage high risk medication regimens after hospitalization include prevention of these high risk regimens and instituting formal care to help manage risky regimens. One tactic to prevent high risk regimens from being prescribed in the first place is through medication reconciliation using computer programs coupled with constant vigilance by the providers delivering care (De Smet, Denneboom, Kramers, & Grol, 2007; Doucette & Andersen, 2005; Doucette, McDonough, Klepser, & McCarthy, 2005). A second, less common way of managing high risk medication regimens is through the provision of home health care.

About 17.9% percent of all patients hospitalized receive home care services (National Association for Home Care [NAHC], 2008; CDC, 2008). Annually, more than 7.6 million people receive home care and, of those, 69.1% are age 65 and over (NAHC, 2008). For all age groups, it is projected that \$57.6 billion will be spent on home care in 2007 (NAHC, 2008). The largest payer (37%) of home care is Medicare (NAHC, 2008).

Although the older adult may have home health care services daily, it is likely that the skilled nursing services to manage the medications will occur once weekly or every other week and may not be initiated until a few days after the return to home. The average length of an episode of care in home care is 46.4 days (Home Health Interactive, 2009). Patients can have multiple episodes of care in one home health care admission. Given that, on average, clients receive only 32 visits per admission (NAHC, 2008), much of the time, both during the episode of care and after the episode of care is finished, patients manage high risk medication regimens on their own.

Fortinsky, Madigan, Sheehan, Tullai-McGuinness, and Fenster (2006) found 18.9% of patients in Medicare certified home health care agencies were re-hospitalized after admission to home health care. Madigan et al. (2001) found a much higher rate (24.4%) of re-hospitalization in a much smaller sample (n = 117) of home health care clients. Rosati and Huang (2007) found a re-admission rate of 19.9% within the first two weeks after discharge. The latest figures available from the Center for Medicare and Medicaid Services (CMS) demonstrate a home health agency hospitalization rate of 29% for all ages based on the OASIS reports done from October, 2008 through September 2009 (CMS, 2010e). These hospitalization rates are disquieting given that home health care is prescribed specifically to keep patients out of the hospital. At the present time, so little research has been done on this population that it is unknown what factors are operating in maintaining such high hospitalization rates despite vigilant monitoring of these medically unstable patients.

In summary, a vicious cycle of harm ensues when too many medications, the wrong medications, or complex medication regimens are prescribed. Patients are hospitalized repeatedly for problems related directly to the medication regimen or for adverse events associated with medication side effects, interactions, or dosing regimens. Repeated hospitalizations increase the risk of iatrogenic issues and subsequent functional status decline, as well as, increase the cost of health care for the individual and the greater society.

Safety and Quality of Care Issues Related to High Risk Medication Regimens

Researchers agree that preventing excess hospitalizations related to over utilization of medications or inappropriate prescribing is considered a desirable systems

outcome (Feinstein, 2002; Lewandroski, 2003). A number of systems initiatives are occurring to improve the quality of care regarding medication management. The Joint Commission, formerly the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), has calculated that 63% of medication errors occur during the transition points either within the hospital, or during admission or discharge from the hospital (JCAHO, 2006). Indeed, in recognition of these untoward costs both monetarily and in human suffering, The Joint Commission made accurate medication reconciliation across the continuum of care an important quality of care goal for its member hospitals (North Carolina Hospital Association, 2006).

Other organizations, besides The Joint Commission, are focusing on efforts in this area demonstrating the importance of this intervention to improve the quality care given older adults. The Agency for Healthcare Research and Quality (AHRQ) has proposed that the Healthcare Effectiveness Data and Information Set (HEDIS) measures used to assess the quality of care in health maintenance organizations include a measure of medication reconciliation for all patients over the age of 75 within 30 days of hospitalization (AHRQ, 2005, Core Measures). The goals of this quality measure are to improve medication appropriateness, decrease polypharmacy, and avoid adverse events (NCQA, 2005). A new quality measure gathered from the Outcome Assessment Information Set (OASIS) data set in home health care, the number of patients who get better at taking their medicines correctly, will also be monitored by AHRQ (AHRQ, 2005, NQMC).

In 2007, the Institute of Medicine (IOM) published a comprehensive report entitled "Preventing Medication Errors" (Aspden et al., 2007), as part of the *Crossing the Quality Chasm* series. This report called for changes in funding mechanisms to study

quality issues, prescribing practices, and patient prescriber interactions. The Centers for Medicare and Medicaid Services (CMS) has several quality measures specifically in home health care related to medication safety. The use of emergent care and hospitalization are frequently directly and indirectly related to medication use or mismanagement (Aspden, et al., 2007). In addition, the improvement or stabilization in self-management of oral medications is directly related to medication safety (CMS, 2010b). Finally, the National Institute on Aging (NIA) has called for studies designed to test prevention strategies and interventions specifically addressing multi-factorial frailty and disability (NIA, 2006). The recognition of the importance of medication prescribing and management of medication regimens is now recognized as an indicator of quality of care. Increasing attention is being focused on outcomes related to medication prescribing and management in all settings and at all levels of government. The changes in the public sector will undoubtedly drive change in the private sector as managers in the private health care systems recognize the drain of profits and the human toll related to the problems due to high risk medication regimens.

Scientific Importance of This Study

Although older adults comprise only 13% of the United States population, 30% of prescription drugs are consumed by this age group (Williams, 2002). The management of high risk medication regimens is a key concept in geriatric education and is probably the most important function of those who specialize in geriatric care. Although medication administration is initiated most often as a medical function, the successful management of medication regimens, the diligent tracking of changes in medication regimens across transitions in care, and the careful monitoring of patients' reactions to their medication

regimens are all functions of nursing care. In addition, advanced practice nurses in many states, as well as physicians, are responsible for discharge planning in various settings, including the hospital, the transitional care unit, the ambulatory setting, and in long term care and assisted living facilities. These providers routinely prescribe medications as part of their duties. Nursing insight as to the interaction of the personal attributes of older adults and the inherent risk of the medication regimen will help to characterize what medication regimen attributes are important to define and to monitor for potentially poor outcomes. The use of data bases collected by nurses in various settings affords researchers an excellent opportunity to understand the effect of medication regimens on outcomes such as adverse events and subsequent hospitalization or re-hospitalization.

Although there is implicit recognition that risk assessment is important to consider in developing a medication regimen, the concept of high risk medication regimens is not well defined and is rarely studied. Indeed, medication regimens are rarely studied outside of institutionalized populations due to the difficulty in processing data collected for administrative purposes, and merging data bases from different agencies or data base platforms. Another major barrier to studying high risk medications regimens in the older adults is a lack of agreement on what factors or concepts constitute high risk medication regimens (Fu et al., 2007; Maddigan, Farris, Keating, Wiens, & Johnson, 2003). For providers, understanding this relationship is important when evaluating the potential for errors in administration, as well as, determining the risk-to-benefit ratio of a particular medication regimen.

Purpose and Specific Aims of Study

It is generally believed if resources, such as using transitional care units, home health care, and intense monitoring medications across transitions in care, are focused on those most at risk for re-hospitalization, readmission rates will decrease. However, re-hospitalization rates have increased by 50% over the last three decades (Jencks et al., 2009). Numerous strategies are employed to prevent re-hospitalization including case management, discharge planning, the use of home health care and transitional care units, and medication reconciliation. Although thousands of dollars per year are invested in medication reconciliation programs and countless hours in human labor are devoted to making sure medication regimens are safe, little is known about the relationship of medications to the end-points of hospitalization or re-hospitalization in many settings, but most especially in the home health care setting. The recognition of those patients at highest risk for adverse drug events and subsequent adverse outcomes allows the nurse to intervene early enough to prevent or decrease the likelihood of adverse events and outcomes from happening.

Purpose of Study

The purpose of this study was to determine if high risk medication regimens independently contribute to the variance in re-hospitalization in home healthcare clients over age 65. A secondary data analysis of OASIS data records and medication records compiled from 15 home health care agencies for all older adults age 65 and over admitted during the calendar year of 2004, were used to examine the relationship between comorbidity (defined by the Deyo modification of the Charlson Comorbidity Index [Deyo, Cherkin, & Ciol, 1992]), a variety of risk factors supported by the literature, high

risk medication regimens (defined by polypharmacy, potentially inappropriate medication regimens and medication regimen complexity) and re-hospitalization.

Specific Aims of Study

The specific aims of this study are:

Aim 1: To describe the medication regimens of older adult home health care clients in terms of polypharmacy, potentially inappropriate medication use, and medication regimen complexity.

Aim 2: To determine what combination of factors (polypharmacy, potentially inappropriate medications, medication regimen complexity) compose the concept of high risk medication regimens.

Aim 3: When combined with other potential risk factors, to evaluate the extent to which high risk medication regimens, as a mediating variable between comorbidity and hospital readmission, account for variance in hospital readmission.

The research questions for this study were as follows:

1. What is the prevalence and characteristics of polypharmacy, potentially inappropriate medication use, and medication regimen complexity for home health care patients age 65 and over?
2. Can a construct of high risk medication regimens be created from operational definitions of polypharmacy, potentially inappropriate medication use, and medication regimen complexity?
3. How much do high risk medication regimens increase the risk of re-hospitalization in home health care patients age 65 and over?

Studying an important endpoint such as re-hospitalization using a multiple mediator design to evaluate three oft studied, but poorly defined concepts (polypharmacy, inappropriate medication use, and medication regimen complexity), may add to the theory building literature and is intended to generate ideas for interventional designs and tool development. Disentangling the effect of comorbidity and other risk factors from medication regimens on re-hospitalization will help clarify the contribution of these variables to this adverse outcome. Other contributions of this study may include identifying secondary data analysis strategies for use in home health care datasets, determining whether the operational definitions developed for high risk medication regimens can be utilized with home healthcare data, as well as generating ideas for intervention design, risk stratification and timing of safety monitoring (Polit & Beck, 2004).

Conceptual Framework

Developing the Conceptual Framework

Conceptual frameworks are used to guide researchers in their quest to discover the nature of phenomena they are studying. These frameworks link ideas about the variables being studied into an organized and coherent whole. A conceptual framework, in effect, becomes a roadmap to guide the researcher over the course of a research career and should help generate ideas for studying the phenomena in question while organizing the existing knowledge about the phenomena.

Madigan, Tullai-McGuinness, and Neff (2002), noted that the study of the impact of medications on outcomes has been atheoretical. In searching the literature, studies were not guided by or associated with any particular theory, nor did the studies use an

explicit conceptual framework to guide the study other than Maddigan et al. (2003).

Therefore, a conceptual framework was developed from the literature using ideas identified as important in medication prescribing patterns, predictors of adverse events, and subsequent patient adherence to the medication regimens (Crossen-Sills, Toomey, & Doherty, 2006; Johnson, Griffiths, Piper, & Langdon, 2005; Maddigan et al., 2003; Sorensen et al., 2005).

Providers often expect that patients or their families should be able to manage very complex therapeutic regimens, while third party payers, such as insurance companies, shorten the hospital stay so the patient is discharged quicker and sicker, making medication management increasingly difficult for the patient with limited physical, psychological, or social supports. Maddigan et al. (2003) specifically examined patient adherence to complex therapeutic regimens. The conceptual framework developed for the Maddigan et al. study was based on Orem's (1991) Theory of Self-Care Deficit.

In the Maddigan et al. conceptual framework (Figure 1.1), patients are expected to be able to accomplish some task that contributes to their well-being or healing called a self-care operation. In the Maddigan et al. framework, the example used is medication management. Self-care agency is the constellation of ever-changing attributes such as cognition, function status, and motivational factors that can inhibit or promote that patient's ability to care for themselves. These attributes can be measured indirectly for example, by assessing cognitive scores, activities of daily living scores, or depression screening scores. Characteristics of a therapeutic regimen (therapeutic self-care demand) interact (depicted by double arrows) with other more stable factors (basic conditioning factors) such as age sex, education, and number of medical conditions as well as the self-

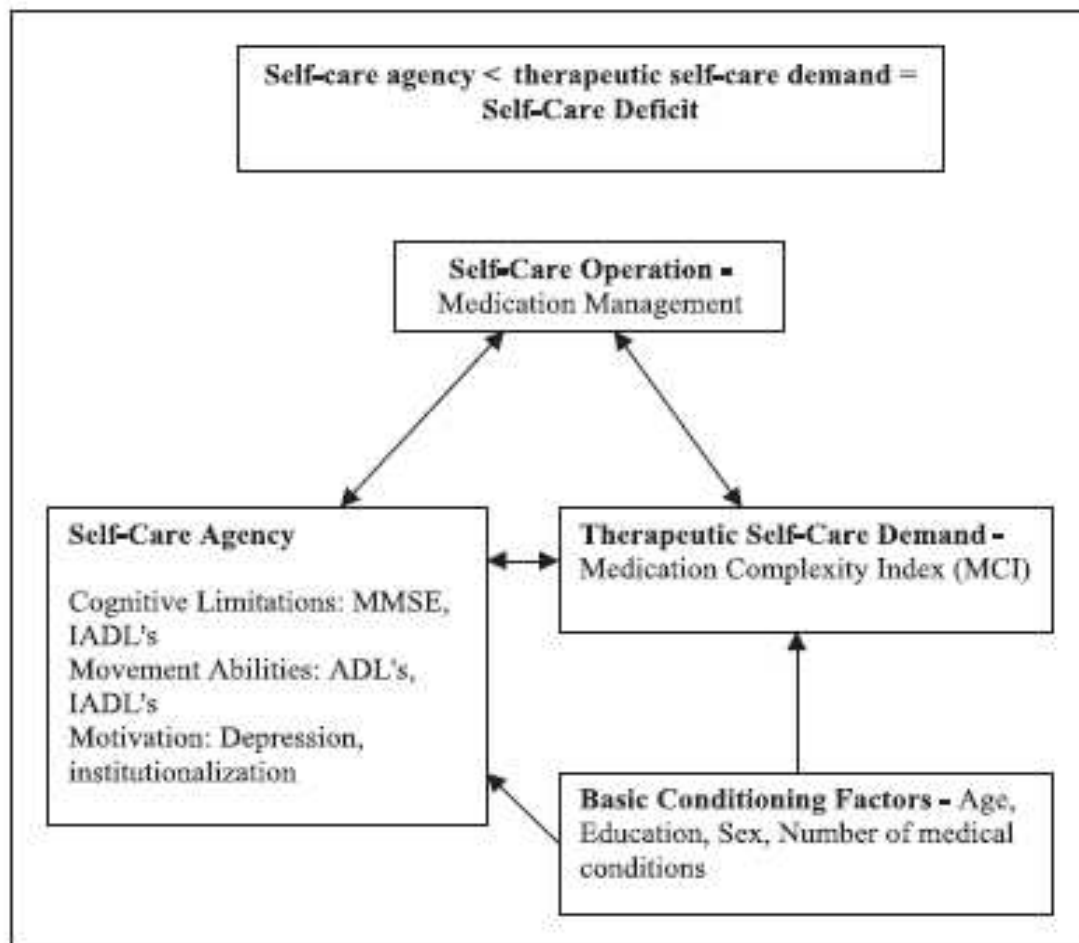
care agency factors to impact the patient's ability to successfully accomplish a self-care operation.

Maddigan et al. (2003) defined a self-care deficit as the mismatch between the patient's capabilities for self-care and what the level of self-care is actually required. The idea of a mismatch between patient capabilities given their current self-care deficits (Self-Care Agency) and the health care provider's expectations as characterized by Therapeutic Self-Care Demand) is implicit in most studies of medication management, but Maddigan et al. (2003) explicitly identified this mismatch as an area worthy of study while specifically studying medication complexity as a factor contributing to this mismatch.

Johnson (2002) concluded medication regimen complexity extends beyond intrinsic factors (numbers of medications, potential for interactions or adverse events) that accompany polypharmacy, but is also related to how an individual perceives the regimen, as well as, the differences in cognitive ability to handle the regimen. In addition, there are circumstances surrounding the individual, such as formal and informal social support that might assist the individual in handling a demanding medication regimen. According to Johnson, adherence also has a role to play in medication regimen management. Patients might or might not adhere to a regimen based on their perception of the risk/benefit ratio, their perception of how the medication works and the amount of real benefit the medication confers, their relationship with the prescribing doctor, the cost of the medication, and whether they need to modify their lifestyle to accommodate the regimen. In essence, what might be an "easy" regimen for one person may be very complex for another person depending on the mix of social supports and cognitive ability the patient possesses. In addition, circumstances are fluid and may change hourly during

the course of a day. From this study, the ideas of social support, cognitive capability, and lifestyle modification became important concepts to examine when studying the riskiness of medication regimens.

Figure 1.1. Illustration of the Maddigan et al. (2003) conceptual framework (used with permission).



Note. MMSE = Mini-Mental State Exam; IADL = instrumental activities of daily living; ADL = activities of daily living.

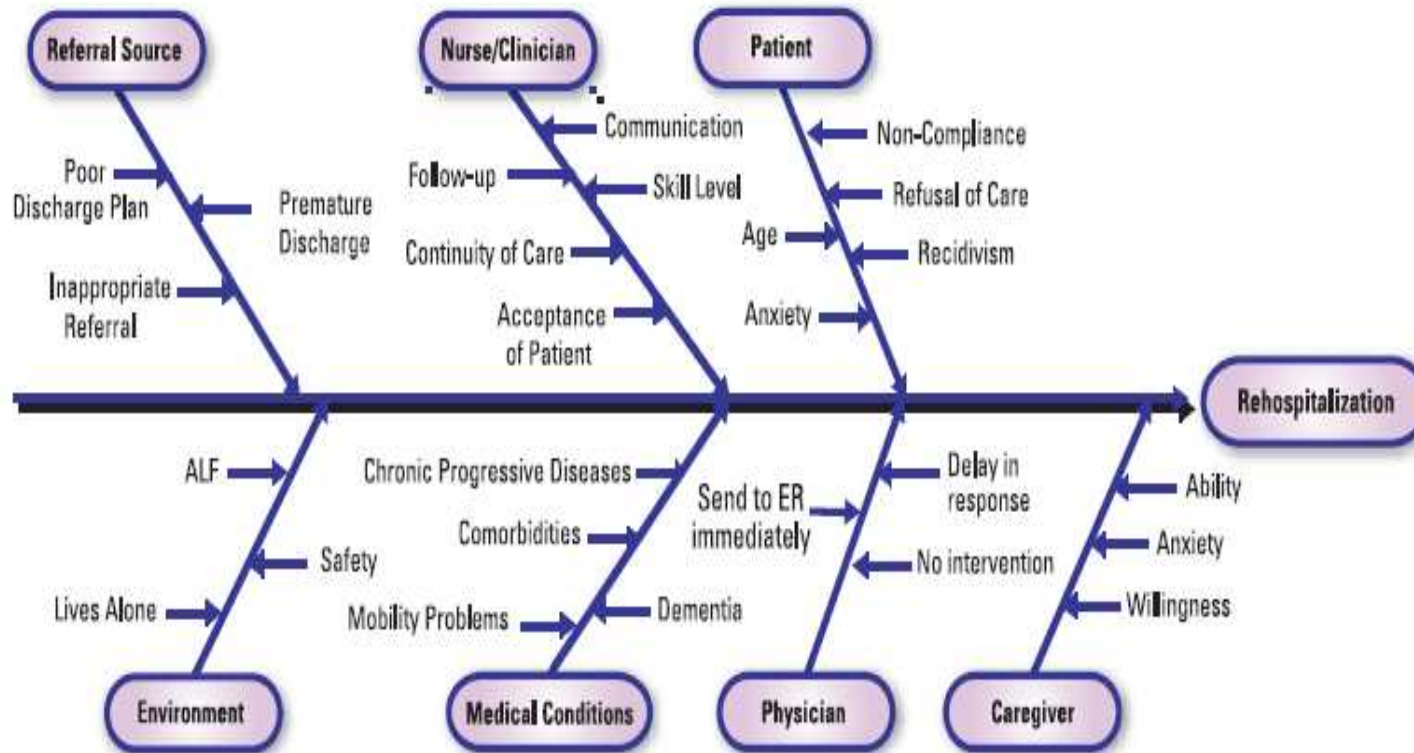
Sorensen et al. (2005) studied the association between the intrinsic risk factors of medications and poor outcomes in Australian home health care clients. Sorensen et al. found lack of a routine, medication duplication, multiple prescribers, and multiple storage locations as medication factors associated with poor outcomes. These factors, although not exactly the same as those identified by Maddigan et al. (2003), nevertheless correspond to the therapeutic demand concept studied by Maddigan et al. Although the number of prescribers and storage locations cannot be accurately identified in this dataset, the idea of lack of routine can be examined by inspecting changes in regimen, timing, and scheduling of medications.

One other source was used to develop a conceptual framework. Crossen-Sills, Toomey, and Doherty (2006) studied common reasons for re-admission back to the hospital from home health care. Using literature review, focus groups of clinical staff and managers, and administrative data analysis, Crossen-Sills et al. developed a root cause analysis (Figure 1.2). The backbone of the fish diagram is the outcome under study (re-hospitalization). Contributing to the outcome, are general areas (environment, patient, nurse/clinician, etc.) which can impact the ability of a patient to remain in the home and are represented by the bones of the diagram. Along a specific bone are factors (covariates) that compose the area and, the level of which, can be measured, studied, and perhaps adjusted to help avoid re-hospitalization.

Several covariates not previously considered for inclusion into the developing conceptual framework for the present study included covariates incorporated in the environmental “bone” such as living alone, covariates considered in the medical

conditions bone such as prognosis, dementia, and comorbidities, and covariates in the caregiver bone such as ability and willingness to provide care.

Figure 1.2. Root cause analysis of clinicians' perceived causes for re-admission from home health care (Crossen-Sills et al., 2006, used with permission).



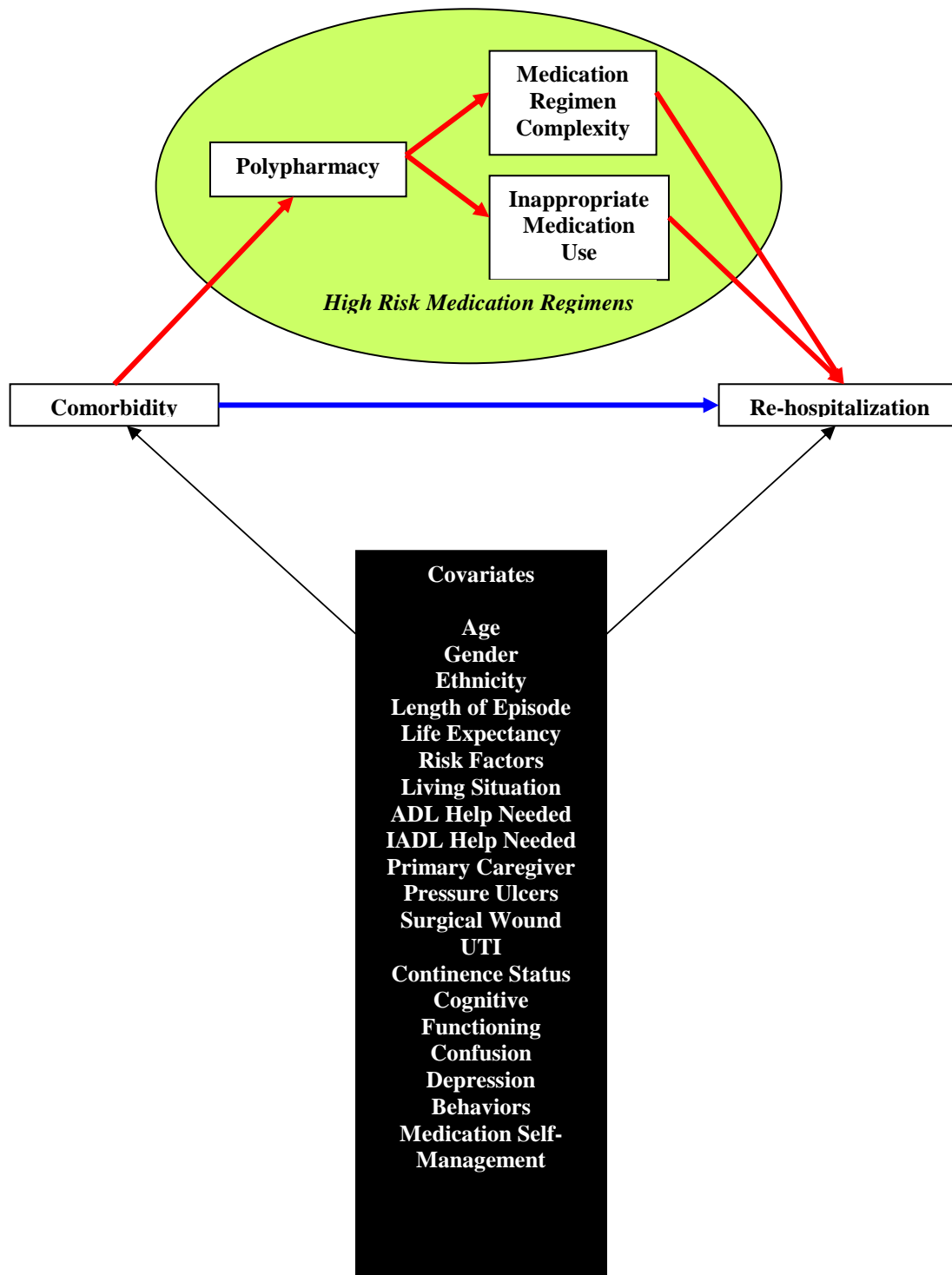
ALF=assisted living facility; ER=emergency room

Description of the Conceptual Framework

The conceptual framework for this study (Figure 1.3) was developed to take into account both the therapeutic demands on the patient and patient factors such as age, living situation, risk factors, assistance needed, cognitive status, and comorbidities. The central idea of the conceptual framework is the concept of high risk medication regimens and the role this concept plays in re-hospitalization. Although Sorensen et al. (2005) listed individual factors related to medication adherence such as the route, preparations steps, and dosing schedules individually, it was evident from the literature review (Chapter 2) that these medication factors could be collapsed in three broad concepts: polypharmacy, potentially inappropriate medications or medical regimen complexity. These three concepts are proposed to capture the inherent risk of a medication regimen, labeled High Risk Medication Regimens.

It was anticipated that high risk medication regimens mediate the relationship of comorbidity to re-hospitalization. Therefore, the measured indicator variables are shown to be embedded in the latent variable of high risk medication regimens to demonstrate that high risk medication regimens are composed of some combination of polypharmacy, inappropriate medications, and medication regimen complexity. Red arrows in Figure 1.3 indicate the direction of this mediating relationship.

Figure 1.3. The Effect of High Risk Medication Regimens on Re-hospitalization: A conceptual framework used to develop analytic framework.



Polypharmacy increases the risk of both inappropriate medications and medication regimen complexity (Cannon, Choi, & Zuninga, 2006; Fick et al., 2001; Fu et al., 2007; Hajjar et al., 2005; Hayes & Kan, 1999; Johnson et al., 2005; Pugh et al., 2006; Viswanathan, Bharmal, & Thomas, 2005); therefore these relationships are shown within the high risk medication regimen concept.

In this conceptual framework, the primary driver of medication prescribing is the patient's individual combination of diseases and illnesses, and the severity of those conditions (comorbidity). Comorbidity has been the most studied and consistent predictor of hospitalization and re-admission in multiple studies (Coleman et al., 2004; Fortinsky et al., 2006; Hasan et al., 2010; Hastings et al., 2008; Parker et al., 2003; Rosati & Huang, 2007). Therefore, the effect of comorbidity on re-hospitalization was chosen as the focal relationship, depicted in Figures 1.3 with a blue line.

Comorbidity has also been found to be predictive of medication errors and adverse drug events (Field et al., 2007). Polypharmacy (Agostini, Han, & Tinetti, 2004; Bedell et al., 2000; Field et al., 2007; Hanlon, Cutson, & Ruby, 1996; Hanlon et al., 1997; MacLaughlin et al., 2005; Rask et al., 2005), potentially inappropriate medication use (Rask et al., 2005), and increased medication regimen complexity (Johnson et al., 2005) have also been predictive of medication errors and adverse drug events, as has high risk medication regimens (Johnson et al., 2005; Sorensen et al., 2005). Although re-hospitalization rates underestimate the adverse events rate, re-hospitalizations become a de facto, but partial, proxy for the occurrence of these events. Therefore, the mediating relationship was constructed from comorbidity through the high risk medication regimen (using the measured indicator variables of polypharmacy, inappropriate medications, and

medication regimen complexity) to the outcome of re-hospitalizations because hospitalization represents a countable adverse event in this dataset.

Other covariates will be examined and are found listed in the black box. These fixed factors such as age and gender, and fluctuating factors such as social support, ADL/IADL assistance needed, and cognition may affect the level of comorbidity and also may have an effect on re-hospitalization. These covariates have been shown to be related to both the predictor variable (comorbidity) and the outcome (re-hospitalization) in various studies, but not consistently so. These additional covariates are depicted in a black box to indicate the variability in findings across previous studies regarding these covariates. The covariate relationships are depicted with black arrows and will be studied in relationship to both the predictor and outcome variables to elucidate the relationships. Although adherence and provider characteristics must be acknowledged as affecting the type of regimens prescribed, and ultimately outcomes (Sherman, 2007; Williams, 2002), neither of these variables can be studied using the dataset for this study. These variables are very complex and merit study outside the limited scope of this study.

Conclusion

Few medication-related studies included conceptual frameworks to guide the development of the research questions being examined. Therefore, development of a new conceptual framework was merited. Along with research questions under investigation, this framework will be evaluated in this study to assess its utility in guiding future work in this area.

In the following chapter the literature review will focus on the four predictor variables (comorbidity, polypharmacy, inappropriate medications, and medication

complexity) and the outcome variable, re-hospitalization (used interchangeably with readmission). The definitions, prevalence, issues in measurement, and gaps in the literature will be discussed regarding these variables and conclusions regarding operationalization of these variables and implications for research will be drawn from the findings of the literature review.

CHAPTER II

LITERATURE REVIEW

Organization of the Literature Review

This study evaluates whether high risk medication regimens or proposed indicator variables (polypharmacy, potentially inappropriate medications, or medication regimen complexity) are a predictor of hospital readmissions for older adults in home health care (HHC) and also whether high risk medication regimens act as a mediator in the relationship between comorbidity and hospital readmission. Therefore, this literature review is organized around each of the main variables tested in this study. The conceptual framework described in the previous chapter guided the literature review and development of the research questions for this study. This chapter begins with an examination of the literature regarding hospital readmission (used interchangeably with re-hospitalization) in home health care. Specifically, issues related to definition of the study variables will be discussed, prevalence studies will be evaluated, definitional issues will be presented, and finally the gaps in knowledge and implications for further study will be presented. The section on hospital readmission will be followed by an evaluation of the literature regarding the concepts proposed to predict hospital readmission in this study: comorbidity, polypharmacy, inappropriate medications, and medication regimen complexity.

The sections describing each predictor variable follow the format listed below:

1. Historical context
2. Definition of the variable

3. Issues in defining the variable
4. Prevalence of the variable
5. Studies using the variable as a predictor
6. Conclusions and gaps in knowledge about the variable
7. Implications for research in this study.

Methodology for Searching for the Literature

Literature from the United States in HHC and community settings was specifically reviewed as differing policies in other countries have a large effect on the number and types of medications used, and index hospitalizations and subsequent readmissions. Databases searched included the Cochrane database, Medline, CINAHL, AHMED, International Pharmaceutical Abstracts, and PsychInfo. Hand searching of reference lists and journals was used to find additional studies. A reference librarian was enlisted to help determine appropriate search terms for all variables as some variables (inappropriate medication use, medication regimen complexity, high risk medication regimens, and home health care) are not defined as Medical Subject Heading (MeSH) terms. The OVID and EBSCO search engines were used to search the chosen databases. Keywords used for searching and search strategies are included in Appendix A.

Inclusion and Exclusion Selection Criteria

The literature was searched from 1990 through 2010, however only studies from 1998 to 2010 were chosen for abstraction, since this time frame captures studies conducted after implementation of the Balanced Budget Act of 1997, the Bush administration's focus on measuring quality, and the implementation of Medicare Part D in 2006. High quality studies or seminal studies from earlier periods were included in this

review if deemed to be appropriate pertinent to the discussion. These studies were included if more recent studies were unavailable or the information presented expanded understanding of the variable in question.

Although qualitative studies, quantitative studies, and grey literature were included in the search for background information, only published randomized clinical trials, comparative studies, cohort studies, epidemiological studies, or meta-analyses were used in the literature review. Either secondary data analyses or primary data collection strategies were considered appropriate for review. All studies were limited to those reported in English with subjects primarily age 65 and over. Excluded were single case studies, opinion papers, and synthesized reviews analyzing primary studies, literature regarding drug use in institutionalized or hospitalized patients, and literature that was about predictors associated with the adverse outcomes, but in the presence of a specific chronic disease or a specific class of drugs. Articles that did not include one of the concepts as a major variable or did not clearly define the concept were also excluded.

After the initial search, over 5,000 articles were returned as pertinent to the study. This number was then limited by language (English), year of publication, type of study, and age of subjects to approximately 2,500 articles. Perusal of abstracts further narrowed the number of articles read in their entirety to 532 articles. Of that number, 74 were deemed pertinent to the present study and chosen for abstraction.

Evaluation Criteria and Abstraction of Studies

Studies evaluated included those which dealt with a population composed of adults age 65 and over. Either prevalence or predictive studies were abstracted, but only studies based in the United States were used for abstraction due to the differences in

health care systems across countries that could dramatically affect the findings of either prevalence or predictive studies. Each article was abstracted based on the Garrard Matrix Method (Garrard, 2004) using author/year, purpose, subjects, inclusion/exclusion criteria, data sources, main findings, limitations, conclusions and implications. Additional criteria, added by this author, included the definition of the concept in question, as well as, any limitations or strengths that definition posed in operationalizing the concept.

Due to the small number of studies on readmission in HHC, no formal metric for judging quality was used, however studies with larger sample sizes, randomized samples, and those that took place in the home care setting were felt to be more pertinent to this review, and in the opinion of this reviewer, carried more weight when drawing conclusions from the review. However, all studies that met the inclusion criteria found pertaining to hospital readmission in home health care were included in the literature review regardless of the quality of the study. Additional studies in other settings meeting the inclusion criteria were also abstracted to augment the findings in the HHC literature, and to fill in the gaps in knowledge where no HHC literature existed.

Hospital Readmission

Historical Context Regarding Hospital Readmission

Considering the cost of hospital readmission, re-hospitalization to the acute care setting from home health care is an infrequently studied outcome measure in the home health care literature (Anderson, DeVilder, Hansen, & Helms, 1996; Anderson, Helms, Hanson, & DeVilder, 1999; Fortinsky et al., 2006; Holtzman, Chen, & Kane, 1998; Li, Morrow-Howell, & Proctor, 2004; Leiby & Shupe, 1996; Madigan et al., 2001; Miller & Weissert, 2001; Rosati & Huang, 2007). None of these studies used large, national data

sets except for Miller and Weissert (2001), and Rosati and Huang (2007), thus limiting generalizability. Even researchers at the Centers for Medicare and Medicaid Services (CMS) had difficulty determining the readmission rate from home health care. On the OASIS website updated by CMS regularly, the acute care hospitalization rate is reported as 29% for home health care patients for October, 2008-September, 2009 (CMS, 2009b). This is historically a fairly stable rate (Rosati & Huang, 2007), yet, Levinson (2006), in testimony for the General Accounting Office, reported home health care readmission rates for Medicare beneficiaries of 47% at the same time the archived report lists home health care hospitalization rate as 28% (CMS, 2010a). Recent studies examining hospital readmission in home health care are prevalence studies using a retrospective approach (Fortinsky et al., 2006; Li et al., 2004; Miller & Weissert, 2001; Rosati & Huang, 2007) or disease specific studies (Kind, Smith, Pandhi, Frytak, & Finch, 2007).

The cost of hospital readmission has been studied in the community setting, but not in the HHC setting. In a recent study done with community dwelling elders, Jencks et al. (2009) found that congestive heart failure, chronic obstructive pulmonary disease, pneumonia, psychosis and gastrointestinal issues were the most frequent medical issues associated with hospital readmissions, while hip and knee surgeries were the most common surgical procedures associated with hospital readmissions. The authors estimated only 10% of readmissions were planned, with \$17.4 billion dollars as the estimated cost of unplanned hospitalizations for Medicare.

Definition of Hospital Readmission for HHC Patients

CMS defines an acute care hospitalization for HHC patients as an inpatient hospital admission that lasts at least 24 hours and occurs during an episode of care which starts and ends in a specific 12 month time period. Excluded from the measure are patients who die while in home care, those who are under 18, non-Medicare or non-Medicaid patients, those receiving services from non-Medicare certified agencies, and those who are long stay patients (episodes of care longer than 12 months). Patients included in this measure are those who are coded on the OASIS assessment as a “1” on M0100 for number 6 (transferred to an inpatient facility-patient not discharged from agency) or number 7 (transferred to an inpatient facility-patient discharged from agency), *and* coded as a 1 on M0855, admitted to an inpatient hospital facility (AHRQ, 2010, NQMC Complete Summary). This definition does not allow for a distinction to be made for patients were originally admitted from the hospital (M0175 coded as a “1”), and those who were originally admitted directly to home health care. This definition may be a very different definition than those used by researchers in the studies reviewed. Theoretically, the CMS hospitalization values should be higher than those determined by researchers who are just evaluating the subset of re-hospitalized patients, but lower than studies which included non-medicare certified agencies.

Issues in Defining Hospital Readmission

In addition to the issue about what location the patient was discharged from initially, other issues include:

1. how long the post-hospital period should be monitored for readmission,
2. when the monitoring should start,

3. whether to count patients referred for admission to HHC but returned to the hospital prior to the patient having the OASIS form completed (the official start of care), and
4. whether procedures, planned hospitalizations, or emergent care stays for monitoring should be counted.

How each of these issues is specified can make a tremendous difference in the reported rates of readmission. Given that most patients are admitted through the hospital to home care, one can assume that hospital admission rates reported in the home health care studies are a reasonably accurate reflection of actual readmission rates. However, the length of time for monitoring the patient to determine the readmission rate varies considerably between investigators. It is also common for patients to return to the hospital before the clinical admission paperwork is finished, despite the administrative paperwork for the admission being started. These patients in transition are not officially counted because their paperwork is not completed, but in reality, they have made a transition in care. While in home care, it is also not uncommon to have a planned hospital visit for transfusions, chemotherapy, or day surgeries that last longer than 24 hours. There are also emergency room “observation” stays that last longer than 24 hours, yet the patient is not officially admitted to a hospital service. In each of these cases, the researcher must be very specific about who is counted as being hospitalized and who is excluded from the count.

Prevalence and Predictors of Hospital Readmission in the Community

Findings from two recent studies of Medicare recipients in the community setting create context for establishing baseline rates of readmission in community dwelling

elders and allow comparisons to be made to home health care populations. In the Hasan et al. (2010) study, subjects as young as 18, were included in the study, giving an expectedly lower readmission rate. Hasan et al. used a national convenience sample from six large academic hospitals across the United States, and found a 17.5% readmission rate within 30 days of hospital discharge in 10,946 subjects over age 18. The retrospective review of the patient records revealed that insurance status, marital status, the Charlson Index score, seeing a regular physician, the physical function SF 12 score, a hospital stay longer than 2 days, and hospital admission in the last year were all predictive of readmission. Jencks et al. (2009), using a 5% sample (> 65,000 subjects) from the Medicare Provider Analysis and Review (MEDPAR) file, found 19.6% of patients age 65 and older were readmitted within 30 days of hospitalization, with 34% readmitted within 90 days of discharge from the hospital.

Prevalence and Predictors of Hospitalization in Home Health Care

Miller and Weissert (2001), in a meta-analysis of 71 studies in home health care, found a 14 - 20% annual hospitalization rate for those patients age 65 and over. It was unclear whether an index hospitalization was needed for the study to be included in the meta-analysis. Interestingly, the hospitalization rate for those who were disabled was almost double that of those who were not disabled. For those who were recently hospitalized, the very old, or the disabled, the annual hospitalization rate was 51.8% similar to the reported hospital admission rate for older home health care beneficiaries reported by Levinson (2006).

Only one HHC study (Rosati & Huang, 2007) with a large sample (greater than 1,000 subjects) was found and this study was limited because the sample was drawn from

one large urban home health care agency and included patients younger than age 65. No distinction was made for patients readmitted to the hospital versus a first time hospital admission. However, using a combination of administrative records and OASIS files, Rosati and Huang (2007) found a 19.9% hospitalization rate for the 46,366 patients during the first 60 days after admission to home health care. More than 50% of those hospitalized were admitted to the hospital within the first two weeks of admission to home care. Predictors for hospitalization included previous use of home health care services, history of falls, hospitalization in the past six months, need for assistance with independent activities of daily living (IADLs), use of more than 5 medications concurrently, difficulty managing medications, wounds, urinary tract infections, and comorbidity indicated by four or more illnesses.

Fortinsky et al. (2006) used a convenience sample from three Medicare-certified Ohio home health care agencies and found a hospital readmission rate of 18.9% within six months of admission to home health care for 922 patients. Eighty percent of patients hospitalized were admitted through the emergency room. Dyspnea, wounds or skin ulcers, case mix level, functional impairment, and guarded rehabilitation prognosis increased the risk of hospital readmission in these elderly home health care patients.

Using a convenience sample of 916 patients re-hospitalized from twelve Midwestern home health care agencies, Anderson et al. (1999) verified that 39% of patients developed a new issue and 37% of patients had an exacerbation of the primary diagnosis within 100 days of admission to home health care resulting in hospital readmission.

Other researchers found social support, disease severity, and medication regimen compliance all predictive of hospitalization in home health care (Anderson et al., 1999; Scharwz, 2000; Li et al., 2004; Rosati , Huang, NavaieWaliser, & Feldman, 2003). Schwarz (2000) evaluated a convenience sample of 60 caregivers of older adults discharged from the hospital to determine whether social support, satisfaction with social supports, depressive symptomology or low use of home health care on the part of the caregivers impacted hospital readmission rates for patients. Schwarz hypothesized that caregivers themselves frequently are unable to cope with the stress of caregiving, thus affecting the quality of caregiving and increasing the risk of readmission for the patient. Giving and receiving tangible support (rides to appointments, reaching out to help others) decreased the risk of readmission. Emotional support, depressive symptoms of the caregiver, and use of home health care did not seem to make a difference in the number of readmissions.

Li et al. (2004) followed 199 patients age 65 and over diagnosed with CHF and discharged from a large Midwestern Hospital to home while using the services of a discharge planner for 14 weeks. Using secondary data, the investigators studied the effect of informal service use (care provided by unpaid family or friends) and formal service use (paid care such as home health care) on hospital readmissions. Length of CHF history increased the risk of readmission after the first two weeks of the study period, while medication compliance reduced the risk of re-hospitalization. The investigators concluded that the importance of improving the likelihood of medication compliance in hospital discharge planning cannot be underestimated.

Not only are patients re-hospitalized at high rates in home health care, but the length of stay in home health care is very short and the reasons for readmission differ from the index hospitalization. Madigan et al. (2001) prospectively studied a convenience sample of 117 patients from three Midwestern urban home health care agencies and found a 24% hospital readmission rate with age as the only predictor for hospital readmission. The reasons for hospital readmission were complex and included both the development of new issues, as well as, worsening of prior issues. The mean length of stay in home health care was eighteen days before hospital readmission. Madigan et al. argue that since the majority of readmissions occur within the first three weeks following discharge, that readmissions much beyond several months are not related to the original hospitalization (the index hospitalization).

Anderson et al. (1996) also found that the 68 patients purposely sampled from 11 home health care agencies were re-admitted to the hospital with different illnesses than the index hospitalization. The most frequent problems for those re-admitted within 31 days of admission to home health care were congestive heart failure and chronic obstructive pulmonary disease. Despite using data collected before prospective payment in home health care, the mean length of stay for home health care patients before readmission was very short at only 11.66 days.

Three studies examined how provision of services affected the outcome of hospital readmission. Holtzman et al. (1998) evaluated whether home health care patients in health maintenance organization (HMO) were re-admitted more frequently than fee for service (FFS) patients in 970 patients discharged from 19 urban hospitals in the cities of Minneapolis and St. Paul using interview, chart review, and MEDPAR data. Holtzman et

al. examined the records of patients with specific conditions including congestive heart failure, chronic obstructive pulmonary disease, stroke and hip fracture and determined that there was no difference in readmission rates between types of payors despite the shorter hospital stays in the HMO patients.

Kind et al. (2007) evaluated how the initial diagnosis and destination after discharge was related to readmission within 30 days of index hospitalization discharge. Kind et al. evaluated the enrollment and claims data of 5,250 Medicare beneficiaries discharged to a rehabilitation center from the hospital after a stroke. These patients were from eleven large, urban HMOs in the Eastern United States. Twenty four percent of the patients in the sample were discharged to home health care agencies. Infection and aspiration pneumonia were the most common reasons for readmission regardless of initial destination (home, nursing home, transitional care) after the index hospitalization.

Using one hospital system in central Washington state, Leiby and Shupe (1992) evaluated whether home health care made any difference in readmission rates compared to patients who were home care eligible, but did not receive home health care (n = 105). These researchers found that home health care made a substantial and significant difference in readmission rates. Those receiving home health care had an unusually low readmission rate of 2.7%. Those not having home health care had a 36.8% readmission rate in the six month period after discharge. All these researchers demonstrated the importance of home health care in keeping patients out of the hospital, whether the patient is in a fee-for-service or a health maintenance organization environment or the destination after discharge from the hospital. Presumably the HHC advantage occurs because the patients are being monitored closely and problems are proactively addressed.

Conclusions and Gaps in Knowledge about Hospital Readmission in Home Health Care

In summary, there is considerable variation in reported hospital readmission rates in home health care, with the Centers for Medicare and Medicaid Services reporting a readmission rate of 28% for those over age 18, but other researchers reporting rates ranging from 19 - 52%. Lower rates were associated with studies that did not use random samples, or had smaller, local samples rather than a national sample. Subjects were also not stratified by age, by surgical procedures versus medical problems, or by comorbidity in most samples, so perhaps the inclusion of younger, healthier patients in samples may have accounted for the lower rates of readmission. In the meta-analysis that did stratify by age (Miller & Weissert, 2001) and in the report by Levinson (2006), older adults had much higher rates of hospitalization. This is likely due to the type of chronic illness older adults are discharged with from the index hospitalization. In the 65 to 84 years old age group, the top three discharge diagnoses are coronary artery disease, congestive heart failure, and pneumonia, while in the 85+ age group, the top three discharge diagnoses are congestive heart failure, pneumonia, and hip fracture (AHRQ, 2008, HCUP). These diagnoses are associated with high mortality rates for older adults and often lead to other comorbid issues (CDC, 2010a; CDC, 2010b).

Studies defined admission rates differently; some authors combined original hospital admissions with readmissions or younger patients with elderly patients. In addition, rates are based on various time periods, with a 30 day admission rate the most common period used for measures. The research supports that hospital readmission occurs early in the home health care episode and that both complex co-morbidities and medication issues have been implicated as potential causes for hospital readmission in

these Medicare beneficiaries. Congestive heart failure and chronic obstructive pulmonary disease are the most expensive, and therefore most studied, diseases as predictors for hospitalization, but many other predictors have also been implicated in hospitalization. The average length of stay in home care is very short before that readmission occurs.

The lack of information regarding hospital readmission for homecare elderly is a serious gap in the literature, especially given that 18% to 50% Medicare eligible elders discharged from the hospital are admitted to home care (Kind et al., 2007; NAHC, 2008; Wolff, Meadow, Weiss, Boyd, & Leff, 2008), double the rate of all hospital discharges that are admitted to home care when using all age groups and all insurances (AHRQ, 2006, HCUP). There is a suggestion in the literature that elders are at a much higher risk for readmission than younger cohorts, but no recent studies have examined that phenomenon. There also is strong evidence that time to readmission is very short, but the influence of the index hospitalization versus other predictors on readmission remains unclear. The cost of this revolving door problem drains significant financial and human resources from the health care system, particularly when it is estimated that 90% of readmissions are avoidable. Clearly, hospital readmission from home health care is an outcome worthy of study.

Implications for Research Regarding Hospital Readmission

Researchers in the past have not frequently stratified risk by age or comorbidity, so studying readmissions in this fashion will help clinicians stratify risk of hospital readmission appropriately. In addition, understanding the predictors of readmission will not only help to decrease cost, but will help to target interventions in an appropriate and timely manner. It will be important to define hospital readmission precisely, and in a

fashion that will make this study comparable to other studies in HHC. Transitions in health care are rife with problems as the Institute of Medicine notes (Aspden et al., 2007).

This is an opportunity to more closely study one of the most common transitions in health care to understand where issues occur. As there is no information specifically on hospital readmission in HHC, this study will be an important addition to understanding the health care trajectory in older adults in HHC.

Predictors of Hospital Readmission: Comorbidity

Historical Context Regarding Comorbidity

Researchers have long recognized that the level of health or the amount of illness that a subject experiences affects outcomes. However, there is less agreement in the research community about how to measure the influence of illness (Yancik et al., 2007). Attempts to fully understand this concept have been elusive (Boyd et al., 2007; Hyder, Rotllant, & Morrow, 1998; Karlamangla et al., 2007; Yancik et al., 2007). Other more quantifiable variables, such as age (Schneeweis et al., 2001), drug counts (Baser, Palmer, & Stepehnson, 2008; Flaherty, Perry, Lynchard, & Morley, 2000), and comorbidity (Baser et al., 2008) have served as proxy measures to quantify health.

Philosophically, there are two basic ways to measure health (Yancik et al., 2007). One method is to evaluate the absence or presence of disease. In this case, the measures chosen will be based on some type of disease count and perhaps disease severity such as comorbidity or multi-morbidity indices (Yancik et al., 2007). The other method is an attempt to define health as a multi-factorial concept encompassing many domains, including social, psychological, economic and physical domains; in this case, the choice of the measure will be more comprehensive, as in a disease burden measure (Broome,

n.d.; Boyd et al., 2007). Boyd et al. (2007) suggests that the choice of measure is strongly influenced by expediency (how much time, dollars, and energy the investigator possesses), the type of data available to the investigator (primary data versus secondary data), analytic efficiency (the power to detect differences), and the type of outcomes measured (mortality, hospital readmissions, expenditures, or adverse drug events). As in all research, the definition of the concept (comorbidity) is critically important to defining the variable operationally (Yancik, et al., 2007).

Definition of Comorbidity

The present study is based on secondary data and includes data points regarding specific diseases and severity of diseases, but not information on the economic, emotional, or social impacts of the disease. Using the Boyd et al. (2007) suggestion for investigative expediency, analytic efficiency, and cross study comparability, the literature review for comorbidity was limited to measures that provided a global/summary score rather than a disease specific scale or an individual domain scores. Measuring health in this fashion is equated with measuring comorbidity (Yancik et al., 2007).

Fried, Ferrucci, Darer, Williamson, and Anderson (2004), in a concept analysis of the differences between disability, frailty, and comorbidity, defined comorbidity “as the concurrent presence of two or more medically diagnosed diseases in the same individual, with the diagnosis of each contributing disease based on established, widely recognized criteria” (p. 258). More recently, the term multi-morbidity has been used especially in the European research community to indicate concurrent diseases and severity (Yancik et al., 2007). Multi-morbidity measures attempt to fully capture all information available in the data set by counting the index disease, as well as, conditions

associated with the co-morbid and index diseases (de Groot, Beckerman, Lankhorst, & Bouter, 2003; Yancik et al., 2007). Comorbidity measures are differentiated from multi-morbidity measures by whether the index disease is excluded from the count.

Technically, comorbidity does not include the index disease (de Groot et al., 2003; Schneeweis et al., 2001; Yancik et al., 2007) in the measure, but often the terms are used interchangeably in the literature (Yancik et al., 2007). Comorbidity is a measure of additional diseases beyond an index disease (Schneeweis et al., 2001; Yancik et al., 2007), which are separate from the original disease, as evidenced by a unique ICD-9-CM or ICD-10-CM three digit code. While Karlamangla et al. (2007) asserts that comorbidity is the “total burden of biologic dysfunction” (p. 296), Baser et al. (2008) defined a comorbidity as “a condition, other than the diagnosis of interest, that may influence the treatment outcome” (p. 946). Clearly the definition of comorbidity is in flux and this fluidity in definition has the potential to greatly change prevalence rates and outcomes.

Issues in Defining Comorbidity

Comorbidity indices originally were developed to predict mortality in inpatient settings (Yancik et al., 2007). However, comorbidity has been shown to be related to a number of other outcomes including hospitalization, readmission, emergency room use, length of stay, costs, utilization, expenditures, and functional status (de Groot et al., 2003; Dominick, Dudley, Coffman, & Bosworth, 2005; Schneeweis et al. 2001). Nonetheless, using a comorbidity measure to capture the amount of illness is not without controversy. Some researchers assert that using a comorbidity score neither improves predictive capability, nor the quality of data collection due to measurement error inherent in the instrument used (Baser et al., 2008; Dominick, Dudley, Coffman, & Bosworth, 2005;

Farley, Harley, & Devine, 2006; Schneeweis & McClure, 2000; Schneeweis et al., 2001).

Schneeweis et al. (2001) asserts that researchers do not even realize age is the most common comorbidity adjustment. Besides excluding the primary disease as a variable of interest, Schneeweis et al. (2001) cast two other criticisms at comorbidity scales.

Schneeweis et al. contend that comorbidity scales only improve predictive capability slightly over age or just a simple disease count, while the variety of scales in use decrease the comparability of studies. Schneeweis et al. also hint that drug-count based indices have additional issues. A drug-count based index (judging the amount of illness based on the number and/or types of drugs prescribed) is unlikely to reflect the real condition of the patient, especially in the sickest of individuals. In these individuals, preventative medications may be discontinued, making the subject appear healthier than they actually are.

Lash et al. (2007) also suggest measurement error may be introduced in a number of other ways as listed below. The source of the data may impact the collection of data when determining comorbidity. If the source is the patient, the re-call may be inaccurate. If information is recorded from the medical records in chart review, the accuracy is improved, but not all the records may be available. In addition, the investigator must determine how far back to review the records and whether permission is granted for all records to be reviewed. Administrative data is usually truncated and focused on maximum reimbursement; therefore Lash et al. suggest research using administrative data may inflate the degree of comorbidity.

When comorbidity is prevalent, the chance of error in measurement of comorbidity is greatly increased (Lash et al., 2007). This is particularly true in elderly

populations where comorbidity, rather than a single disease entity is the rule (Lash et al., 2007), and synergistic diseases (congestive heart failure and diabetes) are related to increased morbidity (Boyd et al., 2007; Yancik et al., 2007). The scales used to measure comorbidity introduce a source of unrecognized error (Lash et al., 2007). This is especially true when diseases are classified. The potential exists for double counting conditions that are associated with the index disease as a co-morbid condition, or conditions associated with the co-morbid disease as a separate disease, thus overweighting the score (Lash et al., 2007). For example, if the disease being counted is diabetes, then neuropathy should not be counted as a separate comorbidity.

Like Lash et al. (2007), de Groot et al. (2003) and Schneeweis and McClure (2000), recognize that comorbidity is no longer being used as just an independent variable, but also as an adjustment for confounding. Schneeweis and McClure contend that the accuracy of the index is affected by both the original outcome the index was developed to measure, and the weighting scheme applied when developing the index. Therefore, Schneeweis and McClure suggest that if the researcher chooses a weighted comorbidity index, the weights need to be re-calculated for the specific study by considering comorbidity as a function of the outcome being studied.

Comorbidity may be such a complex construct, that comorbidity is not able to be measured accurately as all domains have yet to be identified (Baser et al., 2008; Schneeweis & McClure, 2000). Boyd et al. (2007) suggest that using a global score is not good scientific practice. However, the small size of data sets may preclude the use of a measure that evaluates many different domains, while using disease specific indices precludes comparisons across studies (Boyd et al, 2007).

Baser et al. (2008) suggest the low correlation often found between indices has two consequences. According to Baser et al., a low correlation, typically seen between indices, signifies that the indices are measuring different domains. Eliminating one of the measures leaves much of the variance in the model unexplained. The second issue is high correlation between indices. In this case, if the goal of the model is predictive capability, the statistical methods chosen eliminate this concern (Baser et al., 2008). To overcome these issues, Baser et al. suggest using several measures to triangulate the information collected in order to improve the predictive capability of the model chosen and contend that using multiple indices may account for conditions not included in one index alone. Recognizing that there is no “gold standard” for measuring comorbidity (Boyd et al., 2007; de Groot et al., 2003; Lash et al., 2007; Schneeweis et al., 2001), both Lash et al. and Boyd et al. suggest that the investigator must be aware of the limitations of the measurement instrument chosen and strive for accuracy in measurement, and fit of the proper instrument to the data source and domains being analyzed.

Operationalizing Comorbidity

A number of instruments providing a global score with severity weights have been developed to measure comorbidity. Instruments generally fall into three categories for source of data: 1) the patient or proxy (Geriatric Index of Comorbidity, The Total Illness Burden, the Katz Adaption of the Charlson Comorbidity Index), 2) the medical record (Lui Index, Burden of Disease Index) or 3) administrative data (the Deyo modification of the Charlson Index, the Chronic Disease Score, the Elixhauser Index) (Baser et al., 2008; de Groot et al., 2003; Kurichi, Stineman, Kwong, Bates, & Reker, 2007; Lash et al., 2007; Quan, 2006). Three indices in particular are well suited for

secondary data analysis, the Elixhauser index (Elixhauser, Steiner, Harris, & Coffey, 1998), the Chronic Disease Score (a drug-based comorbidity index) developed by von Korff, Wagner, and Saunders (1992), and the Charlson Comorbidity Index with the Deyo modification (Deyo et al., 1992).

. The Elixhauser index was developed for the Agency for Healthcare Research and Quality (AHRQ) in 1997 and was modified in 2003. It was developed to study conditions on admission to the hospital (Kurichi et al., 2007). It is based on 30 ICD-9-CM codes that were associated with increased mortality and length of stay, and expenditures in the inpatient setting (Baser et al., 2008; Stuckenberg, Wagner, & Connors, 2001). This index does not weight the disease conditions for severity. Instead a binary indicator is used to indicate if the disease of interest is present (Dominick et al., 2005). In addition, the Elixhauser Index uses the current hospitalization as well as previous hospitalizations in assessing the comorbid conditions, unlike the Deyo Charlson Comorbidity Index which uses hospitalizations previous to the index hospitalization (Stukenborg et al., 2001). It has not been extensively studied for validity and reliability (Farley et al. 2006, Stuckenberg, et al., 2001). The Elixhauser Index demonstrates equivalence or slightly improved performance in predicting mortality when compared to the Charlson Comorbidity Index (Baser et al., 2008; Kurichi et al., 2007; Li, Evans, Faris, Dean, & Quan, 2008). On the other hand, the Elixhauser index has not been shown to be consistently better than the Charlson Comorbidity Index in predicting other outcomes (Dominick et al., 2005; Farley et al., 2006; Kurichi et al., 2007; Schneeweis et al., 2001). The Chronic Disease Score, developed by von Korff et al. (1992) is also global measure, which counts current medication use and adjusts for age, sex and history of

dispensed drugs (Baser et al., 2008). Little is known about the validity or reliability of this disease index when used as a predictor for readmission.

Charlson, Pompei, Ales, and MacKenzie (1987) developed an early index which has been modified over the years by Deyo et al. (1992), Katz, Chang, Sangha, Fossel, and Bates (1996), and Romano, Roos, and Jollis (1993). Given its long history, ease of use and, accuracy of prediction in multiple settings and for multiple outcomes, the Charlson Comorbidity Index (CCI) remains the most commonly used comorbidity index (Baser et al., 2008). This summary score index was developed to predict inpatient mortality but has been expanded to multiple populations, non-inpatient settings, and used to predict other outcomes with varying levels of success (Baser et al., 2008; Dominick et al., 2008; Farley et al., 2006). This index is a count of 19 diseases with varying weights, ranging from one to six, attached to the diseases which accounted for most of the mortality in the inpatient setting (Baser et al., 2008). It is very accurate in predicting mortality, but has been less so when used to predict other outcomes (de Groot et al., 2003). De Groot et al. (2003) claim that the lessened ability to predict other outcomes is related to the fact that the Charlson Comorbidity Index was developed specifically to measure mortality.

The Deyo modification of the Charlson Comorbidity Index was developed to study the relationship between comorbidity and mortality using administrative databases rather than using chart review to determine the comorbidities. The Deyo modification of the CCI uses ICD-9 coding to detect the 17 co-morbid conditions used to predict mortality included in the CCI score (Kurichi et al., 2007). The modification allows researchers to recover comorbidity information automatically if the electronic data base contains ICD 9 codes.

De Groot et al. (2003), in a literature review, suggest that of the available methods to measure comorbidity, only the Charlson Comorbidity Index (Charlson et al., 1987), the Cumulative Illness Rating Scale (Linn, Linn, & Gurrel, 1968), the Index of Coexistent Disease (Greenfield, Apolone, McNeil, & Cleary, 1993), and the Kaplan Index (Kaplan & Feinstein, 1974) are valid and reliable methods of measuring comorbidity. Other instruments are not considered to have sufficient evidence of validity and reliability as yet. Therefore, because of ease of use with secondary data, comparability across studies, and excellent predictive capability in most settings for many different outcomes, the Deyo modification of the Charlson Comorbidity Index was chosen as the measure for comorbidity for this study.

Prevalence of Comorbidity

Comorbidity is usually defined in relationship to a specific disease. However, where overall comorbidity rates are reported, it is important to understand the definition used for comorbidity. For instance, Fried et al. (2004) suggest that comorbidity, according to the presence of two or more concurrent diseases definition, is 35% in the 65-79 age group and 70% in the 80+ age group. This finding was based on the work of Guralnik, LaCroix, Everett, and Kovar (1989). Comorbidity prevalence can also change based on the population used. For example, Fried et al. also cite work done by Anderson (2002) showing that two thirds of Medicare beneficiaries have two or more diseases. It appears that no matter the definition, comorbidity is an important issue for older adults and based on prevalence alone, would be expected to have a large impact on hospital readmissions.

Comorbidity as a Predictor of Adverse Drug Events Related to Readmission

Comorbidity has also been linked to the occurrence of adverse drug events in a study on 30,000 Medicare enrollees at one large medical center by Field et al. (2007). Using administrative records, clinician reports, hospital discharge summaries, and pharmacist review of pharmacy records, the researchers sought to classify the types of medication errors patients made, and the predictors of those errors. The researchers established that 31.7% of errors occurred in medication administration, 41.9% in modifying medication regimen, and 21.7% in not following clinical advice. Four groups of medications were most often found to be the source of the error: hypoglycemic medications, followed by cardiovascular drugs, coumadin, and diuretics. Although an increasing number of drugs was associated with errors, the CCI score was the strongest predictor of the errors or potential for errors. Neither age, nor gender predicted errors in this sample. Based on the study findings, the authors concluded that the complexity of the medication regimen led to an increased opportunity for errors, and that increased monitoring of patients should occur at transition points (discharge from the hospital) and when changes in the medication regimen are made. This study introduces the idea that CCI was the strongest predictor of medication errors and the possibility that medication regimens are linked to adverse events, thus establishing a potential mediating pathway.

Comorbidity as a Predictor of Hospital Readmission

Only three studies in home health care were found that specifically used comorbidity as a predictor for adverse outcomes such as readmission versus adjusting for comorbidity. Fortinsky et al. (2006) studied 922 Medicare eligible patients from a sample of Ohio Medicare certified home health care agencies. Fortinsky et al. used the Outcome-

Based Quality Improvement (OBQI) definition of hospitalization developed by CMS of being admitted from home to an acute care hospital as an inpatient for at least 48 hours. Using specific OASIS items as predictors (e.g. dyspnea severity, the presence of wounds, skin problems), rather than a global comorbidity score, the case mix score (an indicator of the amount of care needed) dyspnea, wound/skin problems, functional disability, and guarded rehab prognosis were predictive of hospitalization within six months of admission to home health care. In this study, it is impressive that a just few symptoms of disease predicted hospitalization, given that the definition of hospitalization includes a 48 rather than a 24 hour stay and no accounting of diseases or disease severity were used as predictors.

Madigan et al. (2001) defined and operationalized comorbidity as illness and illness severity, and used this measure as one of the predictors of hospital readmission with a convenience sample of 117 patients from three home health care agencies. However, only age, rather than comorbidity, was found to be a significant predictor of hospital readmission.

On the other hand, Rosati and Huang (2007) found that comorbidity, operationalized as OASIS items on primary diagnosis and secondary diagnosis with associated severity rating, was a significant predictor of hospitalization within 60 days of admission to home health care for 46,366 patients admitted to one large Midwestern home health care agency. Unfortunately, none of these studies used a recognized comorbidity index such as the Charlson Comorbidity Index or the Elixhauser Index, but it appears that the investigators used a derived score using OASIS data from the ICD-9 codes and the severity ratings. A derived comorbidity score can be developed from any

combination of several sections on the OASIS form including M0190 (inpatient diagnoses), M0210 (medical diagnoses), M0230 (primary diagnosis and severity rating), M0240 (secondary diagnoses and severity rating), and M0245 (payment diagnoses), therefore can vary depending on the combination of items chosen. Whether using a derived score or a standardized comorbidity tool, researchers must be very specific in which data points were used to develop the comorbidity score.

These studies demonstrate the difficulty of operationalizing comorbidity. None of the measures were comparable and researchers did not specifically describe how the measure was operationalized. However, it is clear the trend is to favor the amount of illness as a predictor of hospitalization.

Given the lack of studies in HHC regarding comorbidity and hospitalization, the literature review was then expanded to include community dwelling older adults in ambulatory care settings. Five additional studies used Medicare or Veteran Administration beneficiaries as subjects and found comorbidity to be predictive of hospital length of stay, emergency room visits, and admission or hospital readmission. Parker et al. (2003) evaluated the records of 6,721 Kaiser Permanente patients in an effort to determine whether using an index based on a drug count, the Chronic Disease Score (a drug-based comorbidity index), was equivalent to the Deyo version of the Charlson Comorbidity Index (CCI) in predicting length of stay in the hospital and readmission at 14 and 30 days after hospital discharge. The investigators used both administrative data and pharmacy outpatient data. The Chronic Disease Score was only significant for predicting unplanned admissions, while the CCI score was a significant predictor for all readmissions and length of stay in the hospital. Adding the Chronic Disease Score to the

model, when using the CCI as the predictor, increased the model's predictive capability significantly. Thus, the CCI was shown to be predictive of more than just mortality, and could be used in predicting both readmission, as well as, length of stay. More importantly, in this study, using both the pharmacy data and the CCI improved the predictive capability of the model.

Hastings et al. (2008) also examined comorbidity, as measured by the CCI, as one of the predictor variables in a study evaluating the outcomes of emergency room visits, hospitalization, or death within 90 days of discharge from a Veterans Administration hospital using administrative records of 972 veterans, age 65 and over. They found that the CCI score, emergency room visits or hospitalization in the previous six months, and triage to the emergency room versus an urgent care clinic, all independent predictors of the outcomes under study.

Other investigators have examined hospital readmission as an outcome. Coleman et al. (2004) studied 1,404 patients age 65 and over, who were part of the Medicare Beneficiary Survey cohort for 1997-1998. The investigators used cost files, use files, administrative data, and the survey answers to determine information about transfers that occurred within 30 days of discharge from the hospital. The investigators found 30.7% of patients transferred one or more times in the first 30 days after leaving the hospital. Predictors of transfers occurring from a less intensive care environment to a more intensive care environment (for example, from home health care back to the hospital) included being a Medicaid patient, specific diseases, visual impairment, and the interaction of comorbidity (measured using the CCI) with diseases, age, vision, and ADL function.

Hasan et al. (2010) also used the CCI to assess the relationship of comorbidity to 30 day readmissions in 10,946 subjects over age 18 discharged from six large urban hospitals across the United States. From telephone interviews and administrative records, this team found the CCI score in addition to insurance status, marital status, having a regular physician, physical function SF12 scores, admission in last year and a length of stay longer than two days predictive of hospital readmission within 30 days for the 17.9% of patients that were re-hospitalized. The odds ratio for the CCI was 1.13 ($p < .001$, CI = 1.08 – 1.19). Unlike Coleman et al. (2004) and Hasan et al (2010), Silverstein, Qin, Mercer, Fong, and Hayder (2008) used the Elixhauser Index to assess the effect of comorbidity on 30 day readmissions in 29,292 Baylor University hospital discharges. In this cohort, there was an 11.72% readmission rate, with age, African American descent, only having Medicare insurance, certain types of medical services, living in long term care and specific diagnoses predicting hospital readmission. As the Elixhauser Index has not been studied as intensively as the CCI in multiple settings, it is possible that the instrument is not validly used to study 30 day readmission.

Conclusions and Gaps in Knowledge Regarding Comorbidity

Major gaps in knowledge about comorbidity, as a predictor, exist in the home health care literature. When comorbidity is used, it is variably defined in this literature. In addition, no focus has been specifically on readmission, but rather on all hospitalizations in the home health care literature, consistent with the CMS quality measures. In the community dwelling literature, the CCI seems to be most often used to measure this concept, but occasionally studies do use the Elixhauser Index which seems to perform as well as or better than the CCI in some areas, but has less predictive capability in other

areas. Neither the Chronic Disease Score nor the Elixhauser Index has been well studied as methods to measure comorbidity. The lack of both a standardized conceptual and operational definition of comorbidity makes comparison across studies difficult and leaves conclusions open to doubt.

Currently, it appears that comorbidity has not been directly linked to any of the mediating variables proposed in this study. Although comorbidity has been studied as a predictor of hospital readmission in home health care, no standardized method has been consistently used to assess comorbidity, therefore the relationship of comorbidity to hospital readmission in this population remains unclear. In the few community studies, the CCI score has been shown to be predictive of hospital readmission, and emergency room use (Coleman et al., 2004; Hasan et al., 2010; Hastings et al., 2008; Parker et al., 2003), adverse drug events (Field et al., 2007), and cost (Charlson et al., 2008; Schoenberg, Kim, Edwards, & Flemming, 2007), as well as, length of stay (Coleman et al., 2004).

Implications for Research Regarding Comorbidity

Given the present gaps in knowledge about comorbidity, it appears that linking comorbidity to the indicator variables for high risk medication regimens will complete the causal chain of events. It presently is unclear whether a link between these variables exists at all, and whether the link is a mediating or moderating link. Untangling the influence of comorbidity from the influence of the proposed mediators on hospital readmission perhaps will help researchers determine whether the focus is on the proper variable in predicting hospital readmissions.

*Predictors of Hospital Readmission: Polypharmacy**Historical Context Regarding Polypharmacy*

Originally, polypharmacy was defined quantitatively as a certain number of medications above a set cut point. In recent years, as elders are living well into their eighties, most elders have multiple chronic conditions, necessitating the use of multiple medications concurrently. A cut point may not be meaningful when comparing studies across time, as the number of medications available for treatment in the older population has increased exponentially in recent years. Researchers now debate the use of a more qualitative definition such as the use of multiple medications, the administration of more medications than are clinically indicated or unnecessary drug use (Hajjar, Cafiero, & Hanlon, 2007). In an effort to be precise, researchers occasionally mix polypharmacy with potentially inappropriate medication use parameters by considering duration of medication use, thus confounding the operational definition of polypharmacy further (Fincke et al., 2005; George et al., 2004; Zarowitz, Stebelsky, Muma, Romain, & Peterson, 2005).

The discussion on the definition of polypharmacy is taking place in the context of a discussion about whether polypharmacy is a reliable predictor of adverse outcomes and adverse drug events (Chrischilles et al., 2007; French et al., 2006; Green, Hawley, & Rask, 2007). Rather, some researchers believe that polypharmacy mediates or moderates the relationship of comorbidity to adverse events or even that polypharmacy was a proxy for comorbidity (Chrischilles et al., 2007; Flaherty et al., 2000).

Recent expert opinion suggests that polypharmacy is not only unavoidable in elders, but is beneficial in improving quality of life, an argument that is counterintuitive

to the general belief that providers should avoid polypharmacy at all costs (Aronson, 2004). In this line of thinking, medications taken for prevention of a future disease or adverse outcome, is worth the risk of increasing polypharmacy. Thus polypharmacy actually becomes a benefit in helping to avoid adverse outcomes. Cases in which polypharmacy is beneficial include statins used to improve cholesterol levels in order to prevent future cardiovascular disease, or aspirin taken as prevention against stroke or myocardial infarction.

Definition of Polypharmacy

Although polypharmacy has been written about frequently in the literature since 1992 when it was first mentioned as a concept in the psychiatric literature (Segal, Cohen, & Marder, 1992). However, to date, there is no consistent operational definition across studies and settings. Polypharmacy has been defined as “the use of multiple drugs administered to treat one or a limited number of conditions” (Segen, Dictionary of Modern Medicine, 1992, p. 565). Researchers have defined and operationalized polypharmacy as ranging from the concurrent use of more than one medication (Agostini et al., 2004; Linton, Garber, Fagan, & Peterson, 2007) to the use of greater than 5-9 medications depending on the setting being studied, and the cut off score being used (Cannon et al., 2006; Flaherty et al., 2000; Hanlon et al., 1997; Ibrahim, Kang, & Dansky, 2005). However, when using a cut point or categories to define levels of polypharmacy, much information is lost in the analysis.

Table 2.1 provides a summary of definitions for polypharmacy that have been used by researchers as well as prevalence rates reported in the studies. A continuous

count seems to be the most common way to operationalize the definition of polypharmacy. However, the exclusion column of Table 2.1 demonstrates wide variation in how medications are counted. Although it is seemingly simple to use a count of medications, in practice, measurement problems arise when using polypharmacy as a variable. Specific questions the researcher must address in defining and operationalizing polypharmacy include:

1. What counts as a medication? Examples of difficult compounds to classify include oxygen, ointments and dressings impregnated with drugs.
2. Should PRN (as needed) medications and over the counter medications be counted when studying polypharmacy?
3. How should combination products and variable dosages be counted?
4. Will medication counts be a continuous count or a categorical count?
5. Are intermittent medications (a course of antibiotics) included in the regularly prescribed regimen?
6. Are all medication routes counted or are just oral medications counted?
7. What is a reasonable cut point to distinguish low levels of drug use from high levels of drug use?

Table 2.1. Summary of definitions for how drugs are counted in studies examining polypharmacy and prevalence.

Author	Definition	Exclusions	Prevalence
Agostini, Han, & Tinetti (2004)	Continuous count	Topicals, OTC preps, herbals, short term antibiotics, PRN meds	Not reported
*Cannon, Choi, & Zuniga (2006)	Categorical counts; polypharmacy > 9 meds	Did not exclude OTC	39%
Chrischilles et al. (2006)	Continuous count	Preparations that did not have NDC numbers	Not reported Mean number of medications: 8.5 20.3% had less than 3 medications
Fincke et al. (2005)	Continuous count	Drugs not prescribed and drugs filled at outside pharmacy	Not reported
*Flaherty, Perry, Lynchard, & Momey (2000)	Continuous count but analyzed by categories, but > 5 drugs considered polypharmacy	Topicals, nasal sprays, artificial saliva and liquid nutritional supplements (protein shakes)	66.1% taking more than 5 meds in those hospitalized
George et al. (2006)	Polypharmacy defined as long term use of at least 2 drugs for 2 or more quarters/year; major polypharmacy >5 drugs	OTC drugs and herbals; counted prescribed only	Not reported
Green, Hawley, & Rask (2007)	Continuous count but polypharmacy >5 drugs	No exclusions	Mean number of medications: 4.0 38% took > 5 meds
Hafner, Belknap, Squillante, & Bucheit (2002)	Continuous count	None listed	Not reported
Hanlon, Schmader et al. (1997)	Continuous count but polypharmacy >5 drugs	Non-VA dispensed drugs, non-prescribed drugs and PRN meds	Not reported
Hanlon et al. (1996)	Continuous count but polypharmacy was ≥ 5 regularly scheduled drugs by a VA physician	Topicals	Not reported; average number of prescribed medications was 6.9
*Ibrahim, Kang, & Dansky (2005)	Five or more systemic, prescribed drugs	OTC drugs, topicals, herbals, ophthalmologic	88% taking more than 5 medications

Author	Definition	Exclusions	Prevalence
Linton, Garber, Fagin, & Peterson (2007)	Continuous count	OTC drugs, herbals	50% taking 5 or more medications
Pugh et al. (2006)	Continuous count of unique oral, topical and injectable meds	Non-prescribed drugs or drugs dispensed from non-VA sources	19.6% exposed to HEDIS always avoid drugs
Schmader et al. (2004)	Unnecessary drugs based on Medication Appropriateness Scores	OTC drugs and herbals	Not reported Mean number prescription drugs on GEM unit: 7.7; non-prescription drugs: 2.7
Steinman, Rosenthal, Landefield, Berthenthal, Sen, & Kaboli (2006 ^b)	> 9 medications	No exclusions	37% polypharmacy rate
Steinman, Landefield, Rosenthal, Berthenthal, Sen, & Kaboli (2006 ^a)	Continuous count	Vitamins, topicals, minerals, PRN meds, herbals; excluded subjects with less than 5 meds	68% taking 6 or more medications
Weaver, Fisher, & Curci (2005)	> 1 medication	No exclusions	70% using more than 5 meds
Williams et al. (2004)	> 5 medications	Non-prescribed drugs	Mean: 6.6 prescribed medications; 5.1 non-prescribed medications
Zarowitz, Stebelsky, Muma, Romain, & Peterson (2005)	More drugs taken than clinically warranted; high risk if > 5 meds	OTC drugs	Not reported

* *Studies taking place in the home care setting.*

Surprisingly, only Flaherty et al. (2000) considered how counting might make a difference in outcomes reported, but then did not report the differences in outcomes for the various cut points considered. The wide range of prevalence rates in Table 2.1 may result from differing methods of counting rather than actual differences in the level of polypharmacy in various study samples.

Issues in Defining Polypharmacy

Other counting issues in polypharmacy research include what constitutes a medication and whether all routes (systemic, oral only, all routes) should be counted, as well as whether medications that are intermittently given or given for a limited time should be counted. Most researchers only study oral routes and eliminate medications that are not routine (PRN) as well as over-the-counter medications (medications purchased without a prescription) from their counts of medications (Table 2.1).

Both “systemic” and “regularly scheduled” medications are problematic in the counting process as topical medications are frequently systemically absorbed, and PRN medications can be used quite regularly. Many of the over the counter drugs potentially have significant side effect profiles for the elderly (Ben-Gay, Motrin, St. John’s Wort, Sudafed), and can be related to adverse events such as gastrointestinal bleeds, changes in clotting times, or acute retention (Bergman-Evans, 2006; Weaver, Fisher, & Curci, 2005). Presently, the trend in research is to count only prescribed medications, and frequently, to exclude OTC preparations and herbals as well as some classes of prescribed drugs such as topicals or instilled drops under the impression that these medications are “safer” than prescribed oral preparations. Again, how these preparations are counted has a large effect on the ultimate findings.

Depending on the database being used, it may not even be possible to account for OTC medications or herbals. Since 19% of Americans use herbals (CDC, 2004) and elders use more than three OTC medications daily (Yoon & Horne, 2001), there is significant debate about the accuracy of the current prevalence rates. Although many researchers using claims data choose to only count prescribed medications, this definition

decreases the prevalence of polypharmacy as elders are high users of both OTC and herbal preparations. It is also important to keep in mind that elders receive drugs through multiple pharmacies, as well as, from family or friends.

The issue of whether to count PRN medications, varying medications and intermittent medications needs to be addressed. All of these medications are part of the medication regimen and can potentially increase the risk of adverse events, so counting them addresses the issue more accurately. Counting the active ingredient versus the actual medication, or whether an active ingredient should be counted multiple times if it appears in different preparations is another issue in polypharmacy. Counting the active ingredient is difficult with regimens that include combination pills or active ingredients in more than one medication (acetaminophen or codeine). If a researcher is trying to measure polypharmacy risk, the count of the actual medications rather than the active ingredient should be made. No matter how polypharmacy is defined, the researcher must be specific and consistent in defining polypharmacy and keep an accurate log regarding how medications were categorized especially when using large electronic databases.

Operationalizing Polypharmacy

Due to the small number of polypharmacy studies in home care, the literature search was expanded to include community settings. In the community setting, two studies had similar polypharmacy rates. Linton et al. (2007), doing a secondary data analysis to determine the prevalence of polypharmacy in 126,682 Tricare beneficiaries, and counting only prescribed medications, found that 50% of the subjects used five or more medications. Weaver et al. (2005) also found high rates of polypharmacy. Using a brown bag review technique (having the patient bring all their drugs to the provider in a

brown paper bag), Weaver et al. examined the incidence of polypharmacy and its relationship to adverse drug reactions in 46 volunteers living in public housing. The incidence of polypharmacy, defined as the use of 5 or more medications, was found to be 70% in this population. Weaver et al. concluded that although the rate is very high, it is possible that counting both prescribed and non-prescription drugs are actually a more accurate determination of polypharmacy.

Fincke et al. (2005), however, found much lower rates of polypharmacy using the definition of 5 or more medications consumed. Fincke et.al. developed three operational definitions for polypharmacy when using large claims databases: cumulative polypharmacy (all scripts filled during a 178 day window), continuous polypharmacy (all scripts filled during two 178 day windows 6 months apart) and simultaneous polypharmacy (the number of scripts active on a particular day). Each definition addressed the duration of drug use in addition to the number of drugs in use. The investigators found a cumulative average of 3.54 drugs per patient, however, 24.5% of patients were taking more than five drugs. When counting continuously filled scripts, the average number of medications per patient was reduced to 1.96 drugs, with only 13% of patients taking more than five medications. The mean number of simultaneous prescriptions was 2.63 medications per patient demonstrating how different counting methods can change the outcomes.

Steinman et al. (2006) evaluated the relationship of three concepts (level of polypharmacy, PIM, and underuse of medications) commonly used to measure quality in two studies using the Enhanced Pharmacy Outpatient Care (EPOC) study data collected in the VA system. Both studies used a subset of 196 patients from the larger randomized

clinical trial. The Steinman, Rosenthal, Landefeld, Berthenthal, Sen, & Kaboli (2006^b) study will be reviewed in this section and the Steinman, Landefeld, Rosenthal, Berthenthal, Sen, & Kaboli (2006^a) study will be reviewed in this section, as well as in the section on potentially inappropriate medication (PIM) use.

In the first study completed by Steinman et al. (2006^b), the correspondence between two other clinical tools used to assess quality of care, the Beers' criteria (Beers, 1997) and the Medication Appropriateness Index (Hanlon, Schmader et al., 1992) were compared to polypharmacy. When studying the quality indicators, polypharmacy was defined as the use of nine or more medications, whether prescribed or not. Low correspondence was found for the three quality measures. Steinman et al. concluded that findings based on these measures would likely lead to vastly different research conclusions and policy decisions. These studies lend credence to the idea that the measures are evaluating differing concepts, or perhaps differing aspects of a larger concept.

The relationship between potentially inappropriate medication use, under use of medications, and polypharmacy was evaluated in the second study (Steinman et al., 2006^a). In this study, polypharmacy was defined as use of multiple medications and excluded topicals, vitamins, minerals, herbals and "use as needed" (PRN) medications. The Beers' criteria (Fick et al., 2003) and a subset of questions from the Medication Appropriateness Index (Hanlon, Schmader et al., 1992) were used to assess medication appropriateness. Although both the Beers' criteria and the Medication Appropriateness Index (MAI) are used to evaluate potentially inappropriate medications, the prevalence rates for potentially inappropriate medication use varied widely between measures. The

use of the Beers' criteria identified inappropriate medication use in 37% of patients, while 57% of patients had inappropriate medication use based on the MAI. Only 22% of patients were identified as using inappropriate medications on both criteria. In the overall sample, over-the-counter medications accounted for 10% of inappropriate medication use. When evaluating the effect of various levels of polypharmacy on inappropriate medication use, those with increasingly higher levels of polypharmacy (≥ 5 medications), had increasingly higher numbers of inappropriate medications. In 42% of patients, inappropriate medication use and medication underuse were present at the same time. The mean number of drugs (both prescribed and non-prescribed) used by patients in this study was 8.1 medications.

Two other definitions of polypharmacy were found in the literature review. These definitions considered length of use of a medication and the relationship of polypharmacy to PIM in defining polypharmacy. George, Vuong et al. (2006) were very specific in defining polypharmacy in a study evaluating the relationship between medication complexity and adherence in 310 people making the transition from the hospital back to the community. In this study, polypharmacy was defined as the long term use of 2 or more drugs at least 60 days per quarter during a year. They also defined major polypharmacy as the concurrent use of 5 or more medications. The average number of medications prescribed at hospital discharge was 10.4 (+/- 3.9) medications.

Schmader et al. (2004), frequent collaborators with Hanlon, evaluated whether a Geriatric Evaluation and Management (GEM) inpatient unit improved outpatient adverse drug reaction rates and suboptimal prescribing 12 months after the index hospitalization for 834 patients in 11 VA medical centers. The GEM outpatient care significantly

reduced the rate of adverse drug events by 35%. The definition of polypharmacy was based on a measure of potentially inappropriate medication use, the Medication Appropriateness Index (Hanlon et al., 1992). The Medication Appropriateness Index (MAI) is a series of ten questions regarding the appropriateness of a prescription. If a patient was found to have potentially inappropriate medication use, they were automatically considered to have polypharmacy. This definition of polypharmacy is unlike others used in the literature and therefore hinders comparison of this intervention study findings to other studies.

Although many investigators adopt a cut point for determining polypharmacy, setting a cut point proactively obscures monitoring trends and makes comparison to studies not using the same cut point difficult. Also, adoption of a cut point may lead to under or over estimation of risk depending on the cut point chosen. Since the mean rate of medication use in HHC is reported variably between 5 to 6.5 medications, using the most common cut point for polypharmacy of five prescribed medications, it is likely that most patients in HHC would have polypharmacy if all medications and routes were counted. Accurate prediction, based on differences between groups, would not be possible in that instance.

Prevalence of Polypharmacy in Home Health Care

Home care patients, on average, consume between 5-6.5 prescribed medications and eight total medications daily, with 19% taking nine or more medications daily (Cannon et al., 2006; Gray et al., 1999; Meredith et al., 2001). Three medication prevalence studies were found in home health care. Ibrahim et al. (2005) studied 139 home health care patients (age 65 and older) to determine the prevalence of

polypharmacy and its relationship to drug-drug interactions. Defining polypharmacy as the use of 5 or more prescribed drugs simultaneously, Ibrahim excluded over the counter (OTC) preparations, herbals, ophthalmologic and PRN medications. On average, patients took 8.9 medications daily and the prevalence of polypharmacy was 88%. Based on the rate of polypharmacy, Ibrahim et al. calculated that potentially, 38.8% of patients could be subject to dangerous drug interactions.

Flaherty et al. (2000) examined the relationship of polypharmacy to hospitalization in 833 home health care patients and found that the 22.7% of patients who were re-admitted to the hospital were taking more medications than patients being discharged back to the community caring for themselves. The prevalence rate of polypharmacy in this group, defined as taking more than five medications, was 66.1%. Unlike other researchers in this area, not only were all medications counted, there was no differentiation between PRN and regularly scheduled drugs, nor were drugs of the same class collapsed into one category. However, Flaherty et al. did exclude topicals, nasal sprays, artificial saliva and nutritional supplements. Flaherty et al. point out that higher numbers of medications in this population may be a proxy indicator for sicker patients, which may be why the hospitalization rate is higher in this population than in other populations studied by different research teams.

Using medical review of OASIS records and the physician orders, Cannon et al. (2006) found polypharmacy in 39% of the 786 home health care subjects with a higher cut point for polypharmacy (nine or more medications). The researchers found patients with polypharmacy to be younger, have higher cognitive function, and using more over the counter (OTC) medications, despite being less able to manage their medications

independently than those who used less than 9 medications. Even though Cannon et al. found a lower percentage of polypharmacy, likely due to a higher cut off limit, nearly 40% of patients still met the criteria for polypharmacy, a figure that should be a cause for concern.

Differences in whether a medication is counted and whether polypharmacy is considered a continuous count or a categorical count will make a significant difference in the prevalence of this variable. The prevalence of polypharmacy in home health care (40-88%) seems to be higher than that of community dwelling older adults (24.5% - 70%). This may be related to how ill those in home health care are, and the frequent adjusting of medication that occurs directly after hospital discharge.

Polypharmacy as a Predictor of Hospital Readmission

Only two studies were found to examine polypharmacy as a predictor of hospital readmission and both were done in home care settings (Flaherty et al., 2000; Rosati & Huang, 2007). Polypharmacy was found to be a predictor of hospital readmissions in both studies. These studies were described in other sections (Rosati & Huang in the hospital readmission section and Flaherty et al. previously in the polypharmacy section).

Polypharmacy as a Predictor of Negative Patient Outcomes Other Than Hospitalization

As there were few studies using polypharmacy as a predictor for hospital readmission, the literature review was expanded to include the relationship of polypharmacy to other negative outcomes. These precursor negative outcomes would likely have the potential to increase hospital readmissions and might potentially be a mediator in the relationship of medication use to readmission.

Although researchers have examined polypharmacy as an independent, or a predictor variable to adverse drug events or adverse outcomes, few studies of this nature were found in the home health care literature. In the community setting with elders, polypharmacy has been found to be an independent risk factor for adverse drug reactions (Agostini et al., 2004; Cannon et al., 2006; Hanlon et al., 2006; Weaver et al., 2005; Zarowitz et al., 2005), adverse drug events (Chrischilles et al., 2007; Field et al., 2007; French et al., 2006; Hafner, Belknap, Squillante, & Bucheit, 2002; Hanlon et al., 1996; Hanlon et al., 1997; Rask et al., 2005; Triller, Clause, & Hamilton, 2005), and medication errors, discrepancies, and non-adherence (Bedell et al. 2000; Field et al., 2007; MacLaughlin et al., 2005). Polypharmacy is also associated with a higher risk of potentially inappropriate medication use (Cannon et al., 2006; Golden et al., 1999; Steinman et al., 2006^a).

Polypharmacy as a Predictor of Adverse Events in the Community

In examining community setting studies, the adverse drug event rate associated with polypharmacy was between 22 - 35% (Chrischilles et al., 2007; Hanlon et al., 1997; Ibrahim et al., 2005; Weaver et al., 2005; Zarowitz, 2005). Hafner et al. (2002) found that warfarin, insulin and furosemide were the three drugs most commonly associated with adverse drug events. Hanlon et al. (1997) evaluated polypharmacy in a subset of 172 older veterans who were part of a larger study using pharmacist interventions to prevent adverse drug events in the General Medicine Clinic at the Durham Veterans Affairs Medical Center. Although thirty-five percent of the sample experienced adverse drug events, none of the predictor variables were found to be significant. Since only the Veteran's Administration (VA) system pharmacy data were studied and the patients had

to have five or more drugs to be in the study, the impact of polypharmacy was likely to be underestimated because medications can also be dispensed from outside pharmacies and over-the-counter medications or herbals were not included in the analysis. There also may not have been enough of a difference between groups to detect because low medication users were not included in the study.

Conclusions and Gaps in Knowledge Regarding Polypharmacy

Serious gaps in the literature about polypharmacy exist. First, the operational definition of polypharmacy seems to be evolving. This may be related to lack of clarity around the conceptual definition of polypharmacy, which is broadly defined as taking more than one medication regularly. Two problems exist around defining polypharmacy: whether a continuous count or cut point should be used and what should be counted as a medication. A consistent and valid definition for polypharmacy is not evident in the literature, however, there seems to be some consensus that five or more medications is an adequate cut point to define polypharmacy, if categorization is desired. The more recent trend is to use both continuous and categorical counts for measuring polypharmacy in the same study. Because researchers studying polypharmacy frequently used secondary data (Cannon et al., 2006; Fincke et al., 2005; Green et al., 2007; Ibrahim et al., 2005; Linton et al., 2007; Zarowitz et al., 2005), it is more difficult to count all medications ordered or consumed (over the counter medications, as needed medications, or herbals and vitamins) in an expedient or efficient way. However, the practice of undercounting medications has led to widely differing polypharmacy prevalence and incidence rates and likely underestimated the influence of polypharmacy on hospital readmission events.

Disagreement regarding counting methods and cut points hamper the ability to accurately study the concept of polypharmacy and compare findings across studies.

Secondly, there are very few studies examining polypharmacy in the United States in community settings and even fewer in home health care. This paucity of research leads to limited evidence about the prevalence and incidence of polypharmacy in the home care setting (Fincke et al., 2005; Ibrahim et al., 2005; Linton et al., 2007; Weaver et al., 2005).

Finally, researchers have linked polypharmacy to a number of intermediate outcomes such as adverse drug reactions, adverse drug events, medication errors, and non-adherence, but few investigators have linked polypharmacy to adverse outcomes like hospitalization, hospital readmission, institutionalization, or death in older patients. It is unclear whether these outcomes have not been chosen due to the difficulty in electronically linking datasets or whether the complexity of studying multiple drugs or drug classes is not likely to be underwritten by pharmaceutical firms who financially support many of the drug studies.

Implications for Research Regarding Polypharmacy

Based on the literature review, a reasonable definition to accurately estimate polypharmacy should include a continuous measure of polypharmacy, as well as, counting all medications, prescribed or otherwise, taken by any route. No loss of data occurs and if a researcher needs to compare rates; categories can always be constructed retroactively. Counting rules for combination drugs, varying dosages and intermittent prescriptions should be clearly specified in the methods section of the study, and limitations and implications of those rules should be described in the discussion section.

Given that most studies use a continuous count of medications, for ease of comparability with other studies, a continuous count will be used in this study. To prevent loss of valuable information by not counting all medications, both PRN medications and over the counter medications will be counted in this study as well as all routes of medication administration. The major limitation when defining polypharmacy more broadly as the concurrent use of more than one medication is that the rate of polypharmacy will be significantly higher than in the present literature findings. However, a higher rate likely reflects the true rate in the HHC community and quite possibly improves predictive capability.

Predictors of Hospital Readmission: Potentially Inappropriate Medications

Historical Context of Inappropriate Medications

The original concept of medication appropriateness appears in the Drug Utilization Review provision of the Omnibus Budget Reconciliation Act of 1990. Under this provision, prescriptions were to be evaluated for appropriateness, necessity, and the likelihood of adverse outcomes if the prescribed drug is given to the outpatient Medicaid patients (Idaho State University, College of Pharmacy, n.d.). This provision in the Act was intended to detect fraud, abuse, overutilization/underutilization, and to prevent untoward reactions to drugs (Idaho State University, College of Pharmacy, n.d.). Each individual state is required to designate a department or research group to direct this auditing program. It is left to the discretion of the individual state government entity as to how to determine the definition/parameters of appropriateness.

Definition of Potentially Inappropriate Medications (PIM)

Conceptually, “potentially inappropriate” medications are more likely to have a narrow therapeutic window due to the physical changes of aging i.e. increased fat to lean muscle ratio, decreased albumin levels, decreased metabolism and excretion (Brandt, 2006; Center for Drug Evaluation and Research, 2002; Fu et al., 2004; Salazar et al., 2007). However, most researchers understand the concept to be drugs that have more risk than benefit to a given patient (Fu et al., 2007).

There are two major ways to operationally define potentially inappropriate drug use: 1) explicit criteria where certain drugs are considered not appropriate for certain populations given the characteristics of that population and how the drug is metabolized, cleared and stored in the body; and 2) implicit criteria where the individual drug is judged inappropriate based on indication, dosage, the potential for side effects and drug interactions (Fick et al., 2003; Hanlon et al., 2002). Separate lines of research have developed utilizing a particular method (explicit vs. implicit), making it difficult to compare outcomes because the definition of PIM is different for each method. Two of the most common criteria are the Beers’ criteria (Beers et al., 1991) and the Medication Appropriateness Index (Hanlon et al., 1992). Both sets of criteria were developed initially for clinical use and now are commonly used as measures in clinical studies.

Issues in Measuring PIM

The Beers’ Criteria. The most common explicit criteria approach to quantify potentially inappropriate medication use is some version of the Beers’ criteria originally developed by an expert consensus panel using a Delphi technique (Beers et al., 1991). The criteria were a list of medications that the experts concluded posed a high risk for

adverse drug reactions in the elderly. The medication list was updated in 1997 by Beers (1997). Zhan, Sangl, Bierman, Miller, and Meyer (2001) reconvened a seven member expert panel to add additional parameters based on the individual's disease context. Adding a disease context required a judgment call as to the appropriateness of the medication being used (Zhan et al., 2001). The addition of the consideration of the disease context was in response to criticism that Beers' criteria did not account for the fact that some drugs could be used in certain situations if monitored closely. Zhan et al. placed the drugs into "never appropriate", "sometimes appropriate" and "use with caution" categories.

Fick et al. (2003) published the most recent revision to the 1997 Beers' criteria incorporating much of Zhan's work and again updating the medication list. In the present form, the list contains 42 specific drugs and 18 classes of drugs to avoid in the elderly. The present revision contains two tables. Table one is a list with drugs that should always be avoided in the elderly and table two are drugs that should be used with caution in the elderly depending on the disease context. This revision now incorporates a severity ranking on the risk for adverse drug reactions (Fick et al., 2003). Although the list of medications to always avoid using in the elderly requires no judgment for inclusion purposes, those that should generally be avoided or should be used cautiously, will require judgment on the part of the investigator and access to additional data points on conditions and outcomes to determine whether those medications should be counted as potentially inappropriate. This level of judgment has implications for how PIM is counted especially if the investigator chooses not to use that section of the Beers criteria.

The Medication Appropriateness Index (MAI). An alternative to the Beer's criteria as a measure for PIM was proposed by Hanlon, Schmader et al. (1992) which uses implicit criteria (judgment of the provider or the pharmacist) to determine the appropriateness of the medication regimen. Hanlon et al. claimed the Beers' criteria were so explicit as to be rigid in application and unable to account for variations in an individual's situation, Hanlon et al. developed a reliable and validated tool, the Medication Appropriateness Index. The MAI consists of 10 questions regarding the appropriateness of prescribing the medication. Areas to be examined include whether there is an indication for the medication's use, the medication is correctly dosed, the frequency of dosing is appropriate, the duration of the medication use is appropriate, the patient has functioning of pathways for metabolism and clearance, and the medication is effective in treating the patient's disease (Hanlon et al., 1992).

However, the MAI has a number of limitations that preclude the use of this measure by researchers other than pharmacists. Implicit definitions of inappropriate medication use rely on a pharmacist's or clinician's judgment of whether these criteria are met or not and as a result, are difficult to use in secondary data analyses. In order to use the MAI as developed, the researcher must be very knowledgeable about medications, have access to: 1) the patient's disease condition, 2) at least two time points to determine duration of treatment, and 3) the outcome of treatment in order to determine whether the disease is actually responding to the medication. In addition, primary data collection in longitudinal studies is expensive to perform and is subject to attrition over time. However, the MAI appears to be favored by European researchers over the Beers'

criteria as the questions it contains are neither country specific, nor formulary specific (Gallagher, Barry, & O'Mahoney, 2007).

To overcome these issues, often only a portion of the MAI is used. In most research studies not being done by Hanlon or his associates, the MAI is being confined to three questions, but unfortunately, the psychometrics of using just three questions has yet to be assessed. Only the full tool, as it was initially developed, has been demonstrated to be psychometrically sound (Samsa et al., 1994).

Operationalizing PIM

There is heavy dependence on the Beers' criteria as the basis for measurement of inappropriate medication use. However, the Beers' criteria are primarily a clinical tool rather than a psychometrically tested measurement tool. Consequently, many researchers remain dissatisfied with the Beers' criteria. Researchers frequently modify the Beers' criteria, rather than using it as it was developed, by dropping medications or adding other medications which creates challenges when attempting to compare studies done at different points in time and leaves the results of studies in question. Explicit criteria such as the Beers' criteria are also dependent on changes in prescribing practice, the timing and release of new drugs, and reimbursement practices that influence trends in prescribing. This makes comparing findings over time extremely difficult. In addition, it appears the Beers' criteria are being refined in preparation for standardization for use in national quality assurance studies. The Beers' criteria is used more frequently than the MAI for clinical and in research purposes, possibly because the Federal government is championing a version of the Beers' criteria through the HEDIS audits and the development of quality indicators of medication use in nursing homes. This will

influence the criteria towards standardization in both clinical practice and research. The widespread adoption of the HEDIS criteria (AHRQ, 2005, Core Measures) have the potential to dramatically change how health care is delivered due to a focus on outcomes which are measured in the clinical arena.

Although lengthy, the Beers' criteria are still easily manipulated when using electronic databases, making it more suitable than the MAI for epidemiological research. The Beers' criteria are likely to be favored over the MAI in this instance because it is far easier to use with large administrative data sets. The separate tables in the 2003 version of the Beers' criteria allow investigators a choice of using strictly explicit criteria, which improves ease of use with administrative databases, or having a hybrid version of the criteria when adding the implicit judgment table.

Despite a lack of psychometric testing, all of the major agencies (Agency for Healthcare Quality and Research, Centers for Medicare and Medicaid Services, National Health Service of Great Britain) have compiled lists of medications that are based on the Fick et al. (2003) updated Beers' criteria or the idea of explicit criteria and use these lists as portions of quality measures. The Beers' criteria have been judged by the 2003 panel to be appropriate avoidance advice in all geriatric settings (Maloney, 2004), therefore the 2003 version of the Beers' criteria will be used to operationalize PIM in this study (Appendix C).

Prevalence Studies Using the MAI

Studies examining the prevalence and incidence of PIM using the MAI have not been done with home health populations. Consequently, the studies reviewed are those that were conducted on community populations. The majority of the research in this area

uses large secondary data sets collected by the government to explore inappropriate medication prescribing and the use of potentially inappropriate medications in community dwelling elders. Hanlon, Schrader, Hajjar, Pugh, and Sloane frequently collaborate on research projects, and conduct the vast majority of research examining PIM. These researchers have spent many years examining inappropriate prescribing and outcomes in multiple settings ranging from nursing homes, hospitals and community settings. Their data are primarily from the Duke University Epidemiologic Studies of the Elderly (EPESE) and from the Veterans Administration (VA) system. Fu et al. (2004, 2007) use the MAI to evaluate inappropriate medication use in relation to utilization of services and cost using the Medical Expenditure Panel Survey (MEPS) data while Zhan et al. evaluate PIM using a subset of Beers' criteria drugs for drug-drug and drug-disease interactions using both the MEPS data (2001) and the National Ambulatory Medical Care Survey (2005).

Despite being the developer of the MAI and having a rich data set containing interview data appropriate for use with the MAI, Hanlon, Fillenbaum, Schmader, Kuchibhatla, and Horner (2000) used the 1997 version of the Beers' criteria to evaluate PIM in 3,314 elders enrolled in the EPESE study. Using the Beers' criteria, Hanlon et al. found the prevalence of potentially inappropriate medication use to be 27% in the first wave and 22% in the second wave of subjects in this study. In a second study, again using EPESE data from the fourth wave of 3,234 subjects, Hanlon et al. (2002) compared the 1997 Beers' criteria (Beers, 1997) and the Drug Utilization Review (Knapp, 1991) criteria to evaluate the relationship between potentially inappropriate medication use and functional status decline and mortality. The Drug Utilization Review (DUR) criteria

developed by Knapp are very similar to the MAI criteria. Potentially inappropriate medication use, as assessed with the Drug Utilization Review criteria, was 21% as opposed to a 28% potentially inappropriate medication use rate based on the Beers' criteria.

Hanlon also worked with Hajjar et al. in a series of studies using data from the Veterans Administration system to determine the prevalence and predictors of potentially inappropriate medication use at hospital discharge, as well as, the predictors of falls. Hajjar et al. (2005) studied a subset of 384 patients from a Geriatric Evaluation and Management unit study (Hanlon et al., 1996) to evaluate the prevalence and predictors of potentially inappropriate medication use at hospital discharge. Hajjar et al. linked potentially inappropriate medication use and polypharmacy in this study. The investigators considered potentially inappropriate medication use as unnecessary drug use based on the full MAI criteria. Polypharmacy was defined in a novel way by considering polypharmacy to be any positive score on the MAI. Hajjar et al. found that 44% of elders had unnecessary drugs at hospital discharge and nearly one third of the unnecessary drug use was accounted for by gastrointestinal medications, central nervous system medications, vitamins and minerals.

Finally, Hanlon and Hajjar worked with Rossi et al. (2007) to determine the prevalence and predictors of unnecessary drug use in 128 community dwelling elders. In this study, potentially inappropriate medication use was defined by an inappropriate rating on three questions from the MAI on indication, effectiveness, and therapeutic duplication of drugs. Using only these questions, Rossi's team found 58.8% of patients

were using an unnecessary drug. Lack of effectiveness was the most common reason for the drug being classified as unnecessary.

Other than Hanlon et al., only Williams et al. (2004) and Steinman et al. (2006^b) used the MAI for assessing potentially inappropriate medication use. The two Steinman et al. studies were described in the polypharmacy section. Of particular note, Steinman et al. (2006^b) used just three questions from the MAI, which departs from how the MAI was validated. Nonetheless, Steinman et al. still had high rates (57% - 82%) of potentially inappropriate medications. Williams et al. did not report a prevalence rate.

Since the MAI measures appropriateness based on parameters such indication, duration, and dosage, the high rates of PIM using this measure are particularly troubling, and may be indicative of the poor state of education regarding acceptable prescribing practices for geriatric patients. Clearly elderly patients, already at high risk for adverse drug events, are particularly vulnerable to PIM issues. A less sophisticated measure, such as the Beers' criteria although perhaps easier to use in research, may demonstrate a lower prevalence of PIM due to the difference in definition of PIM.

Prevalence Studies Using the Beers' Criteria

Inappropriate medication use in home health care was examined in only two studies. In 2006, using the 1997 Beers' criteria, Cannon et al. (2006) found a 31% potentially inappropriate medication (PIM) use in a sample of 786 Medicare patients from one hospital system. Only polypharmacy was found to be a significant predictor of PIM use. In this study, age, gender, race, sensory function, cognition, ADL independence, ability to manage medications independently, and financial status were not significantly associated with PIM. Flaherty et al. (2000) had a prevalence of 20% PIM in

patients that were hospitalized in the study, while those who were discharged to the community actually had a higher PIM rate of 27%. Flaherty et al. used the earliest version of the Beers' criteria (Beers et al. 1991). Both studies are described in detail earlier.

Many more studies were found evaluating PIM in the community setting. Pugh et al. studied over one million records of veterans in the VA system in two studies which demonstrated the large difference in PIM use when different measures are used to determine PIM use. In the first study Pugh et al. (2005), using the 2003 revision of the Beers' criteria (Fick et al., 2003), identified a 33% rate of potentially inappropriate medication use. Pugh et al. then adjusted for diagnosis, dose and duration of medication use and found a 23% of potentially inappropriate medication use rate using the Zhan criteria (Zhan et al., 2001). In a follow up study, Pugh, Hanlon, Zeber, Bierman, Cornell, and Berlowitz (2006) determined the potentially inappropriate medication use rate using the HEDIS criteria (which excludes estrogen use). In this study, the HEDIS criteria were updated with 22 additional drugs from the 2003 revision of the Beers' criteria. Pugh et al. found 19.6% of patients were exposed to the HEDIS indicator for "always avoid" drugs was similar to the rate found when using the 1997 Beers' criteria helping to support the assertion that PIM remained stable in this population despite updating the criteria to include newer medications.

Zhan et al. did two prevalence studies using the 1997 Beers' criteria as the base for a subset of 33 medications that were vetted by a seven person expert panel to be particularly troublesome when used with elders (Zhan et al., 2001). This version of the Beers' criteria was also used by Simon et al. (2005) to determine the prevalence of

potentially inappropriate medication use in a secondary data analysis of 157,517 health maintenance organization patients. Simon et al. found a 28.8% prevalence rate of potentially inappropriate medication use, which is higher than the PIM rate (21.3%) found by Zhan (2005). Both sets of findings were much higher than the 4.2% PIM rate in the Viswanathan et al. (2005) study examining ambulatory subjects using a modified version of Zhan's revision of the Beers' criteria. However, Viswanathan et al. were not able to use dose or duration parameters due to data limitations.

Other researchers (Curtis et al., 2004; Golden et al., 1999; Fick et al., 2001; Fick et al., 2004; Hanlon et al., 2002; Rigler, Perera, Jachna, Shireman, & Eng, 2004) completed prevalence studies in various settings and also defined potentially inappropriate medication use using the 1997 Beers' criteria without modification. The prevalence rates in these studies varied from 21% to 69.4%. When researchers use the 2003 Beers' criteria, potentially inappropriate medication rates vary from 23% (Pugh et al., 2005) to 77.7% (Franic & Jiang, 2006).

Which medications are evaluated may account for much of this variation. For example, Rigler et al. (2004), using claims data, chose not to include medications that were prescribed less than 50 times per month, while Cannon et al. (2006) chose to evaluate all drugs used, rather than just those prescribed.

Although the MAI and the Beers' criteria are operationalizing the concept of PIM very differently, prevalence rates are very similar with a 23-78% prevalence rate with the Beers' criteria and a 21-82% prevalence rate for the MAI. It appears that no matter the definition for PIM there is wide variation in prevalence of PIM. This variation may be

due to what is counted (all medications, all routes versus just prescribed medications, specific routes), as well as the concept of PIM differing across definitions.

PIM as a Predictor of Adverse Events and Readmission

There have been few predictive studies done using PIM as a predictor for adverse drug events or adverse outcomes such as emergency room use, hospitalization, or death. All of these studies reviewed have been in community settings. All of the researchers used some version of the Beers' criteria as a predictor for these adverse events.

Several studies evaluated PIM as both an outcome and predictor. Fick et al. (2001), using a matched pair analysis of 2,336 elderly Medicare subjects, found that PIM was predicted by the number of providers a patient had and PIM, in turn, predicted costs and utilization (doctor visits as well as emergency room visits). In this study, PIM was defined by the 1997 Beers' criteria (Beers, 1997). Fick, Mion, Beers, and Waller (2008) also found that those with PIM use had 1.5-2 times the risk of higher utilization of health care (inpatient, outpatient, office visits and emergency room use) than those who did not have PIM in their regimen. Rask et al. (2005) also used the 1997 Beers' criteria and compared the outcomes to the Canadian version of the Beers' criteria, the McLeod criteria (McLeod, Huang, Tamblyn, & Gayton, 1997). Rask et al. evaluated 406 elderly patients in manage care and found that those who had PIM had more chronic conditions and were on more drugs than those who did not have PIM. In this study, PIM was not found to be predictive of adverse drug events.

Other studies examined PIM as a predictor of adverse outcomes. Hanlon et al. (2002) compared the Beers' criteria to the Drug Utilization Review measure in the EPESE study described in the prevalence section and found mortality was not

significantly associated with potentially inappropriate medication use as defined by either measure. Functional status decline was not associated with potentially inappropriate medication use when defined by the Beers' criteria, however, when potentially inappropriate medication use was defined by the Drug Utilization Review criteria, it was strongly associated with functional status decline. Hanlon et al. concluded that implicit criteria (Drug Utilization Review or Medication Appropriateness Index) for determining potentially inappropriate medication use were more sensitive to assessing high risk medication regimens than are explicit criteria (Beers' criteria). Zuckerman et al. (2006) also studied functional status decline more indirectly by using nursing home placement as the outcome when studying PIM as a predictor. In 487,383 Medicare enrollees with employer supplemental insurance, Zuckerman et al. used the 2003 Beers' criteria to define PIM and found PIM was associated with a 31% increase in nursing home placement.

Fu et al. used the Medical Expenditures Panel (MEPS) data in two studies to evaluate PIM using the Beers' criteria. In a 2004 study, Fu et al. evaluated the 1996 Medical Expenditures Panel data from 22,601 adults age 65 and older and found PIM to be predictive of reporting poor health status. Fu et al. (2007) used the 2000-2001 MEPS data and evaluated PIM (defined by the 2003 Beers' criteria) to study 720 elders continuously enrolled in five rounds of the Medical Expenditures Panel. Fu et al. found that PIM (prevalence rate of 27.8%) was a significant predictor of health care expenditures and utilization (prescriptions, office visits, emergency room visits) and estimated that PIM was responsible for \$7.2 billion dollars of incremental expenditures in the United States in 2001. Not only was PIM a significant predictor for higher

expenditures and utilization, PIM was associated with higher number of medications being used. Finally, Hustey, Wallis, and Miller (2007), used the 2003 Beers' criteria and examined 352 consecutive admissions to the emergency room. These researchers found that 32% of patients had PIM on admission to the emergency room and 13% of those discharged to home from the emergency room also were given PIM prescriptions.

Conclusions and Gaps in Knowledge Regarding PIM

The literature related to PIM use is less mature than the polypharmacy literature primarily due to the difficulty in determining an operational definition. Competing schools of thought exist regarding how PIM should be defined, what are the appropriate methods to measure PIM, and whether the methods used in studies are measuring the same concept. It is important to choose tools to study potentially inappropriate medication use that accurately reflect the concept, are simple to use, and provide reliable and valid measurement. Few researchers use the full-length MAI, as it is cumbersome to use. However, there is no agreed upon scoring rubric for the Beers' criteria and thus, another gap in the literature is that the Beers' criteria, as well as the simpler three question version of the MAI, remain untested for psychometric properties. The lack of an agreed upon operational definition hinders estimating prevalence rates, costs, and utilization.

Assessing prescribing and medication use practices surrounding potentially inappropriate medications is the heart of medication quality assurance programs. There is a growing body of literature comparing methodology and tools to define PIM in an effort to stabilize the definition of potentially inappropriate medication use. Recent studies are now comparing the Beers' criteria to both the MAI and the Zhan/HEDIS criteria (Hanlon

et al., 2002; Pugh et al, 2005; Raebel et al., 2007; Rask et al., 2005; Schmader et al., 2004; Steinman et al., 2006^a; Viswanathan et al., 2005; Zhan et al., 2005; Zuckerman et al., 2006). As a result, there is movement towards a hybrid type measure which combines implicit and explicit criteria.

Versions of the Beers' criteria (Beers et al., 1991) remain the most widely used tool to determine the use of potentially inappropriate medications both in research studies and in clinical applications (Cannon et al., 2006; Curtis et al., 2004; Fick et al., 2001; Fick et al., 2004; Golden et al., 1999; Green et al., 2007; Pugh et al., 2005; Pugh et al., 2006; Rask et al., 2005; Rigler et al., 2004; Viswanathan et al., 2005; Zhan et al., 2001). Although choice of the Beers' criteria makes sense for comparing studies to one another because of its common usage and long history, the Medication Appropriateness Index is appealing simply because it clearly evaluates *why* a medication is inappropriate and also allows for individual variation. However, databases generally are not yet standardized or linked electronically, so this tool is more problematic when measuring potentially inappropriate medication use especially in epidemiologic studies. These limitations make it unlikely that this measure will be widely adopted in practice by non-pharmacists, as the MAI has not been shown to have a substantial advantage over simpler, explicit criteria such as the Beers' criteria.

There are other significant gaps in the literature regarding PIM, especially in the home health care literature. Although both the MAI and the Beers' criteria reflect differing concepts, the rates of PIM are surprisingly similar. Only two studies in home care deal with PIM, therefore data must be extrapolated from the studies of community dwelling elders. However, alarmingly high prevalence rates have been demonstrated in

HHC settings. This is especially troubling in that home healthcare is specifically used to monitor inappropriate medication use (Madigan et al, 2001; Schwarz, 2000). Estimates of PIM in community dwelling elders range from 21% to 88% depending on the measure used and what medications (prescribed only or all medications) are counted. However, most studies with large sample sizes have established PIM prevalence between 21-29% in the community. Knowing that home health care patients are more likely sicker and more functionally impaired, undoubtedly the rates of PIM in home health care are not reflected in community studies. Since research, policy and reimbursement are based on these findings, the lack of sound estimates is a concerning trend.

Given the age and the existence of multiple diseases in the HHC population, the potential for PIM and subsequent adverse drug events is very high. However, no studies using PIM as a predictor of adverse events exist in HHC. The association has been established between potentially inappropriate medication use and adverse drug events, functional status decline, emergency room use, cost, utilization, and nursing home placement in community dwelling elders (Fick et al., 2001; Fu et al., 2007; Hanlon et al., 2006; Hustey et al., 2007; Rask et al., 2005; Zuckerman et al., 2006). Although Hanlon et al. (2002) studied the influence of PIM on mortality, PIM was not found to be predictive of mortality. Other than Fu's work on inpatient costs, hospital readmission or even hospitalization does not seem to have been an endpoint for studies of inappropriate medication use.

Once again, the lack of knowledge is concerning especially in light of the Fu et al. (2007) findings of the incremental cost of health care expenditures when PIM is present. PIM seems to be an understudied concept in HHC. This is a troubling trend given the

level of comorbidity and the numbers of medications seen in this population, but most especially since nursing services are specifically prescribed to assist with medication management, yet neither the prescriber nor the caregivers are recognizing PIM.

Implications for Research Regarding PIM

It is clear that studies need to be completed not only about the prevalence of PIM in HHC, but also about the influence of PIM on adverse drug events, adverse outcomes, and utilization. In addition, the link between comorbidity and PIM has yet to be established. Therefore, not only will a prevalence rate be determined for PIM in this study, a link between comorbidity and PIM, and between PIM and hospital readmission will be examined.

Predictors of Hospital Readmission: Medication Regimen Complexity

Historical Context of Medication Regimen Complexity

Medication complexity is not a particularly new concept (Conn et al., 1991), but the exact parameters of what composes complexity and how to measure those parameters has caused a number of researchers to mention the concept, but blithely ignore the precise definition. For researchers, the impact of this concept is just beginning to be appreciated since a critical mass of polypharmacy and potentially inappropriate medication use literature demonstrates equivocal findings regarding outcomes such as adherence, cost and adverse outcomes in elders. Clearly the concepts of polypharmacy and PIM alone are not powerful enough to explain the variance seen with adverse drug events or adverse outcomes. In addition, there is an intuitive sense by clinicians that the concepts of polypharmacy and inappropriate medication use may not provide enough explanation for

what is being observed in the clinical setting regarding adverse drug events and subsequent adverse outcomes.

Unlike the other two proposed mediators, polypharmacy or PIM, medication regimen complexity is an active area for qualitative research (Elliott, Ross-Degnan, Adams, Safran, & Soumerai, 2007) and psychometric testing (George et al., 2004; George et al., 2006) indicating the emergence of a new concept. Qualitative researchers have attempted to elucidate how people set up and manage their regimens or make decisions about modifying medication regimens based on the complexity of the medication regimen (Elliot et al., 2007).

The development of the concept of medication complexity is lagging that of polypharmacy and potentially inappropriate medication use. Around the time that the first studies in medication regimen complexity appeared (Conn et al., 1991), implementation of the Drug Utilization Review provision of the Omnibus Budget Reconciliation Act of 1990 also occurred. The idea of inappropriate medications could have been funded more generously due to the focus of government policy on Drug Utilization Review. The lack of literature addressing medication regimen complexity may also be indicative of the difficulty in separating adherence issues from medication regimen complexity, as well as, difficulty in operationalizing medication regimen complexity.

Definition of Medication Regimen Complexity

A sparse evidence base for this concept is not unexpected, as this concept is theorized to be composed of many factors. Medication complexity encompasses the idea that medication regimens are “difficult” for the elder to manage based on their cognitive ability, present disease acuity and unfamiliarity with their regimen (Hayes & Kan, 1999;

Johnson et al., 2005; Maddigan et al., 2003). Medication regimens include the following characteristics: multiple medication doses, changes in dosing regimens, multiple administration times, multiple routes, and unusual preparations such as cutting pills in half or measuring liquids (Conn et al., 1991; George et al., 2004). It is assumed that as difficulty of the regimen increases, the potential for taking too little or too much of a drug increases due to errors in preparation and administration of the drug regimen (Conn et al., 1991, Field et al., 2007). These errors are likely to increase the probability for adverse events and subsequent hospitalization (Field et al., 2007; Johnson et al., 2005).

Medication regimen complexity factors may additionally include, or are moderated by, multiple patient characteristics such as cognitive ability, education, caregiver assistance, and perception of the regimen's simplicity, effectiveness and cost (Conn et al., 1991; George et al., 2004; Sorensen et al., 2005).

Issues in Measuring Medication Regimen Complexity

Medication regimen complexity can be influenced by the environmental context in which medications are taken such as a supervised settings, prescribing by more than one provider, and the lifestyle changes made to accommodate the regimen (George et al., 2004; Johnson, 2002; Johnson et al., 2005; Sorensen et al., 2005; Travis et al., 2007).

Another challenge in measuring this concept is that changes in individual characteristics change the level of risk at any one point, making the assessment of medication regimen complexity a dynamic target (Johnson et al., 2005; Maddigan et al., 2003). Nonetheless, in the existing tools to measure this variable, there is acknowledgement that although variations in the individual's attributes occur, the attributes of the medication regimen can be measured and assessed separately from the

individual's attributes (George et al., 2004). For example, Gurwitz et al. (2003) found most adverse events related to medication use were related to the prescribing and monitoring phase rather than to patient adherence or medication consumption errors.

Operationalizing Medication Regimen Complexity

All studies, in any setting and in any country, were included in this literature review that contained an explicit definition of medication complexity due to the lack of literature in this area. Early studies considered medication complexity as doses x frequency (Conn et al., 1991). However, Conn et al. recognized that patient adherence is influenced by medication factors beyond just the number of medications being consumed. Conn et al. believed multiple factors comprise medication complexity such as number of doses, routes, preparation steps, and variable dosing schedules. Therefore, Conn et al. used a validated ($r = .89$) and reliable instrument in test-re-testing ($r = .80$ to 1.0) tool called the Medication Complexity Index developed by a graduate student (Kelley, 1988, unpublished), The Medication Complexity Index (Kelley, 1988, unpublished) provided a summative score for the number of prescribed regularly scheduled medications (excluding PRN medications), the number of doses per day, additional directions that need to be followed when taking the medication, and the mechanical actions (crushing tablets, mixing powders) needed to prepare the medication regimen for consumption. Maddigan et al. (2003) used a variant of the Medication Complexity Index which provided a summative score for the number of tablets per day taken, the number of daily doses and any additional directions need to take medications successfully, but excluded mechanical actions to prepare the dose of medication (such as measuring liquids or drawing up medications in syringes). It was unclear whether the medications included all

medications or just prescribed medications and whether the medications counted were just regularly dosed medications or included PRN medications. Johnson et al. (2005) also modified the Medication Complexity Index (Kelley, 1988, unpublished) to include total number of medications, frequency, and administration activities.

However, George et al. (2004) alleged that not only was the Medication Complexity Index outdated in dosage forms, but also had inappropriate weightings and a poor design making it difficult for the user to record information. In the redesign of the Medication Complexity Index, George et al. accounted for route, dosing frequency and additional directions which include mechanical actions to prepare the medication, multiple unit dosing (2 tabs, 2 puffs), variable dosing (Coumadin 2 mg Monday through Friday, 3 mg on Saturday and Sunday), specific timing (at 3 p.m.), and alternating dosing (NPH insulin 7 units in a.m., 5 units at bedtime). The revised index, the Medication *Regimen* Complexity Index (MRCI), was found to be valid (Kendall's $W = 0.9$, Spearman's $\rho = 0.9$) when tested on the medication regimens of 134 patients with moderate to severe chronic obstructive pulmonary disease. A team of pharmacy researchers established face, content and criterion validity, while two raters evaluated inter-rater and test/re-test reliability ($r > 0.9$). Convergent (Spearman's $\rho = 0.9$) and divergent validity (Spearman's $\rho = 0.34$) were also confirmed.

Studies Using Medication Regimen Complexity as a Predictor

No studies were found that examined the prevalence of medication regimen complexity in any population in any setting. However, there were a few studies that evaluated medication regimen complexity as a predictor of outcomes such as adherence

or self-management of medications. Most took place in the community setting and will be used to help understand what is happening in the HHC setting.

Conn et al. (1991), in two seminal studies, examined the relationship of medication regimen complexity to adherence. The studies were completed using a prospective cohort of 178 and 98 community dwelling elders respectively. Conn et al. quantitatively evaluated how difficult a medication regimen was to self-administer by evaluating adherence. Adherence, as measured by self-report and pill count, was not related to medication complexity in either study, although the relationship was in the expected direction (Conn et al., 1991).

Hayes and Kan (1999) examined the effect of medication regimen complexity on knowledge of newly prescribed medications in 63 elders discharged from the emergency room in a correlational study. Using the Medication Complexity Index (Kelley, 1988 unpublished), Hayes and Kan found that increased medication complexity, from the addition of the new medications, was significantly associated with less knowledge about the new medications.

As previously described, Maddigan et al. (2003) used the Medication Complexity Index developed by Kelley (1988, unpublished) to study a random sample of 301 hospitalized subjects in a medication self-management program. Maddigan et al. examined the variables associated with the ability to self manage the medication regimen and found that medication regimen complexity was a significant and independent predictor of the ability to self-manage medications. There was also a significant interaction between medication regimen complexity and the score on the Mini Mental Status Exam (MMSE). People with intact cognitive ability were unaffected by medication

regimen complexity, while those with a cognitive deficit were significantly affected by medication complexity.

Johnson et al. (2005) also developed and tested a set of predictors for elders at high risk for adverse medication events using a sample of 111 community dwelling elders in Australia using the Medication Complexity Index (Kelley, 1988, unpublished). Significant factors associated with medication complexity included taking five or more medications per day, 12 or more doses per day, more than one prescriber, availability of caregivers, forgetting to take medications, and compliance. The Medication Complexity Index (Kelley, 1988, unpublished) score was significant for predicting adherence. Johnson et al., unlike George et al., felt that this tool was a good predictor of high risk patients.

George et al., (2006) used the newly designed Medication Regimen Complexity Index tool to evaluate the relationship of medication complexity to adherence in 310 hospitalized subjects at the time of their discharge to the community. Unlike findings from other studies, there was no association between number of medications, complexity of regimens, dosage form or dosing frequency, and non-adherence. George et al. concluded that other factors, such as additional instructions, contributed to non-adherence patterns.

Travis et al. (2007), in a correlational study, used a convenience sample of 154 family caregivers' in the 2004 National Caregivers Study. Travis et al. used the Kelley MCI (1988, unpublished) to define medication complexity. Travis et al. found that caregivers experienced a 34% increase in their hassles score for every 10 point increase

in the Medication Complexity Index score, and using these results, developed the Family Caregiver Medication Administration Hassles Scale.

Conclusions and Gaps in the Literature Regarding Medication Regimen Complexity

Medication regimen complexity was poorly defined in the literature and primarily was discussed in relationship to specific diseases such as diabetes, HIV/AIDS and cancer (Martin et al., 2007), despite the fact that elders are the group most likely to experience this phenomenon on a regular basis. Perhaps the negative findings of Conn et al. (1991) and George et al. (2006) have discouraged researchers from further study of this concept, because few researchers have examined the nature of complex medication regimens and how complexity affects adverse outcomes or adverse drug events.

Similar to the concepts of polypharmacy and PIM, there is little agreement as to its conceptual or operational definition of medication regimen complexity in the few studies that do address this concept directly. Some researchers believe that there are multiple concepts being measured under the umbrella term of “medication regimen complexity”. Therefore, the measure itself is not clean enough to precisely describe the impact of the measure on the particular outcome being studied. The lack of studies, refining the definition and operationalizing the concept, presents a barrier to further study.

Presently, there are few tools to measure this concept. Conn et al., (1991) reported that the Medication Complexity Index (Kelley, 1988, unpublished) is both a reliable and valid measure from which the summary score was developed based on the total medications per day, the frequency of the medications, and administration activities. Although the Medication Complexity Index is reported to be reliable and valid,

psychometric testing has never been published. The design of the Medication Regimen Complexity Index (George et al., 2004) is indeed an improvement over the original Medication Complexity Index (Kelly, 1988, unpublished), however it remains unwieldy to use in clinical practice as well as with large databases due to the number of subscales (three) that need to be completed and the judgment calls involved in calculating a score for each medication. Continued exploration of this area is warranted due to evolving conceptual and operational definition issues. Despite these issues, the Medication Regimen Complexity Index (George et al., 2004) is presently the only validated and reliable non-disease specific measure addressing medication complexity in the published literature. This comprehensive tool measures all the factors found in the literature considered to compose medication complexity, has been found to be valid and reliable (at least in COPD patients) and appears to fit well with the proposed conceptual framework for this study. Given the tool's complexity, it is cumbersome to apply, even in the research setting. Unfortunately, there is no remedy for this problem until new tools are developed, so the Medication Regimen Complexity Index (Appendix D) was the tool chosen to measure medication regimen complexity for use in this study.

Other gaps in knowledge include information on the prevalence of medication regimen complexity in older adults in any setting, but particularly in HHC where the elderly are particularly vulnerable to medication mishaps and adverse drug events due to comorbidity, cognitive deficits, and lack of social support. So far, only a few studies have examined the influence of medication regimen complexity on adherence or medication self-management, but no other outcomes appear to have been studied in the elderly.

Implications for Research Regarding Medication Regimen Complexity

The Medication Regimen Complexity Index (George et al., 2004) has not been tested in a large sample yet. In addition, medication regimen complexity has never been tested as a predictor of adverse drug events or adverse outcomes, such as readmission, with a cohort of older adults in any setting. Comparisons of this concept as a predictor of these events and outcomes has not been tested against other potential medication related predictors. This study will be a contribution to addressing these gaps in the research literature.

Overall Summary and Conclusions

In this chapter, the argument has been built that not only is little known about hospital readmission or readmission from home health care, but the link between the proposed predictors and hospital readmission is not firmly established, especially in home care. Because the proposed predictor variables are conceptually complex and the literature is of relatively recent origin, investigators must use caution in operationalizing these variables because small changes in definitions can change research outcomes in dramatic ways.

By limiting the studies for this review to the United States (medication regimen complexity studies being the exception), it is more difficult to draw conclusions about the trends in studies due to a smaller number of studies overall. In addition, the literature in the field of home health care is generally clinical in nature and only a few studies have been conducted since the implementation of the Balanced Budget Act of 1997, which changed how hospitals are paid and home health care is provided (Kilgore et al., 2009; Smith, Maloy, & Hawkins, 2000; Wilensky, 2000). Although hospital readmission has

been studied, literature about the predictor variables in home health care is almost non-existent. Therefore, when necessary, the review included information from ambulatory settings, with the proviso that researchers would assume that any findings from the community setting are likely to be adversely affected in the HHC setting due to the increased degree of comorbidity likely to be experienced by these patients.

Although there is implicit recognition that risk assessment is important to consider in developing a treatment regimen, the concept of high risk medication regimens appears to be poorly defined and is rarely studied. No studies were found mentioning the construct of high risk medication regimens, although many studies were found mentioning high risk medications, usually in conjunction with list of medications that are considered high risk for either adverse drug reactions or events. A major barrier to studying high risk medications regimens in the elderly is a lack of agreement on what factors or concepts constitute high risk medication regimens (Fu et al., 2007; Maddigan et al., 2003). Thus, this construct is awaiting further refinement.

Medication counting issues continue to plague efforts to accurately assess the prevalence of the predictor variables in the HHC and ambulatory populations. Additionally, few researchers have linked any of these concepts (polypharmacy, PIM, and medication regimen complexity) to adverse outcomes, such as hospital readmission, as an endpoint for the study. A small number of investigators have linked medication related concepts together, mostly in comparing one measure of an operational measure of a concept to another operational measure. Occasionally, a researcher used polypharmacy and PIM as predictors in the same study. No investigators have used all three concepts together as predictive variables and no researchers have examined these concepts as

mediating variables. Only a few studies evaluated the relationship between comorbidity and polypharmacy and/or potentially inappropriate medications, but none evaluated the relationship between comorbidity and medication regimen complexity.

Another vexing issue is how to disentangle the effect of comorbidity from the effects of other covariates, especially medication regimens. The potential for confounding frequently leaves the conclusions drawn from studies open to debate. Yet, few researchers have examined the influence of comorbidity on medication regimens. Nor have many researchers evaluated the influence of comorbidity and medication regimens together on adverse outcomes such as hospital readmission in any setting, but especially in home health care patients (Bero, Lipton, & Bird, 1991; Flaherty et al., 2000; Fu et al., 2007; Johnson & Bootman, 1995; Madigan et al., 2001; Winterstein, Sauer, Hepler, & Poole, 2002).

Nonetheless, it is clear that all of these variables are worthy of study. For this study, a continuous count of all medications will be used to measure polypharmacy, while the Beers' criteria (Fick et al., 2003) will be used to measure potentially inappropriate medications. The Medication Regimen Complexity Index (George et al., 2004) will be used to operationalize medication complexity and the Charlson Comorbidity Index with the Deyo modification (Deyo, et al., 1992) will be used to measure the number of illnesses and illness severity.

In the following chapter, each of these variables described in the literature review will be operationalized and the methodology for the study will be outlined in detail. The analytic frameworks will be developed from the conceptual framework presented in

Chapter 1 and the literature review discussed in this chapter. Chapter 3 will culminate in an analytic plan that purposes to address questions posed in the review of the literature.

CHAPTER III

METHODOLOGY

This chapter focuses on the methodology used in this study. The study design, data sets, and sample are first described. A detailed discussion of the predictor variables, covariates and outcome variable is then presented with supporting rationale for the use of the particular measure. The choice of analytic software is reviewed and rationale for selection is discussed. Finally, the underlying assumptions for the analytic plan and the analytic plan are depicted and described.

Design

Secondary data were utilized to test the predictive potential of comorbidity and high risk medication regimens for re-hospitalization in elderly home health care clients. Analytic strategies included discriminate analysis, factor analysis, correlation analysis, logistic regression, and structural equation modeling (SEM). This study extends the classic Baron and Kenny (1986) mediational design initially using SEM to test two mediation hypotheses. The first hypothesis uses a single latent variable, arbitrarily named high risk medication regimens, as a mediator in the relationship between comorbidity and hospital readmission while the second model tests a multi-mediational approach in the same relationship using indicator variables for high risk medication regimens (polypharmacy, potentially inappropriate medications, and medication regimen complexity). Other potential models arose from the reiterative process of SEM and were also tested in the same fashion as the hypothesized models. In addition to the main predictor variables (comorbidity and high risk medication regimens), other covariates

were chosen based on the literature review and the availability of data, and then included in the model based on bivariate logistic regression results.

The use of secondary data previously collected from home health care agencies only allows for an exploratory, between-subjects design rather than an experimental or quasi-experimental design as no intervention was intended in the natural setting. Because many of the variables were measured either at the beginning or end of the episode of care, it is difficult to determine a causal sequence using multivariate techniques (Polit, 1996). Though no causal relationships can be determined through the multivariate analysis, path analysis or SEM can be used to isolate the contribution of interrelated variables to the dependent variable (Polit, 1996). Therefore, SEM was used to elucidate the effects of the independent variables on the outcome of re-hospitalization and the strength of that effect, as well as, the influence that interrelated variables have on each other (Byrne, 2010; Polit, 1996).

Although a matched pair design was considered, there are sufficient outcome events to allow valid conclusions to be drawn from the SEM. A matched pair design would have been useful in a situation where it is suspected that there will not be enough outcomes to draw valid conclusions. However, the t-test in a matched pair design would be limited to determining whether those who were hospitalized were different from those who were not, rather than how much variance is accounted for by the particular predictors chosen.

*Description of Data Sets**OASIS Record*

The Outcome and Assessment Information Set (OASIS) data set (Shaughnessy et al. 1994; Shaughnessy, Crisler, Schlenker, & Hittle, 1998; University of Colorado, 2010) is used in all Medicare certified home care agencies as documentation for patients in Medicare certified home care agencies. The OASIS-B form has 79 items that are completed within five days of the start of home health care or within 2 days of transitions of care such as hospitalization, institutionalization, discharge or death, although the number of items completed can vary based on the reason for the assessment (CMS, 2006; CMS, 2009b). In addition, the OASIS instrument is completed every 60 days for those patients needing continuing home health care, as well as at discharge where an additional eight items are included describing the circumstances of the discharge from home health care.

The OASIS instrument is the basis for reimbursement and tracking episodes of home health care (CMS, 2001), so accuracy in documentation is generally assumed to be very good. However, the instrument was originally developed specifically for documentation of services provided by the home care agency in order to evaluate home health care outcomes (Shaughnessy et al., 1998).

The OASIS form is a relatively comprehensive assessment tool completed by the home care nurse to track whether emergent care happened anytime during the episode of care, hospitalizations, days to hospitalizations, length of stay, functional status, cognitive status, medication self-management ability, life expectancy, prognosis, wound information, sensory status, behaviors, risk factors, patient support from family and

friends, and living situation as well as specific support services needed (CMS, 2006). In addition, this assessment records 1) two inpatient diagnoses (M0190) treated during the last 14 days (no surgical, E-codes [cause of injury or poisoning codes] or V-codes [classification of factors influencing health status and contact with health care providers other than a disease or injury which may influence present or future care]), 2) four medical diagnoses (M0210) related to the need for a treatment change in the last 14 days (no surgical, E or V codes allowed), 3) the primary diagnosis (M0230) for which the patient is receiving home care (V-codes allowed) and 4) up to five diseases (M0240) or chronic conditions (no surgical codes; V-codes and E-codes allowed) (Advance, 2009; Barrett, Steiner, and Cohen, 2005; CMS, 2006). The reason for admission to home health care might not be a disease or the disease that has the most important effect on the patient's prognosis. The five secondary diagnoses usually serve to support the primary reason for admission to home health care. Therefore, because the number of disease fields is both truncated and focused on admission to home health care, these OASIS items may not present a complete picture of comorbidity. However, as OASIS data is used for billing purposes as well as to track improvement in the patient's condition, it is expected that there will be little overlap in diagnoses, and it is likely that all the fields will be completed. Given that there are 12 fields to complete, a relatively comprehensive view of comorbidity is expected. Madigan and Fortinsky (2004) acknowledged that the OASIS tool has good face and construct validity and found the interrater reliability kappa statistics ranged from .66 to .91 in their testing of the tool.

The OASIS form has been revised a number of times after originally being developed at the University of Colorado, Center for Health Services and Policy Research

in 1995 (Shaughnessy et al., 1998). The version used in this study was the OASIS B-1 implemented in October of 2003.

Medication Record

The medication record contains the prescribed medication regimen augmented by the home health care nurse's observations of what medications are in the patient's home with patient verification of the non-prescribed medication regimen. The medication record is *not* a record of what the client has actually consumed, but rather the "medication regimen plan". Thus, the medication record is free of adherence issues and represents the potential for side effects and interactions in its purest form. Given that one of the primary reasons home health nurses are assigned to patients is for medication management, it is assumed that patients were likely consuming the medications as prescribed in the medication record. However, in this data set, the degree of adherence to the medication regimen is unknown. Further, because the rationale for the prescriptions is not provided, the ability to judge the appropriateness of a regimen is restricted because limited information is given regarding the total number of diseases, the length of time the patient has been on a particular medication, and whether the dosing is appropriate given the total disease constellation. Thus, a judgment of the toxicity of the medication regimen for the particular patient is not possible and inappropriate medications must be determined using a guide that does not take these factors into account.

Variables included on the medication record that were used in constructing the predictor variables include dummy agency and patient identification numbers, names of medications (both generic and brand), route, number of pills or amount of liquids used to provide the dose, the dose of the medication, the frequency of dosing, timing of dosing,

any other special instructions (alternate dose, limited doses, changing amounts, ecetera), as well as the start and stop dates which allowed assignment of the medication to an episode of care. No information exists to support the reliability or validity of these records. However, it is assumed that these records are fairly accurate as this documentation is part of the legal record of a patient's care.

Sample

The sample data were generated from a convenience sample of 15 Medicare-certified home health care agencies using records from all open cases during the calendar year of 2004. These agencies had a variety of owners: ten county agencies, two hospital-based agencies, one for-profit agency and two not-for-profit agencies. The demographic profile of these patients should mirror that of home health care clients in the Midwest as fourteen of the fifteen agencies were located across the Midwest. Eight agencies had over 3000 visits a year (range 3165-24,000 visits/year). An open record included only those patients actually receiving care at the time of the study (N = 3,199). These cases may have carried over as open cases from 2003 into 2004. Patients may also have had their case opened several times during the course of the year. Patients were followed until 12/26/2006 and accumulated 18,067 OASIS records (patients can accumulate multiple records during the episode of care) and more than 80,000 medication records. Given the range in size and types of agencies, the sample drawn from these agencies should reflect the type of patients cared for in Medicare certified agencies in the mid-section of the United States. Conclusions drawn from this sample cannot necessarily be generalized to home health agencies in other sections of the United States. In addition, conclusions are applicable only to Medicare certified agencies. .

It must be recognized that those who are able to go home directly from the hospital without home health care likely either have good social supports in place or are more functionally competent than those who are admitted to home care. It is possible only the hardiest of older adults can remain in their home without supervision or assistance. There may be a systematic bias operating that favors healthier, more functionally competent older adults to go home without services or family support. These patients would not appear in the home health care population at all.

On the other hand, the frailest of older adults are not likely to appear in the home health care population. Those who are frail, either cognitively or physically, may already be living in or discharged to a skilled or assisted living facility. It is also likely that older adults who suffer from cognitive and functional deficits, or have labile diseases not living in an institutionalized setting, are living with family members. Thus, the frailest of our population are not likely to show up in home health care either.

Medicare prospectively pays for home health care in 60 day increments called episodes of care (CMS, 2010d; CMS, 2010c; TriWest Provider Services, n.d.). The episode is a continuous period of time during which the patient received one or more home care visits. The episode of care, as defined by Medicare, starts at the first billable service date and ends either within 60 days or when the patient is discharged from home health care (TriWest Provider Services, n.d.). However, for this study, an episode of care was defined as the number of days of care provided beginning at the start of care assessment date through the date of the discharge summary. Therefore, only those patient episodes of care with at least two OASIS records (“start” or “resumption” of care assessment, and a discharge assessment) and a medication record (N = 2,772) were

eligible for the study. In addition, only episodes of care which indicated that the patient was age 65 and over on January 1, 2004 ($n = 2,277$) were retained for the study.

As the outcome was re-hospitalization, based on the OASIS assessment definition of an inpatient stay, only those episodes of care associated with an inpatient hospital stay in the two weeks prior to initiation of home health care services ($n = 1,229$) were evaluated. Specifically, to be included in the study, subjects' episode of care must indicate a discharge from an inpatient facility (coded as 1 [from hospital] on M0175) and had M0100 coded as 1 (start of care/further visits planned). Some subjects may have had a stay in a transitional care setting in the two weeks between discharge from the hospital and admission to home health care, however as long as those subjects' episodes of care indicated that they entered home health care within two weeks of hospitalization, their records were retained for analysis.

A number of patients in this population could have been hospitalized, but would not be included in the final sample for a number of reasons. Single adults, if not able to care for themselves, are likely not to go home immediately after hospitalization, but instead spend a longer time in a transitional care setting. Also, those who have more chronic diseases such as congestive heart disease, chronic obstructive pulmonary disease, or dementia may need longer rehabilitation stays and thus miss the two week window for being included in the final sample. Lastly, since Medicare pays for 21 days for rehabilitation, it was expected that a number of patients, especially those with surgeries, would likely be excluded from the final sample, due to a longer stay for rehabilitation. Excluding these patients may bias the sample, but including them confounds the findings related to the effect of long term and transitional care received after hospitalization.

Therefore, when a stay in transitional care, skilled nursing facilities, or rehabilitation exceeded two weeks, the subject was not included in the sample.

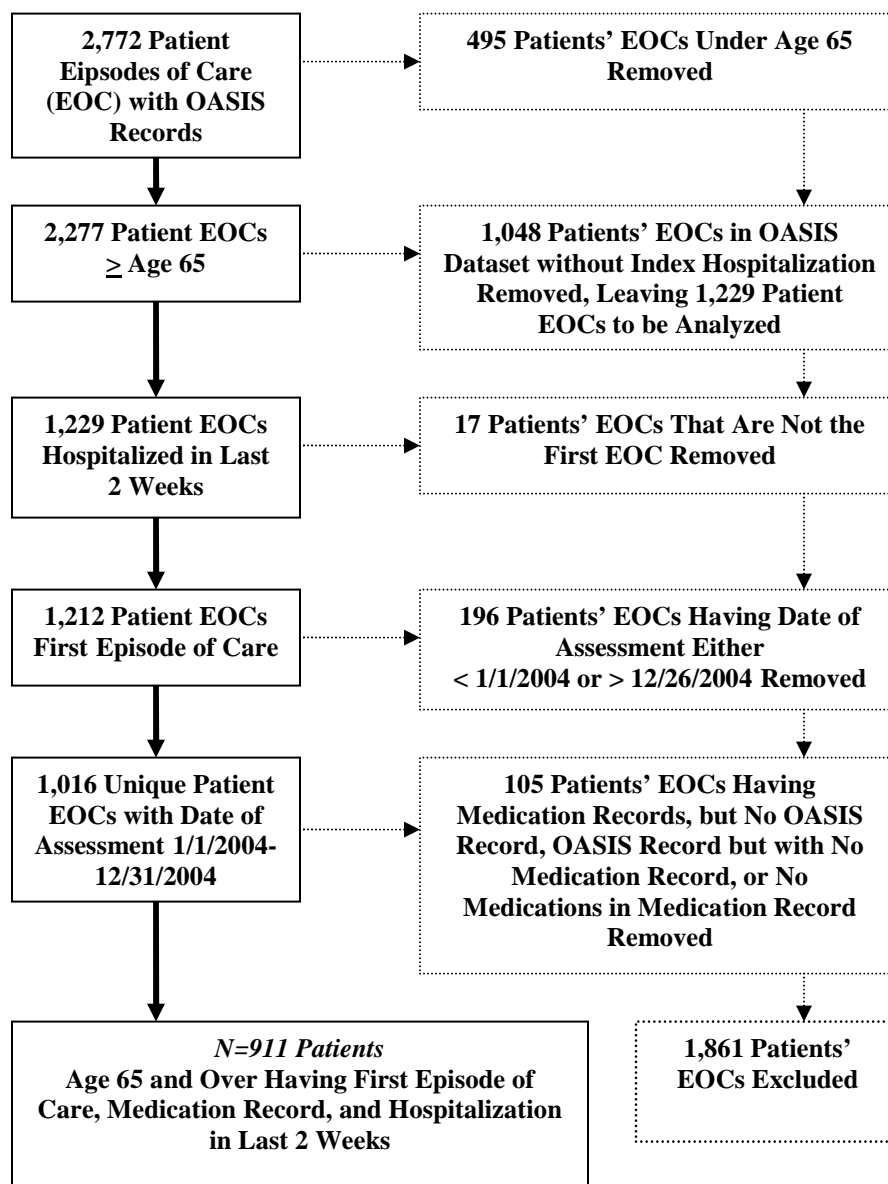
The sample was further refined to include only the first episode of care for the calendar year 2004 (n = 1,212). The first episode of care for this study was defined as the case being opened for the first time in 2004 after an initial inpatient stay and did not include episodes that began as a resumption of care following hospitalization, as these patients would have been in the home health care system continuously for a long time prior to their hospitalization. A resumption of care episode indicates that the patient's record was held open while the patient was in the hospital. A discriminate analysis using a propensity score was done to demonstrate that patients with a resumption of care episode had different characteristics than those who were in their first episode of care.

The last step in working with the OASIS file was to eliminate patient episodes of care that were open prior to January 1, 2004 or did not indicate closure of the episode of care before December 26, 2006 (n = 1016). Those patients with first episodes of care which carried over from 2003 did not meet the inclusion criteria and those that remained open beyond 2006 did not have an associated outcome that could be evaluated.

Finally, the OASIS data set and the medication records for these subjects were merged and episodes of care with incomplete, missing, or invalid medication records were eliminated from the sample (n = 911). At this point the episode of care represents unique patients during one period of time, and therefore, throughout the remainder of the paper will be referred to as subjects or patients. Excluded cases (episodes of care) were: 1) cases where the start of care was prior to 1/1/2004 (coded as M0090 Date of Assessment \leq 1/1/2004) or lasted beyond 12/16/2006, 2) cases opened beyond the first

episode of care (M0100 coded as 1 but showing up as multiple dates of assessment in M0090), 3) patients not age 65 or older during the calendar year of 2004, 4) or patients admitted from the community, transitional care, or nursing homes (M0175 coded as 2, 3, 4, 5 or N/A) without a qualifying hospital stay. In addition, patients who were not taking medications during that episode of care were excluded as well as, patients who did not have two OASIS records indicating a beginning and end date for the episode of care. After applying the inclusion and exclusion criteria, the study sample consisted of 911 patients with both a complete OASIS record and a medication record (Figure 3.1).

Figure 3.1 Inclusion of patients in the study based on their episodes of care.



Variables

Predictor (Independent) Variables

The predictive variables of interest (comorbidity, polypharmacy, inappropriate medications, and medication regimen complexity) are continuous variables at the interval level. Three variables were used to define high risk medication regimens (polypharmacy, inappropriate medications, and medication regimen complexity) and were operationalized consistent with measurement practices and tools discussed in the literature review.

Comorbidity. Conceptually, comorbidity is the interaction of multiple diseases and their severity on a particular outcome beyond the disease being studied (Hall, 2006; Perkins, et al., 2004). As discussed in chapter two, by definition, comorbidity measures exclude the primary diagnosis, although authors have included the primary diagnosis when calculating the summary score in comorbidity measures (D’Hoore, Bouckaert, & Tilquin, 1996; Fried, Bernardini, & Peraino, 2001; Hall, Ramachandran, Narayan, Yani, & Vijayakumar, 2004; Quan et al., 2005). However, Hall (2006), in defining what comorbidity is, and is not, states that “comorbidity is not multimorbidity, which is the coexistence of ≥ 2 diseases in the same patient without identifying an index disease” (p. 850). Authors may, in keeping with the definition of comorbidity, choose not to use the primary diagnosis (Quach et al., 2009; Zhang, Iwashyna, & Christakis, 1999).

The Deyo adaptation (Appendix B) of the Charlson Comorbidity Index (Charlson et al., 2008; Charlson et al., 1987; Deyo et al., 1992) was chosen to operationalize comorbidity because this tool can be used to evaluate data from a secondary source using ICD 9 codes, rather than by patient report or provider judgment (Hall, 2006). It is commonly used to quantify comorbidity, and has been shown to be both reliable and

valid in a number of settings to predict many types of outcomes (Kurichi et al., 2007).

Hall (2006) compared four commonly used comorbidity indices: the Cumulative Illness Rating Scale, the Charlson Comorbidity Index (CCI), the Kaplan-Feinstein Classification, and the Index of Co-existent Disease. Hall found the Charlson Comorbidity Index possesses face and content validity, good interrater and test-retest reliability, and demonstrates excellent predictive validity. The Charlson Comorbidity Index has been used with elders in many settings, but no specific reliability values were found when used in home health care.

The design of the Charlson Comorbidity Index includes the primary diagnosis as one of the diseases scored (Deyo, et al., 1992). The primary diagnosis is the reason for admission to the institution or service. However, as admission to home health care is often based on the rationale for a skilled nursing service or the need for physical therapy, the primary diagnosis may be different than the primary diagnosis used to hospitalize the patient. The primary diagnosis is used to support the reason for admission to home care. Primary diagnoses for home care could include diagnoses such as generalized weakness, deconditioning, or gait instability which support the need for therapy. Primary diagnoses could also support the need for skilled nursing services such as wound care, tube feedings, or diabetic teaching/monitoring, but not be directly related to the primary hospital diagnosis. In addition, some of the primary care diagnoses were planned to be used as a separate predictor, therefore the primary diagnosis in this study was not used in calculating the Charlson Comorbidity Index score.

The Deyo adaptation of Charlson Comorbidity Index, commonly used in research studies, was scored as designed, but excluded the primary diagnosis. A summary score

for 17 diseases listed on the Charlson Comorbidity Index was used to calculate the Charlson Comorbidity Index score. The Deyo modification allows for an age adjusted scoring system, if age is not considered a separate variable. However, in this study, the age adjusted score was not used as age was considered a separate variable.

In the OASIS record, overlap can occur in the fields used to collect the comorbid conditions. Potentially, patients could have up to 11 comorbid conditions. Comorbid conditions chosen to be included in the Charlson Comorbidity Index score were obtained from four OASIS items: secondary diagnoses (five diagnoses from MO240), two inpatient diagnoses in MO190, and four diagnoses from treatment changes (MO210). Only each *unique* comorbid condition included in the OASIS record was used to score the Charlson Comorbidity Index. These raw score weights associated with the diseases listed on the Charlson Comorbidity Index were then summed for each patient. These individual summative scores were then used in the modeling process.

Primary diagnoses were evaluated separately from the Charlson Comorbidity Index (Figures 4.1 and 4.2) using data collected from the OASIS item M0230. Diagnoses for the primary diagnosis item were collapsed into 51 disease categories using a combination of the Clinical Classification Software (AHRQ, 2009, Clinical Classification Software) and expert opinion. If the primary diagnosis appeared in one of the 51 categories, it was coded as a 1 for that category and if the patient did not have the condition, a zero was coded for that category. Only two primary diagnoses were included in the analysis as separate covariates, congestive heart failure and diabetes, as these two categories did not include other disease entities, they are major diagnoses associated with prolonged hospital stays, and there were enough cases to analyze.

A number of issues arise when attempting to use a summative comorbidity score in this particular data set due to both the type of data available and how the sample was defined. Because there is no hospital discharge summary, patients with lengthy active problem lists may not have an accurate comorbidity score due to truncation of the OASIS diagnoses used to determine comorbidity to 11 fields. In addition, only the hardest of frail older adults actually are admitted to home care within the time frame defined for the sample. Elderly who are extremely frail are likely not to be admitted to the hospital in the first place, or are already in long term care or hospice. Neither of these groups is likely to be in the population of home health care patients.

If frail elders are admitted to the hospital and they survive hospitalization, they will likely be admitted to a transitional care, skilled nursing, or rehabilitation unit for longer than two weeks, thus not included in the study sample. This is especially likely to be the case for those with chronic diseases such as congestive heart failure, diabetes with complications, cancers, dementia, and chronic obstructive pulmonary disease. Since the hardest and the frailest elders are less likely to be in home health care, home health care clients are likely to have lower comorbidity scores than the general population. Chronic diseases account for many of the scores on the Charlson Comorbidity Index, are common in the elderly population, and are most probably listed as a primary diagnosis for many home health care patients. Therefore, it is expected that the comorbidity score average in the study sample chosen would be lower than if the primary diagnosis was included or post-hospital timeframe for inclusion in the study were expanded to capture those who were in rehabilitation settings for longer periods of time.

However, if the primary diagnosis were included, the study would be evaluating multi-morbidity rather than comorbidity (Hall, 2006). It was also felt that including the primary diagnosis as part of the comorbidity score would introduce more bias than if the primary diagnosis were excluded in the summative score. A substantial portion of the primary diagnoses are likely related to rehabilitation needs rather than diseases. Counting the primary diagnosis of those subjects with rehabilitation related primary diagnoses would underweight the comorbidity index, but selectively so. Therefore, if bias was introduced due to not using the primary diagnosis, systematic bias affecting all subjects was preferable over introducing a selective bias.

Polypharmacy. Polypharmacy was operationalized as a continuous count of the planned use of all regularly taken medications (whether prescribed or over the counter), via any route, listed in the medication record during the first episode of care. Unlike many other studies, PRN medications (those used as needed) were included in the count as were drugs that have a limited dosing time (antibiotics). Although listed in the medication record, oxygen was not considered a medication, nor was normal saline used as a diluent or a vehicle for IV medication. Combination drugs (Tylenol #3) were counted as one drug, rather than counting the active ingredients as separate drugs. Variably dosed drugs (warfarin), were counted only as one medication. Over-the-counter drugs (Tylenol, Maalox, Dulcolax) that had a regularly scheduled time or dosing schedule attached to the drug were considered prescribed drugs for both this count and for the medication regimen complexity count described below. This decision was based on the rationale that a provider had to intervene to tell the patient the timing and the maximum dosing allowed. In addition, polypharmacy was operationalized as a categorical variable (less than nine

medications = 0; nine or more medications = 1) based on this continuous count.

Polypharmacy counts have not been tested for psychometric properties.

Potentially Inappropriate Medications. The Beers' criteria (Fick et al., 2003) were used in this study to determine potentially inappropriate medications (PIM). These criteria, were developed through a Delphi method (Beers et al., 1991), using expert agreement to determine the level of risk for a particular medication, but there remains a need to determine the predictive ability of this tool. However, there appears to be consensus in the medical community that this tool has face validity (Maloney, 2004).

Although not developed to provide a numerical score, the tool (Appendix C) is useful in identifying the level of risk in medication regimens. Fick et al. (2003) added a new feature in the criteria that gives the potential for adverse reactions as high risk or low risk. According to Fick et al., there are two ways to consider PIM: 1) medications that are inappropriate to use in older adults no matter the diagnosis or condition (Table 1, p. 2719), and 2) consideration of the diagnosis or condition in determining whether a medication is considered inappropriate (Table 2, p. 2721). A consensus panel of 12 experts used a Delphi method to determine medications that were ineffective for use or posed a high potential for adverse reactions in the older adult. Fick et al. then used a five point Likert-like scale to have the experts rank the adverse reactions on a severity scale. Medications that posed a risk of severe adverse outcomes were ranked as having a *high* severity ranking, while those which posed a risk, but the degree of severity was less, were ranked as *low* on the severity ranking.

In the present study, medications identified by Fick et al. (2003) that were considered always inappropriate (Table 1) were given a score of 2.5 if the severity

ranking was high and a score of 2 if the severity ranking was low. For medications in which diseases or conditions were considered (Table 2), those medications ranked as high risk were scored as 1.5, while those medications ranked as low risk were scored as 1.0. Medications listed on both tables were given the highest score listed. Each individual's scores were then summed to provide an aggregate score for each individual's total PIM score. An absolute count of drugs per patient that were listed on the Beers' criteria was also used in the descriptive analysis.

Medication Regimen Complexity. Medication regimen complexity was measured with the Medication Regimen Complexity Index (Appendix D) developed by George et al. (2004). The Medication Regimen Complexity Index maximally leverages the information in the medication record by developing a weighted score in three subscales (route, dosing frequency and additional directions or preparation). The subscale scores are then combined as a summary score. Not only was a summary score used in the analysis, but this variable was also dichotomized using a score of 20 or above as indicating high medication regimen complexity. This cut point value was arbitrarily chosen, as George et al. do not provide guidance at what point regimens are considered complex.

The Medication Regimen Complexity Index was scored as designed using all three subscales. George et al. was able to show both convergent (Spearman's $Rho = 0.9$, $p < .0001$) and discriminate validity (Spearman's $Rho = 0.34$, $p = 0.1$ for age and $p = 0.487$ for gender). Interrater and test-retest reliabilities were greater than or equal to 0.9 for both the total test and the subscale evaluations. Other options found in the literature to

measure this concept use portions of the scale questions in an unweighted fashion and were deemed not to be suitable for this study due to reliability or measurement issues.

Other Continuously Coded Covariates

Age. Age is a continuous variable and was determined from the difference between the OASIS start of care assessment date and the birth date. Once the age was determined, the birth date was deleted from the file. Subjects who were included in the study were at least 65 at the start of the study year (2004). Age was also categorically defined based on the continuous variable and coded as 1 for ages 65 to age 74, coded as 2 for ages 75 to age 84, and coded as 3 for ages 85 and older.

Gender. M0069 was recoded for a gender variable. Males were recoded as 1 in order to be the reference category and females were recoded as 2.

Ethnicity. M0140 was recoded for an ethnicity variable. Any ethnicity other than Caucasian was recoded as 0, and Caucasian recoded as 1.

Episode Length. The episode length variable was constructed from two items on the start of care OASIS assessment, M0090, the date the assessment is completed, and M0906, the date of discharge, transfer or death of the patient from the OASIS discharge assessment. The date of assessment documents the initial visit by home care providers and for this study was considered to be the start of care. Medicare does allow for the OASIS form to be completed over more than one visit, and when that is the case, the last date when the assessment is completed is recorded as the start of care (CMS, 2010b). Ideally, the date of assessment and the date of transfer would be the same when a patient is discharged, transfers or dies, however, it is possible that forms are completed retroactively. Therefore, since the date of assessment might not accurately reflect the

actual transfer date, M0906 was used as the date to calculate the end date for the episode of care. These dates were then used to calculate an episode length in days.

The episode length variable was constructed both as a continuous variable as described above, but also was constructed as a dichotomous variable based on the continuous variable length. The two categories were an episode length of less than 30 days (coded as 1) or an episode length of greater than or equal to 30 days (coded as 0).

Dichotomously Coded Covariates

Functional status (Barnes et al., 2008; Fortinsky et al., 2006; Gillum & Obesisan, 2010; Hasan, et al., 2010; Miller & Weissert, 2001), medication self management (Ellenbecker, Frazier, & Verney, 2004; Madigan, 2007; Rosati & Huang, 2007), cognitive impairment (Panza et al., 2010), comorbidity (Gillum & Obesisan, 2010), depression (Boyle, Porsteinsson, Cui, King, & Lyness, 2010; Bula, Wietlisbach, Bernand, & Yersin, 2001; Panza et al., 2010; Sheeran, Byers, & Bruce, 2010), living arrangements and social support (Muramatsu, Yin, & Hedeker, 2010; Schwarz, 2000), primary caregiver (Li, et al., 2004), wounds (Fortinsky et al., 2006; Rosati & Huang, 2007), ulcers (Fortinsky, et al., 2006; Rosati & Huang, 2007), continence status (Pettersen & Wyller, 2006), urinary tract infection (Rosati & Huang, 2007), risk factors such as smoking or drinking (Gillum & Obesisan, 2010), and life expectancy (Crimmins, Kim, & Seeman, 2009; Joehl, 2005) may all be predictive of adverse drug events, adverse outcomes, and poorer prognosis. Although in the OASIS assessment many of these variables are coded with numerous categories, each of these covariates was recoded in a dichotomous fashion with 0 being the absence of the condition and 1 indicating that the condition is present. For many of the OASIS items, the status in the prior two weeks and the current status are

both recorded. However, only the current status was used, as current status is verified by the clinician, while the prior two week status is subject to recall bias and was not able to be verified. The description and the development of each of the covariates tested are described in the following paragraphs.

Functional Status Measures. Functional status encompasses two areas. The first area is that of providing seven basic areas of care, called activities of daily living (ADLs). The ADLs are: grooming, dressing, bathing, toileting, transferring, ambulation, and eating. The second area is independent activities of daily living (IADLs). These activities require a higher level of cognitive ability to perform them successfully and the loss of function in this area can be an early indicator of dementia (Allaire & Willis, 2006; Barnes et al., 2008; Wadley, Okonkwo, Crowe, & Ross-Meadows, 2008). The IADLs scored on the OASIS assessment include planning and preparing light meals, use of transportation safely, ability to do own laundry, housekeeping/cleaning tasks, shopping, handling finances, and the ability to use the telephone.

In the original data, item MO380 details the type of primary caregiving help needed for each patient. The items for this variable include ADL help, IADL help, environmental support, psychosocial support, advocacy help, financial agency help, and health care agency. Each of these items, if checked as needing help in the particular area in the original data, were scored as one, meaning the patient received help in this area or a zero, meaning the patient was independent in this area. Both the ADL and IADL variables were retained with their original coding as measures of functional status.

Consideration was given to a summative score and using the specific category (e.g. for example help with bathing or mobility) information for each ADL or IADL

(M0640-M0800), but the ADL and IADL individual items did not have a 1:1 correspondence to any of the presently validated tools in use. The categories on the OASIS items for functional status often overlapped and discrimination of the type of help needed was so fine that a constructed summative score on the need for ADL or IADL help would have undue influence on the outcome. Therefore, dichotomous scoring of these two variables was used.

Medication self-management is an important skill not typically measured in IADLs but which has been found to be a predictor of hospitalization in other studies (Kuzuya et al., 2008; Madigan, 2007). The OASIS assessment allows for determining medication self-management. For this study, only management of oral medications (M0780) was considered as a separate covariate. Intravenous medication routes and injectable medications were captured in the Medication Regimen Complexity Index score (discussed later). If the subject is able to set up their medications and take medications independently at the proper dosage and time, they were coded as a 0 and considered independent. All other levels of dependence for this question, people with no oral medications prescribed, or the level of independence was unknown, if checked on the original data, were collapsed and recoded as a 1.

Finally, cognitive impairment was determined from OASIS item M0560; if the first category (alert, oriented, able to focus and shift attention, comprehends and recalls task directions independently) was checked in the original data, this item was scored as a 0, and the patient was considered as having no impairment. Any other category checked on this OASIS variable was recoded as a 1 indicating that the patient had some level of cognitive impairment.

Problematic Behaviors. A number of predictors were chosen to be evaluated in this realm. Disruptive behaviors demonstrated at least weekly (M0610) included memory deficits, impaired decision making, verbal disruption, physical aggression, socially inappropriate behaviors, and delusional/paranoid behaviors. Clinicians could mark more than one category in this OASIS item. Two items were chosen as potential predictors, memory deficit and impaired decision-making. Memory deficit includes the failure to recognize familiar persons/places, the inability to recall events of the past 24 hours, or significant enough memory loss to require supervision. Impaired decision-making includes failure to perform usual ADLs or IADLs, inability to appropriately stop activities, or jeopardizing safety through one's actions. If in the original data set, these items were checked, the item was then coded as a 1. If the item was not checked, the subject was considered not to have a deficit in that area and was coded as 0. The original coding for these items was retained for the analysis.

Depression has also been associated with a poor prognosis (Boyle et al., 2010; Bula et al., 2001; Panza et al., 2010). Depressive feelings that are reported or observed (M0590) were also coded in a similar fashion. Categories for this item included depressed mood, sense of failure or reproach, hopelessness, recurrent thoughts of death, or thoughts of suicide. In the original data, if any of these items were checked, the item was coded as 1, indicating the feeling was reported by the patient or observed in the patient by others. If the item was not checked, it was coded as 0, indicating that the feeling was not reported or observed. These categories were then collapsed to yield a recoded variable of 1 if any depressive feelings were observed or reported, or a 0 if these feelings were not observed or reported.

Lastly, risk factors (MO290) such as heavy smoking, obesity, alcohol dependency or drug dependency were treated in a similar fashion as depression. If the individual risk factor was checked on the OASIS variable, the item was coded as a 1, indicating the patient engaged in this behavior. If the item was not checked, it was coded as a 0, indicating that the patient was presumed not to be engaging in this behavior. A variable was then developed by collapsing these items into a single score indicating the subject engaged in the risky behavior (coded as 1) or was presumed not to engage in the behavior (coded as 0).

Patient Support Measures. Those living with others are more likely to be re-hospitalized than those living alone (Jacob & Politek, 2008; Landia et al., 2004). OASIS item M0340 was used to test this theory. If this item was originally coded as 1 (lives alone), it was re-coded as a 1. All other codes (2-6) were recoded as a 0 indicating that the subject did not live alone. For the descriptive analysis, this item was also categorized for study using living alone as the reference category (coded as 1) and all other categories if checked coded as follows: living with spouse or significant (coded as 2), living with other family member (coded as 3), living with a friend (coded as 4), and living with paid help (coded as 5), and living with spouse and children (coded as 6). Although the last category in the OASIS form is living situations that did not include the above, since no patients had this category checked, the code for option six was changed to a collapsed category for patients who had checked both living with spouse and living with other family members.

The need for caregiving assistance (M0360) was also assessed to determine whether this item is associated with re-hospitalization. This item has seven potential

mutually exclusive categories that could be checked listing the types of people who would be taking the lead responsibility for caregiving including 1) no one person, 2) spouse or significant other, 3) daughter or son, 4) other family member, 5) friend, neighbor, community member or church member, 6) paid help, and 7) unknown. The unknown category was dropped as a variable, and the remaining categories were recoded as 1 through 6. If no corresponding items were checked, it was presumed that the patient was independent in care and this situation was coded as a 0.

A number of other covariates, including continence status (Anaphalen & Gibson, 2008), the presence of surgical wounds (Fortinsky et al., 2006; Rosati & Huang, 2007) or pressure ulcers (Fortinsky, et al., 2006; Rosati & Huang, 2007) have variously been suggested as predictors of hospitalization or poor outcomes. The urinary continence status is assessed by item M0520 on this version of the OASIS. If the original coding was 0, meaning the patient was continent, anuric or had a urostomy for urinary drainage, the subject was re-coded as 0 indicating the subject was continent. If the subject was coded a 1 (incontinent) or two (requiring a urinary catheter), the item was re-coded as 1.

The presence of a surgical wound could suggest a faster recovery and fewer re-hospitalization episodes as patients who are deemed surgical candidates are generally robust enough to undergo surgery. Those who are the most debilitated are more likely to be treated medically or considered for palliative care. OASIS item M0482 assesses the presence of surgical wounds with a 0 indicating no surgical wound, and a 1 indicating the presence of a surgical wound.

On the other hand, the presence of a pressure ulcer may be predictive of a poorer prognosis and/or outcomes. Patients with pressure ulcers are generally less mobile for a

variety of reasons and have poorer circulation and nutrition. Therefore, the OASIS item M0445, the presence of a pressure ulcer, was coded as originally appeared on the OASIS form, with 0 indicating the absence of a pressure ulcer and 1 indicating a pressure ulcer was present.

Diseases. Two disease categories, congestive heart failure and diabetes, have been shown to be associated with higher utilization, including admission to the hospital (Anderson et al., 1996; Holtzman et al., 1998; Li et al., 2004; Rosati & Huang, 2007). When the ICD-9 codes were collapsed into fewer meaningful categories for the primary diagnosis, many of the disease categories contained multiple types of diseases in order to have enough cases to analyze. However, the data collected for these two primary diagnoses categories (congestive heart failure and diabetes) were free of other diseases, making these constructed categories useful for analysis. For each disease, if the patient had the disease, they were coded as 1, and 0 was used for lack of the disease.

Life Expectancy. The final item used as a predictive covariate was item M0280, life expectancy. This item was coded as it appears on the OASIS assessment form, with 0 being a life expectancy longer than 6 months and 1 being a life expectancy shorter than six months.

The Outcome (Dependent) Variable

Re-hospitalization. The outcome variable, re-hospitalization, rather than first hospitalization, was chosen as the outcome variable as this is a persistent and costly problem that home health care is intended to prevent. Consideration was given to using adverse events as the outcome variable, but the data were incomplete and less reliably collected for this variable.

Re-hospitalization was scored as a 1 if OASIS item M0100 number 6 or 7 (discharge to an inpatient facility) is checked on the discharge record and item MO855 is scored as a 1. All other options checked for this item were scored as a 0 meaning that the patient was discharged to someplace other than the hospital. Consideration was given to an outcome of time to discharge rather than a dichotomous outcome of discharge to the hospital versus discharge to any other venue. However, the research interest was in whether high risk medication regimens were an independent predictor of the outcome. Without disentangling the effect of comorbidity and high risk medication regimens, predicting time to outcome could be confounded by the effect of comorbidity.

Analytic Software

After preparation of the individual data sets, the medication record data set and pertinent variables from the OASIS data set were merged to form the analytic data file. Prior to merging, records were checked for completeness and accuracy in Excel file versions of each data set. The databases were then converted to Predictive Analytics SoftWare/ Statistical Package for Social Sciences (PASW/SPSS) files and the files merged to form the analytic file. PASW/SPSS, version 18 Grad Pack (2009) was used to analyze the data. Analysis of Moment Structures (AMOS), Version 18, was the statistical package used to develop the SEM.

Analytic Plan

Introduction

In this section, the analytic plan will be reviewed in detail. First, a discussion of the mediation hypotheses will be presented followed by a discussion of the assumptions underlying the chosen analytic techniques. Next, the structural equation model will be specified. A detailed analytic plan, focusing on each aim and the associated research questions suggested by the attainment of the aim, is then presented. Finally, this chapter concludes with a discussion of the ethical issues in this study.

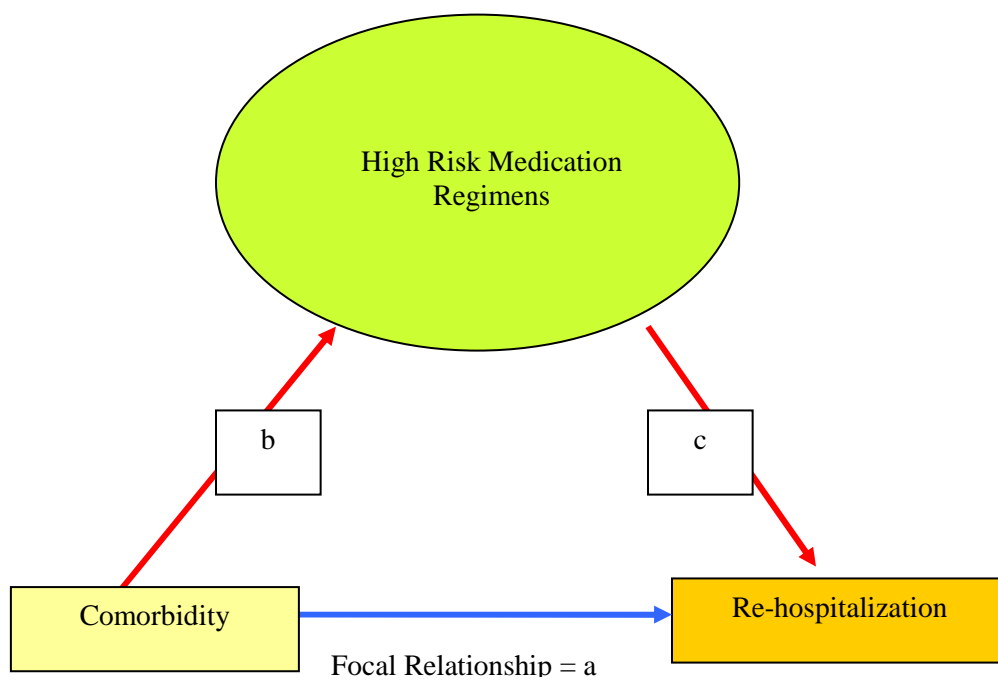
Choosing the Analytic Techniques

The focal relationship (Aneshensel, 2002) tested was the relationship between comorbidity and re-hospitalization, examining the hypothesis that with increased comorbidity, the odds of re-hospitalization would increase. Comorbidity has been most associated with the likelihood of hospitalization and readmission and thus was chosen as the main predictor variable for the focal relationship (Aneshensel, 2002). Other fixed factors such as age, gender, cognitive impairment, social support, episode length, and functional status were included as covariates and tested for moderating influences on the focal relationship and the mediating relationships.

However, a latent variable, high risk medication regimens, composed of some combination of polypharmacy, inappropriate medication use and medication regimen complexity, is believed to exert a mediating influence on this relationship (Figure 3.2). If the mediating relationship exists, Baron and Kenny (1986) state that the significance of the focal relationship should be extinguished. It is now recognized that partial mediation exists when the focal relationship is diminished, but not entirely extinguished when the

mediating variable is considered (Kenny, 2009, Mediation). Determining whether there is a mediation relationship between the predictors and the outcome variables is complicated by the fact that the proposed mediator is a latent variable i.e. not directly observed.

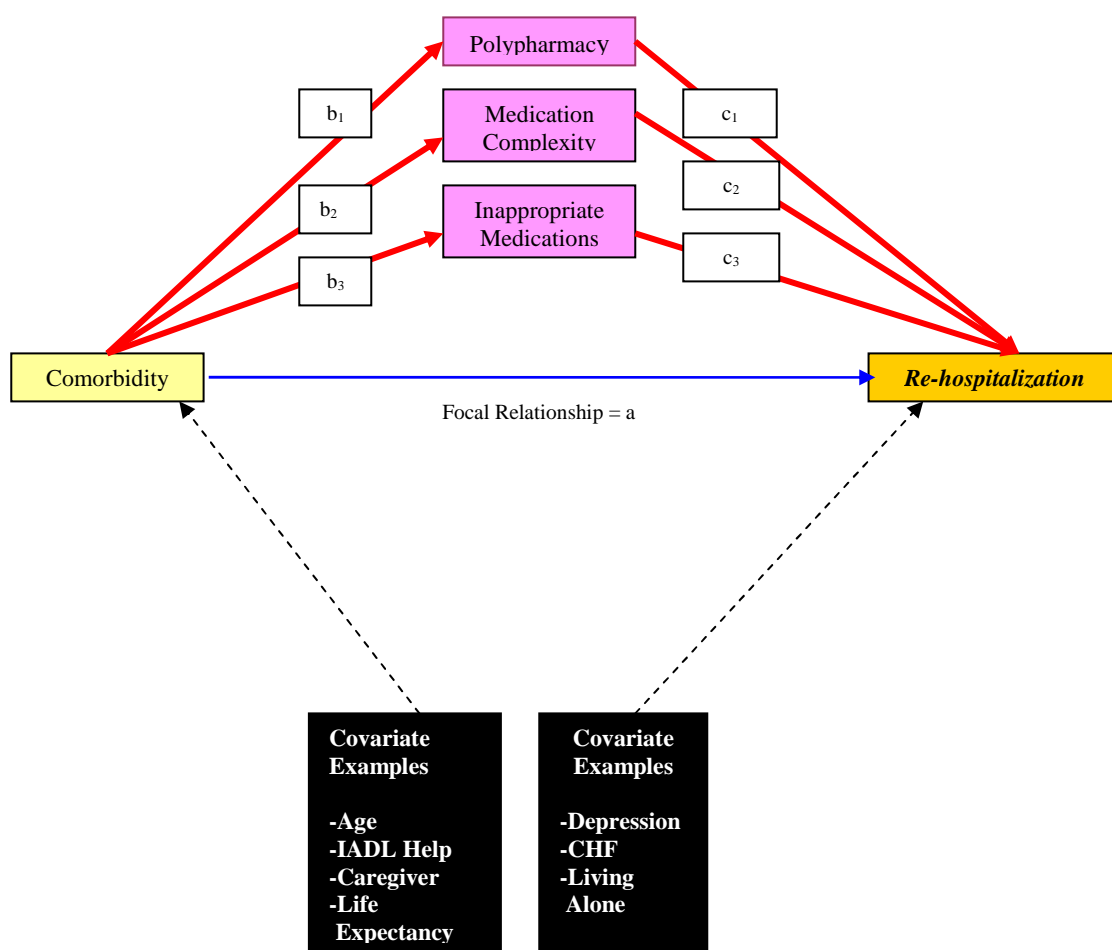
Figure 3.2. The conceptualization of the analytic framework.



Mediation differs from moderation in that when mediation occurs, a variable is inserted into the pathway of the focal relationship that is related to both the predictor variable and the outcome variable. In full mediation, the causal pathway is in essence shifted to the indirect path i.e. the direct path is extinguished and the effect on the outcome variable is displayed through the mediating variable. In partial mediation, the effect occurs through both pathways, but the strength of the direct path (the focal relationship) is lessened. In moderation, on the other hand, the effect of the moderating variable is on the focal relationship. The effect of the predictor on the outcome changes with varying levels of the moderating variables. Moderators typically weaken the effect of the predictor variable on the outcome, but can increase the effect, or even reverse the effect of the predictor on the outcome (Kenny, 2009, Moderator Variables).

Two problems exist when considering a classic mediation model as the analytic framework for this study. The first issue is the relationship that the observed mediating variables (polypharmacy, inappropriate medications and medication complexity) have to high risk medication regimens and also to the outcome variable, re-hospitalization. Each factor has to be tested individually, in addition to be tested in combination, for the presence of a mediating relationship (Figure 3.3). Usually, classic mediation analysis using multiple regression is done on just one variable at a time. Using multiple variables as mediators while analyzing the mediating hypothesis with a multiple regression technique is a new area of statistics and is still being developed (MacKinnon, 2008). In addition, the predictor variables, although treated as continuous variables, do not meet the assumptions of multiple regression (normal distribution, linear relationship) making it difficult to obtain an accurate solution in the analysis when using multivariate techniques.

Figure 3.3. A proposed multivariate analytic model.



MacKinnon (2008) provides guidance as to how to solve for a multi-mediational model using multivariate analysis with variables that meet the assumptions for multiple regression. However, few authors have considered this model when the outcome variable is dichotomous because logistic regression techniques must be used with dichotomous outcomes. Therefore, an analytic technique such as SEM is used in order to accommodate non-normal data, non-linear relationships and dichotomous outcomes.

The second issue is accounting for the latent variable, high risk medication regimens. At the initiation of this study, the factors composing high risk medications were unknown as this concept is poorly defined in the literature. Given the conceptual model, it also was expected that both inappropriate medications and medication regimen complexity would either be co-linear or perhaps share a sub-mediating pathway with polypharmacy (Figure 3.4), as increasing polypharmacy levels are likely to increase the likelihood of either increased complexity or inappropriate medication use occurring. Multivariate techniques do not allow for the exploration of the relationships that are poorly defined. Therefore, based on MacKinnon's work (2008), path analysis for a latent variable mediation model i.e. structural equation modeling (SEM) was chosen as the appropriate technique for the analysis (Figure 3.5).

Figure 3.4. Analytic framework with polypharmacy functioning as a possible mediating variable in the relationship between comorbidity and medication complexity and inappropriate medication use.

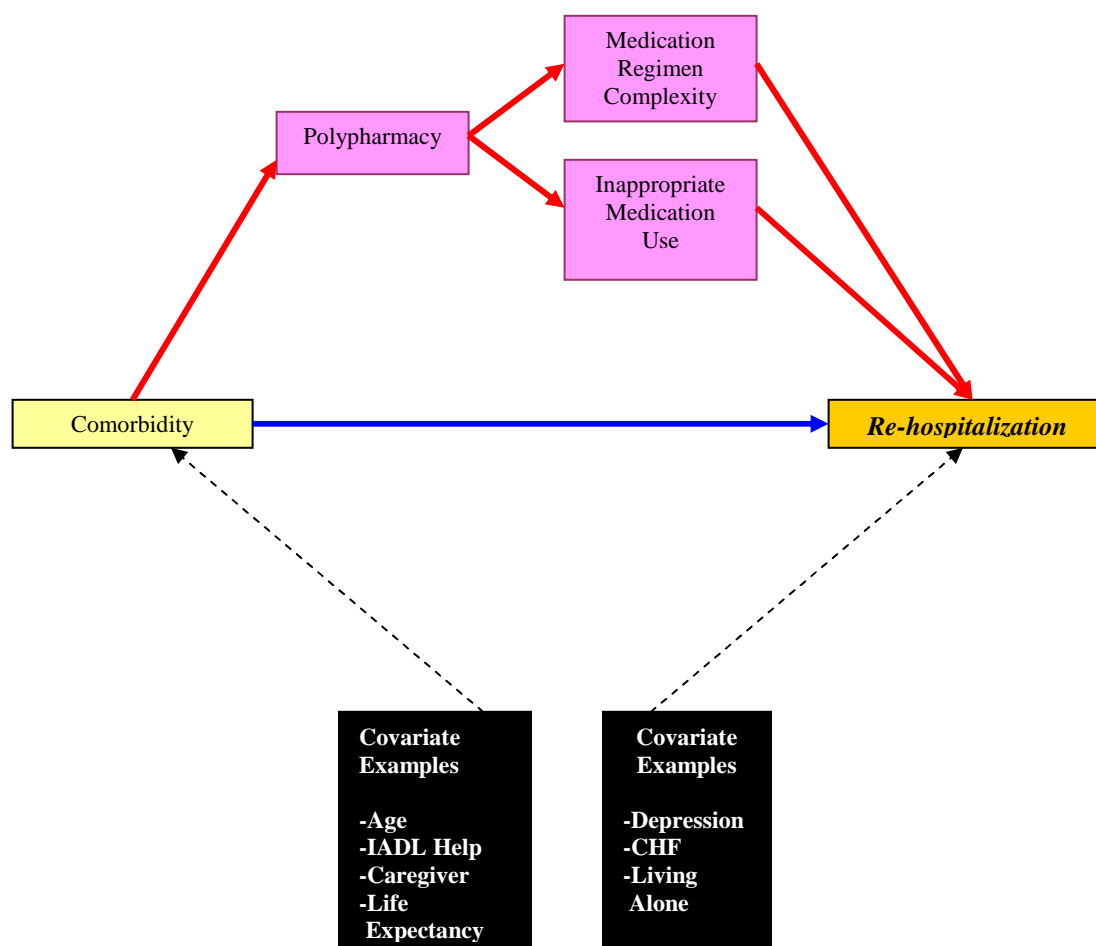
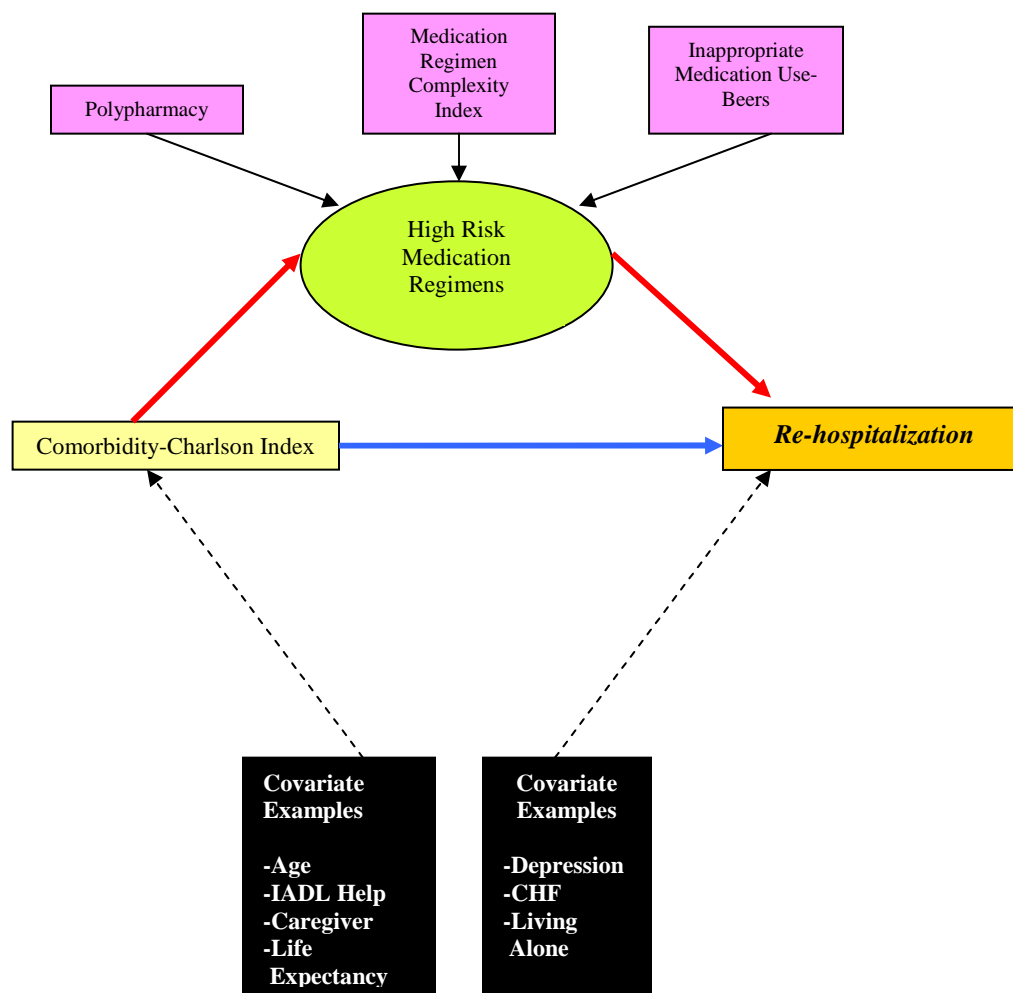


Figure 3.5. Proposed path diagram with focal relationship in blue and the mediating relationship shown in red.



Assumptions Underlying the Analytic Techniques

Path analysis modeling and structural equation modeling (SEM) are based on two primary techniques, linear regression and logistic regression. Because path analysis is based on solving simultaneously a series of regression equations with similar assumptions, in general, assumptions for linear regression must be met when using path analysis. Linear regression included the following assumptions: 1) the variables are related in a linear fashion, 2) homoscedasticity (equal variances around the regression line), 3) variables are interval level or can be treated as interval level variables, 4) outliers are not included in the analysis, 5) the data are continuous (not truncated), 6) the data are normally distributed, and 7) all variables are tested in the model (Garson, 2009a). If data are related in a non-linear fashion, using linear regression will underestimate the beta weights, however minor violations of this assumption are tolerable (Garson, 2009a). Regression is relatively robust to violations of homoscedasticity, as well as truncated data, but the researcher must use caution in interpreting the results in both situations (Garson, 2009b).

For path modeling, the model must be recursive, i.e. the causal flow is one direction (Polit, 1996; Garson, 2008). In addition, assumptions for linear regression should be met (Polit, 1996). In particular, 1) variables should have a linear relationship or should be transformed if non-normally distributed, 2) there should be an appropriately sized sample (10-20 cases for each variable), 3) there should be low co-linearity between variables, and 4) the sample cannot have missing values for the variables (Garson, 2008).

A critical assumption, which when violated invalidates the path analysis, is that the *disturbance* or *residual error* terms are applied only to one variable. This is because

disturbance terms represent not only variance due to variables that have not been included in the model, but also measurement error from the particular observed variable (Garson, 2008). Finally, variables should be measured without error (Polit, 1996) and residuals should not be correlated with other residuals (Polit, 1996; Garson, 2008) or with more than one variable (Garson, 2008).

Strictly speaking, path analysis is completed with observed variables; when one or more latent variables are included in the model, the more powerful SEM modeling is used. Fortunately, SEM is robust to many of the assumptions underlying path analysis and can be used in situations when there are non-linear regressions, non-recursive models or correlated variables, measurement error, or error terms (Polit, 1996; Garson, 2009b). SEM uses regression equations to evaluate how well two proposed models “fit” the existing correlation matrix of multiple prediction variables (Garson, 2008, Path Analysis).

The strength of SEM is modeling complex relationships among various predictor variables and pathways that can be modeled (Garson, 2009b). In SEM, each variable is both a predictor and outcome in order to assess the influence of one variable on another variable and then simultaneously linking the regression equations together (Garson, 2009b). Therefore, the beta weights predicted in the model are susceptible to change if the position of a variable is changed in the model or additional variables are added to the model (Garson, 2009b). In addition, a summative factor analysis needs to be completed to assess which factors compose the latent variable. SEM, using a two step process allowing for both confirmatory factor analysis for the latent variables, as well as, the model fitting process, is the ideal vehicle for this type of analysis (Garson, 2009b; Byrne, 2010).

Although a normal distribution of indicator and latent variables is desirable, most SEM programs have methods that can handle non-normal distributions of these variables, such as the bootstrapping program in AMOS (Garson, 2009b). In addition, SEM can model categorical data, multi-collinearity among variables and correlated error terms (Garson, 2009b).

A final consideration is interpreting the meaning of a dichotomous outcome used in a path analysis. Not all statistical packages have a logit link function that allows the researcher to model the probability of an outcome as a latent model and then link the probability to the outcome such that variability in the outcome is accounted for by the predictor variables (Garson, 2009b). A number of programs are available for SEM that include the logit link function including MPlus, EQS, LISREL, and AMOS. Linear structural equations analysis (LISREL), distributed by SPSS, is the oldest of these programs and is found most often in the psychological and sociological literature (Garson, 2009b). Both MPlus and AMOS can accomplish the same tasks but have powerful graphics. AMOS contains an interface with the SPSS statistical package used to analyze the data (Garson, 2009b; Byrne, 2010), so therefore was chosen as the program to accomplish the structural equation modeling.

Specifying the Model

Three SEM models were developed. The first model was Figure 3.3 in which the proposed mediating variables each exert their influence on the outcome of hospitalization. A second model (Figure 3.4) retains the individual medication variables. However, polypharmacy was conjectured to be related to inappropriate medication use and medication regimen complexity in a mediating fashion. This sub-mediating

relationship occurred because as polypharmacy levels increased, the odds of both inappropriate medication use and medications regimen complexity both increased. Although the potential for co-linearity between medication regimen complexity and potentially inappropriate medications exists, based on previous studies these variables appear to measure entirely different concepts. Thus, in this analytic model, polypharmacy was expected to function both as a predictor variable for medication complexity and inappropriate medication use and also as a mediating variable for the mediating hypothesis. Although not a strictly collinear relationship, this pathway explains the relationship between the three observed mediating variables.

When the observed mediating variables (polypharmacy, potentially inappropriate medications and medication regimen complexity) are treated as indicator variables for the latent variable, high risk medication regimens, a far more satisfactory and likely more accurate model, is developed because the indicator variables each have their own measurement error. Therefore, the analytic model in Figure 3.5 was also chosen to be tested.

Although presently not recursive models, there are many influences on re-hospitalization. Indicator variables (the proposed mediators) for the latent variable are shown as purple boxes, the latent variable (high risk medication regimens) as a green oval, other covariates as in the black box, the main predictor variable (comorbidity) as a yellow box, and the outcome variable in an orange box. The focal relationship tested in the mediating model is shown with a blue arrow. The proposed mediating pathway is depicted with red arrows. It is possible that variables such as age, cognitive status, functional status, and support may moderate the focal relationship causing the focal

relationship to vary over different levels of these variables (Kenny, 2009, Moderator Variables). However, these variables are designated as covariates in the model because the precise nature of their influence was not initially known. Covariates could also be placed to influence re-hospitalization as well as the indicator variables. Adherence may also influence comorbidity, the type and number of medications prescribed, and re-hospitalization. However, studying the influence of this latent adherence variable on the outcome as well as the predictors was outside the scope of this study.

Analytic Plan

In this section, an overview of the tasks to be accomplished through the analysis will be discussed. Next, a short discussion of the data preparation ensues, followed by a discussion of the preliminary data analysis and potential violations of underlying assumptions that might cause the analysis to be inaccurate. Finally, the detailed analytic plan and statistical tests for each aim and associated research questions generated by the aim will be offered (Table 3.1). This chapter ends with a discussion about missing data and Institutional Review Board (IRB) considerations.

Steps in the Analysis

This analysis takes place in a series of steps culminating in the choice of a predictive model. The steps include: 1) determining whether underlying assumptions for regression modeling were met, 2) determining the degree of co-linearity existing between the independent variables, 3) assessing whether a focal relationship exists between comorbidity and hospitalization, 4) assessing which covariates are related to the predictor variables, 5) evaluating which covariates directly influence re-hospitalization, 6) examining which variables actually represent high risk medication regimens, 7) assessing

whether high risk medication regimens actually influence re-hospitalization rates, 8) determining how much variance in the outcome is accounted for by the predictors and the covariates, and 9) examining whether the focal relationship is either extinguished or reduced with the mediating variable included in the model.

Preparing the Data for Analysis

Initially, personal identifiers were stripped from both data sets. Both the medication record and the OASIS record were then examined to assess the level of incomplete records and errors in the data. For the medication record, an analytic plan was developed with the assistance of Dr. Stephen Schondelmeyer, University of Minnesota, School of Pharmacy. Dr. John Holmes, University of Pennsylvania Medical School, helped develop the analytic plan for the OASIS data. Dr. Jihoon Ryoo, University of Minnesota, assisted with developing the analytic plan for the study after consultation with Dr. Melanie Wall, University of Minnesota, School of Public Health, Dr. Robert delMas, University of Minnesota, College of Education and Human Development, and Dr. Joseph Gaugler, University of Minnesota, School of Nursing.

Medications were coded as generic preparations and evaluated for errors in spelling of compounds, routes or dosages. Data such as disease codes were collapsed into categories for analysis and variables were re-coded in both data sets for analysis. Subjects without both a medication record and two OASIS records were dropped from the data analysis. Dummy identifiers were developed prior to merging the two data sets. Very few data points were missing, so no imputation was necessary. Outliers were examined once the data sets were merged.

Examining the Data for Violations of Underlying Assumptions

Before any analysis occurred, the question of whether there was a difference between those patients coded as a 1 for reason for assessment (start of care) and those coded as a 3 (resumption of care) on item MO100, was answered using discriminate function analysis and developing a propensity score model. Essentially, this step determined the composition of the sample used for analysis. According to Howell (2007), this type of analysis is used to distinguish if two groups are different from each other. It is based on logistic regression techniques, but the resulting probabilities are then compared in an ANOVA test to see if the groups differ in their characteristics. When the ANOVA test statistic shows a difference between the groups, the researcher is justified in treating the groups as different samples because their characteristics differ. This assumes that the propensity analysis is powered correctly with an appropriate sample size and alpha level in order to detect significant differences. In this analysis, the descriptive data from the recently hospitalized first episode group (episode type 1) were compared to the group that had resumption of care (episode type 3) to ensure that these two groups were comprised of subjects who differed on the parameters in question.

Once the sample was chosen, underlying assumptions for the various analytic techniques were assessed by examining the distributions of the variables. Keeping in mind that logistic regression procedures are robust to most violations of linear regression assumptions (Howell, 2007), histograms (dichotomous variables) and frequency curves (continuous variables), as well as skewness and kurtosis statistics were used to assess the normality assumption. Residual plots were assessed for violations of the homogeneity, homoscedasticity, and independence assumptions. Finally, since the models were

developed using a series of regression equations, the assumption that the variables are linearly related were assessed by monitoring scatter plots of Y on X for non-random patterns. If violations of these assumptions occur, when appropriate, variables were transformed.

Initially, descriptive statistics included determining rates of re-hospitalization, social support, cognitive and functional impairments. In addition, means for age, comorbidity scores, number of medications and inappropriate medication used, complexity scores, and length of service in HHC were calculated. Re-hospitalized patients were compared to those who were not re-hospitalized on characteristics pertinent to the analysis. Once these steps were accomplished, the primary analysis could be done.

Analytic Questions to Be Answered

There were five major tasks this analysis was designed to accomplish:

1. Describing the first episode home health care population and the medication use patterns associated with initial care and evaluating whether these patients are different from home health care patients who are not in their first episode of care through both the use of descriptive statistics and discriminate analysis.
2. Determining which medication related variables compose high risk medication regimens.
3. Determining which variables should be included in the SEM analysis.
4. Evaluating the influence of the predictors on the outcome variable through SEM.
5. Evaluating the proposed mediational model.

Linking Aims to the Analytic Plan

Aim 1. To describe the medication regimens of older adult home health care clients in terms of polypharmacy, potentially inappropriate medication use, and medication regimen complexity.

The first research question generated by examining this aim, “What are medication regimens patterns in home health care (HHC) patients?” was answered through the use of descriptive statistics such as the mean and frequency distributions. Histograms and frequency distributions, as well as skewness and kurtosis calculations were used to evaluate the underlying assumptions for later modeling.

Aim 2. To determine what combination of factors (polypharmacy, potentially inappropriate medications, medication regimen complexity) compose the concept of high risk medication regimens.

Polypharmacy (PP), potentially inappropriate medications (PIM) and medication regimen complexity (MRC) have been studied as components of high risk medication regimens in other settings and with other populations. Prior to testing whether they are indeed components of high risk medication regimens, it was important to first ascertain whether these concepts are overlapping concepts. Correlation matrices were studied to determine how much variance these concepts share.

After examining the correlation matrices, a simple factor analysis was performed to determine whether high risk medication regimens are composed of one, two or three of the proposed mediational variables. Previously, authors have mentioned high risk medication regimens as a factor related to hospital readmission, however, investigators

do not define or test this particular factor. For this study, both the individual medication variables were tested, as well as a model including high risk medication regimens, as it was hypothesized that the latent variable will likely be more predictive than any individual medication variable and likely more predictive than a multi-mediational model such as Figure 3.3. Because a high risk medication regimen is a latent variable, the mediating relationship is determined by representing high risk medication regimens through the observed mediating variables (polypharmacy, inappropriate medications, medication regimen complexity). These mediating variables were designated as indicator variables in the factor analysis.

A summative factor analysis was done to assure that the indicator variables compose the latent variable in the second model. In factor analysis, the researcher seeks patterns in relationships between many independent variables so that outcome variables can be explained by a smaller number of independent variables called factors (Darlington, n.d.). Factor loadings are used to determine the number of factors and the specific factors composing the latent variables.

Aim 3. When combined with other potential risk factors, to evaluate the extent to which high risk medication regimens, as a mediating variable between comorbidity and hospital readmission, account for variance in hospital readmission.

This aim first establishes the relationship between the predictor variables, determines the most parsimonious model, accounts for the variance in re-hospitalization by the predictor variables and the covariates, and finally tests the mediating relationship. These steps are described below.

Step 1: Determining the relationship between covariates. Correlation matrices were used to help determine the level of co-linearity between the covariates and whether the covariates and predictor variables even have a relationship to the outcome variable of re-hospitalization. In addition to determining whether a relationship exists, correlation matrices depict the strength and direction of the relationships which assists the researcher in developing the analytic model, and helps to determine which covariates will be included in the model. When studying the relationship between covariates, the goal is to have low correlations between variable pairs, otherwise it can be assumed that the variables are measuring the same concept. This redundancy will over estimate the effect of the two variables on the outcome, akin to double counting an item. To study the correlations between variables, at least one of the variables must be continuous in nature.

In those pairs with high coefficients (> 0.9), one of the covariates was removed from the analysis (Lomax, 2007, p. 208) as the covariates are presumably measuring the same concept. However, because the hypothesis was that the mediating variables (polypharmacy, inappropriate medications and medication regimen complexity) play a role in influencing the outcome, no matter the level of co-linearity between comorbidity and any of the mediating variables, all of the mediating variables were kept in the final model. There was no expectation of high co-linearity between comorbidity and the mediating variables.

On the other hand, a correlation between the predictor variables and the outcome variable is desirable as these are the relationships that are being tested. If no correlation existed, there is no reason for examining the relationship between the individual predictor and the outcome in the first place.

After the correlation matrices were studied, binary logistic regression was used to execute the final step in determining the relationship of the twenty-one covariates to comorbidity in this preliminary analysis. Chi square test statistics were examined for significance. Those variables that are significant were kept as covariates in the final model.

Step 2: Choosing variables for logistic regression. Once proposed mediation relationships were examined, logistic modeling was used to choose other covariates for inclusion in the SEM. When using regression modeling procedures, the researcher must choose the order in which the variable or blocks of variables are added to or eliminated from the model. For the logistic regression modeling in this study, a number of methods were considered for order of entry of the variables (all possible subsets, simultaneous, forward selection, and backward elimination) to develop the model in an effort to ensure that the model remained stable despite the method used.

A sequential modeling procedure, all possible subsets regression modeling (Lomax, 2007; Howell, 2007), is favored when there is little literature to support precisely which variables are predictive of re-hospitalization in home health care clients. The predictor variables chosen to be tested were based on variables that predict hospitalization in other settings such as ambulatory care and long term care (see literature review) and those that were not strongly co-linear. In all possible subsets regression modeling, each model using each combination of predictors is analyzed and the model yielding the largest adjusted r^2 is chosen as the final model. In this study, 15 possible models could be examined using the variables for comorbidity, polypharmacy, PIM, medication regimen complexity (one 4 predictor model, four 3 predictor models, six 2

predictor models, and four 1 predictor models). Though labor intensive, both Lomax and Howell suggest this is the most appropriate sequential modeling procedure for exploratory research, rather than stepwise procedures, as there is no a priori selection of variables. Lomax suggests that with stepwise procedures, oftentimes noise is selected rather than crucial predictors and important predictors are removed from the model because the partial correlation confidence intervals for numerous variables are too narrow to be significant, while Howell maintains not only does this procedure take an enormous amount of time, it has great potential to capitalize on chance findings.

In simultaneous selection, all the variables are entered at once based on a priori knowledge of the variables (Lomax, 2007). In the backward elimination method, all variables being considered for the model are loaded into the model for the first run. Then, the least significant variable or block of variables is eliminated with each subsequent run until only significant variables remain in the model (Lomax, 2007). Howell (2007) contends that this procedure is simple and intuitive to use, but also capitalizes on chance in finding suppressor variables (predictor variables that have a positive influence on the outcome variable through one path and a negative influence on the outcome via another path). In contrast, according to Lomax, forward selection modeling builds the model by adding each variable in sequence based on some prior knowledge about what variables are likely to be significant. Variables are added to the model based on the expected contribution to the model, with the variable having the largest contribution entered first and with subsequent variables each contributing to a lesser degree to the model. When comparison of each step to the previous step is no longer significant, based on the likelihood ratio test with maximum likelihood estimation, the model building process is

halted and the model is complete. The remaining variables not selected into the model should not be significant predictors, while those selected into the model should be significant predictors (Lomax, 2007). According to Howell (2007), the forward regression is the best procedure for selecting variables as the best compromise procedure. In this case, forward selection was used to initially develop the model, and because the literature was equivocal about the predictors, backward elimination was chosen as the most appropriate procedure and was relied upon as the arbiter of the final logistic regression model.

The Wald test and associated significance level were used to choose variables to include in the reduced logistic model and subsequently, the SEM. Garson (2009, SEM) suggests that the Wald statistic, used to test the null hypothesis that the regression coefficient is significantly different from zero, is an acceptable method of determining which variables to keep in the logistic model when large sample sizes are used. The variables with the largest Wald statistic, according to Garson, would have the most impact on the model if removed from the model.

Step 3: Determining the degree of influence the latent variable, high risk medication regimens, and its indicator variables, have on re-hospitalization. This step helps establish the causal chain of events. Since, given this particular data set, there is no way of studying events in a time sequence or taking multiple measurements over time, the causal chain must be determined using statistical modeling. Byrne (2010) claims path analysis used to test causality establishes which indicator variables make up the latent variables. Path analysis, in the form of SEM, was used to determine how much variance each of the chosen variables contribute to the final outcome by using the logit link

function contained in the AMOS program. Finally, each model was tested for goodness of fit and the model with the highest statistic was chosen as the appropriate model for causation. Evaluating the direct (focal relationship) and indirect effect (mediating relationship) of predictor variables, path coefficients on the outcome variables enables the researcher to explain how much influence (effect) the mediator has on the outcome and what percentage of variance is due to a particular variable.

Step 4: Determining the mediating relationship. This is the final step in determining whether a mediational relationship exists. If complete mediation exists, the focal relationship will be extinguished when the mediators are added to the model. If partial mediation exists, the focal relationship will have a decrease in the significance level when the mediators are added to the model. Since there is a mix of both dichotomous and continuous variables in the model, multivariate analysis could be a reasonable choice to evaluate the full model for mediation. Both Polit (1996) and Howell (2007) suggest that multivariate analysis using a series of multiple regression equations can be used in evaluating dichotomous variables without substantially increasing the standard error when the number of subjects is large or the number of variables is not too large. However, the alternative method to multivariate modeling would include evaluation of the direct and indirect paths in the SEM model (Garson, 2009b).

According to Baron and Kenny (1986), mediation is established through a series of steps. Typically, the Baron and Kenny steps are used when the analytic technique is simple regression modeling when the endpoint is the logistic or linear regression model findings. However, with SEM, the work of modeling is done before the final

determination of whether a mediation hypothesis is confirmed. Therefore, the steps were modified to accommodate the SEM.

These steps are described by MacKinnon (2008) in the chapter on the *Multiple Mediator Model*. First, the main (focal) relationship must be established between the independent variable (comorbidity) and the outcome of re-hospitalization. The two variables must be correlated. In order to include these variables in SEM, they should be significantly correlated ($r > .3$), but not so highly correlated ($r > .9$) that they might be considered to measure the same concept. These bivariate correlations are done for the focal relationship (comorbidity and readmission), and also between the predictor variable and the potential mediators (polypharmacy, PIM and medication regimen complexity) used as indicators for the latent variable (high risk medication regimens) or the latent variable itself, and finally between the potential mediator indicator or latent variables and the outcome variable (readmission). Once these relationships are established, these variables could be considered in the SEM process for mediation. If the relationship is not significant, typically the particular mediating variable would not remain in the proposed mediation model. Each of the steps in establishing relationships between the main predictor, the potential mediators, and the outcome variable must be significant in order for the mediation hypothesis to be considered. If any of these correlations were not significant, further analysis of the data would have been fruitless in trying to determine whether mediation existed.

Once these preliminary steps are completed, then the chosen variables are examined using SEM. Two SEM models were run. The first, using just the focal relationship, was run to determine the focal relationship pathway coefficient. Then the

model with the proposed mediator(s) included was run and the focal relationship was compared to the modeling done when only the focal relationship was used. If the path coefficient decreased, but is not extinguished, partial mediation is occurring, but if it completely extinguished, full mediation is occurring. If the path coefficient is decreases to zero (fully extinguished), it can be assumed that the predictor's effect on the outcome is due to the mediating influence of the variable(s) on the outcome. The analytic plan described above is summarized in Table 3.1.

Table 3.1. Analytic plan summary.

Aim	Research Question	Analytic Technique
Preliminary Analysis	Is there a difference between reason for assessment (#1 and #3) groups?	Discriminate Analysis
1. To describe the medication regimens of older adult home health care clients in terms of polypharmacy, potentially inappropriate medication use and medication regimen complexity	1. What is the prevalence and characteristics of polypharmacy, potentially inappropriate medication use, and medication regimen complexity for home health care patients age 65 and over?	Descriptive Statistics
2. To determine what combination of factors (polypharmacy, potentially inappropriate medications, medication regimen complexity) compose the concept of high risk medication regimens	2. Can a construct of high risk medication regimens be created from operational definitions of polypharmacy, potentially inappropriate medication use and medication regimen complexity?	Summative Factor Analysis
3. To evaluate the extent to which high risk medication regimens account for variance in re-hospitalization when combined with comorbidity and other potential risk factors	3.0 How much do high risk medication regimens increase the risk of re-hospitalization in home health care patients age 65 and over?	Logistic Regression, Correlation Analysis, & SEM
	3.1 What is the effect of high risk medication regimens on re-hospitalization?	Effects Decomposition
	3.2 Do high risk medication regimens mediate the relationship between comorbidity and re-hospitalization?	Comparing Models

Missing Data

Attrition was not a factor in this study as the data have been previously collected. However, the presence of missing data was an issue for this study. Hot deck imputation (Davern, lecture notes, 2008) was used when more than 5% of the data were missing.

Ethical Issues

The study protocol was submitted to the University of Minnesota, Office of Research for initial review and comment. There were no risks to individuals participating in this study as secondary data were used for the analysis. An expedited Institutional Review Board (IRB) review was granted. The investigator completed the required IRB coursework for the University of Minnesota including Safeguarding Personal Health Information on Computers, Privacy and Confidentiality in Research, Protection of Human Subjects, Responsible Conduct of Research, Managing Health Data Securely and Conflict of Interest. Subject confidentiality was ensured throughout the entire study. Data were subject to Health Insurance Portability and Accountability Act guidelines and ethical data collection practices.

Other than a birth date, data were de-identified by the vendor before data were sent to the research team. Further, the individual home care agencies were assigned a dummy number prior to the data set being sent to the investigators. In addition, each individual was assigned a number by the vendor that is not identifiable by others. Therefore, no identifying data were available to the researcher except birth dates which were re-coded to age and then removed from the analytic files. The original data files, as well as data preparation and analytic files, were kept on CD ROM in a locked filing cabinet in the principal investigator's locked office, as well as electronically, on a secure,

password protected research website maintained by the University. Preparation and analytic files were also kept on a password protected laptop computer in the researcher's possession

The data were freely shared within the research team consisting of the funded principal investigator, a statistician, three PhD students, and a Master's degree graduate student all from the University of Minnesota, School of Nursing. A professor in the University of Minnesota, School of Pharmacy, a statistician from the University of Minnesota, College of Education and Human Development, and two collaborating researchers, who were senior scientists at outside institutions, also viewed de-identified data. Any data that were publicly accessed were de-identified and stored in a format that was already analyzed. The research team met monthly in order to discuss issues that arise during the course of the month with both the analysis and progress of the study. Meeting minutes were part of the permanent record and were kept throughout the course of the study. A thorough data preparation log was kept regarding initial preparation steps, recoding of variables and analytic techniques.

Inclusion of Women, Minorities and Children

As expected that many of the subjects were women. Given the composition of home health care, the subjects were more likely to be Caucasian, and indeed, this was the case. No children were participating in this study as the inclusion criteria were limited to those over age 65 and using home health care in the community.

Conclusion

This chapter began with a discussion of the study design, descriptions of the data sets, the sample, and the variables chosen for study. A number of potential analytic

models were devised and merits of each model were compared. An analytic plan was developed and the rationale for using SEM versus multivariate analysis was presented. It was shown that SEM would possess the sophistication needed to answer the research questions posed. The chapter ended with a discussion of the ethical issues unique to this study.

In the next chapter, the results of the full analysis will be presented. The findings related to the various steps of the analytic plan outlined in this chapter will be discussed and the utility of various models compared. The best fitting model will then be discussed in detail and the answer to whether a potential mediation model exists will be revealed.

CHAPTER IV

RESULTS

Introduction

In previous studies, high risk medications are mentioned, but the components proposed to consist of high risk medication regimens are not defined or tested. Some of the individual components proposed to comprise high risk medication regimens (polypharmacy and potentially inappropriate medication use) have been examined as a precursor to adverse events, but only polypharmacy has been studied as a predictor of readmission. These findings from this study will begin to define the concept of high risk medication regimens and add to the knowledge of risk factors for hospital readmission in the elderly home health care population.

In Chapter 3, the analysis approach to address each of the study aims and the specific measures were described. This chapter will describe the findings for each of the aims described in Chapter 1. These aims include: 1) describing medication regimens of older adults in home health care, 2) determining the factors composing high risk medication regimens, and 3) determining whether high risk medication regimens account for variance in hospital readmission above that accounted for by comorbidity alone.

In this study, each aim builds upon the findings of the previous aim. However, various data analyses are also described which lay the foundation for accomplishing the aims. Because secondary data are used for this study, development of the analytic data set using propensity scores is described. Prior to reporting the results of each aim, descriptive statistics are used to portray the characteristics (covariates) of the study sample. In preparation for model building, correlation analyses of the overall sample are presented

evaluating whether demographic characteristics are independent from one another.

Readmitted and non-readmitted home health care patients are compared and contrasted according to their demographic characteristics.

Following the sample development description and the descriptive analysis, each aim is then described, as well as the associated results. Medication regimens are examined using both descriptive statistics and correlation analysis. To evaluate the concept of high risk medication regimens, the findings from the confirmatory factor analysis are presented. To develop and test the structural equation model (SEM) that will evaluate the extent that high risk medication regimens account for variance in hospital readmission, logistic regression modeling is first employed to determine the covariates significant enough to include in the SEM. Both the factor analysis and the logistic regression model findings are crucial in selecting the variables listed in the black box depicted in the analytic models described in Chapter 3, and that are included in the SEM testing and development.

Lastly, each model is presented in the order the model was developed, based on the testing of the previous model. Although the fit indices are presented in one table, to promote ease of comparison across models, each model and the critique of the model will be presented separately. Full test statistics will be presented only for the best fitting model in the body of the paper.

Initial Development of the Data Set

When using secondary data, researchers must sift through data points usually collected for reasons other than research, in order to determine which variables are pertinent in answering the research question. The answers must be found in the existing

data, unlike studies using primary data, in which the research questions drive the data collection. Thus, the first step in a secondary data analysis is developing the analytic data set, that is, the subset of the data that actually has the potential to answer the proposed research questions. In this study, two datasets were merged in order to develop the analytic dataset. OASIS records and medication records for patients age 65 and older, admitted to 14 Midwestern and 1 East Coast home health care (HHC) agencies for their first episode of care during the calendar year of 2004 were merged to develop the analytic dataset. An additional inclusion criterion included only patients who were admitted to home health care (HHC) after a hospitalization, as opposed to entering HHC from the community or other facility.

It was important for demonstrating generalizability, that the final sample reflects the characteristics of the population in question (those age 65 and over). In addition, in order to make generalizations to the home health care population, the sample of those patients age 65 and over must reflect the population of home health care clients (the entire dataset). Since the entire dataset was all open cases for the calendar year of 2004, if the sample of those aged 65 and over reflects the entire dataset, conclusions are likely to be generalizable to the population. On the other hand, if excluding patients, those patients must either be different enough to warrant separate analysis or so similar that no bias is introduced.

A stepwise process using propensity scores at each exclusion step was employed to determine if the included patients were significantly different from excluded patients at each step of the exclusion process. Ensuring that the final sample was relatively homogeneous helped to control for extraneous factors (type of episode, episode start date,

and young adults) that might have confounded the results. The propensity scores were developed based on each exclusion criterion, and significance of one-way ANOVA evaluated to ensure that those excluded from the study were different enough from the included patients to warrant a separate analysis. Although the original database included 2,772 patients, only the records of 911 patients who were initially hospitalized, were age 65 or older, and had complete records, for the purpose of this study, were evaluated.

Table 4.1 summarizes from what venue patients entered home health care in the previous two weeks in the complete dataset (including all those age 18 and over) compared to just the sample of those age 65 and over, and to the final sample. Although patients frequently entered home health care directly from the hospital, patients also could enter home health care from other institutional settings, or even directly from the community setting. Approximately half of the subjects in both the complete dataset and in the sample of those ages 65 and older came from the hospital in the previous two weeks. About 20% in both the complete dataset and the age 65 and older sample came from another institutional setting such as a rehabilitation setting, skilled nursing facility, or a nursing home. A larger percentage (28%) of both of these groups (the complete dataset and the age 65 and older group) had no institutional stay in the previous two weeks and was likely ongoing recertification cases. The final study sample drawn from the age 65 and older sample eliminated the 46% of patients who did not have a qualifying hospital stay. Many of the patients in the final study sample (13%) also had a rehabilitation stay or a skilled nursing facility stay in the previous two weeks. Although 6% fewer people in the final study sample had a skilled nursing facility stay, the percentages for other institutional stays were quite similar suggesting that the study

sample was not very different from the subjects in the complete dataset or from those age 65 and older.

Table 4.1. Location of patient in the previous two weeks before admission to home health care.

Disposition Location	All Ages/Entire Dataset (n = 2,772)	Age 65 and Older (n = 2,277)	Study Sample (n = 911)
Hospital	55.2%	54%	100%
Rehab	3.5%	3.4%	3.5%
Skilled Nursing Facility	14.8%	16.8%	9.8%
Nursing Home	0.9%	1.1%	0%
Other	0.3%	.2	0.1%
None	28.4%	28.5%	N/A

Table 4.2 summarizes the demographic characteristics of the dataset at each step of the exclusion process. Figure 4.1 depicts the diseases used for the primary diagnoses observed in the various samples used in the propensity study. A description of the sample after each exclusion step is described in the following paragraphs.

Step 1: Description of the Sample that Included All Ages

The initial secondary dataset included all episodes of care opened in 2004 (N = 2,772). This population of patients included age groups, from young adults (age 18 and over) to those who were elderly. As indicated in table 4.1, 48% of the population (n=1330) was admitted to home health care without an index hospitalization in the previous two weeks. Of those admitted without an index hospitalization, 28% (n = 776) were not admitted from any inpatient facility, meaning either the episode of care was for recertification or the patient was admitted to home health care directly from the

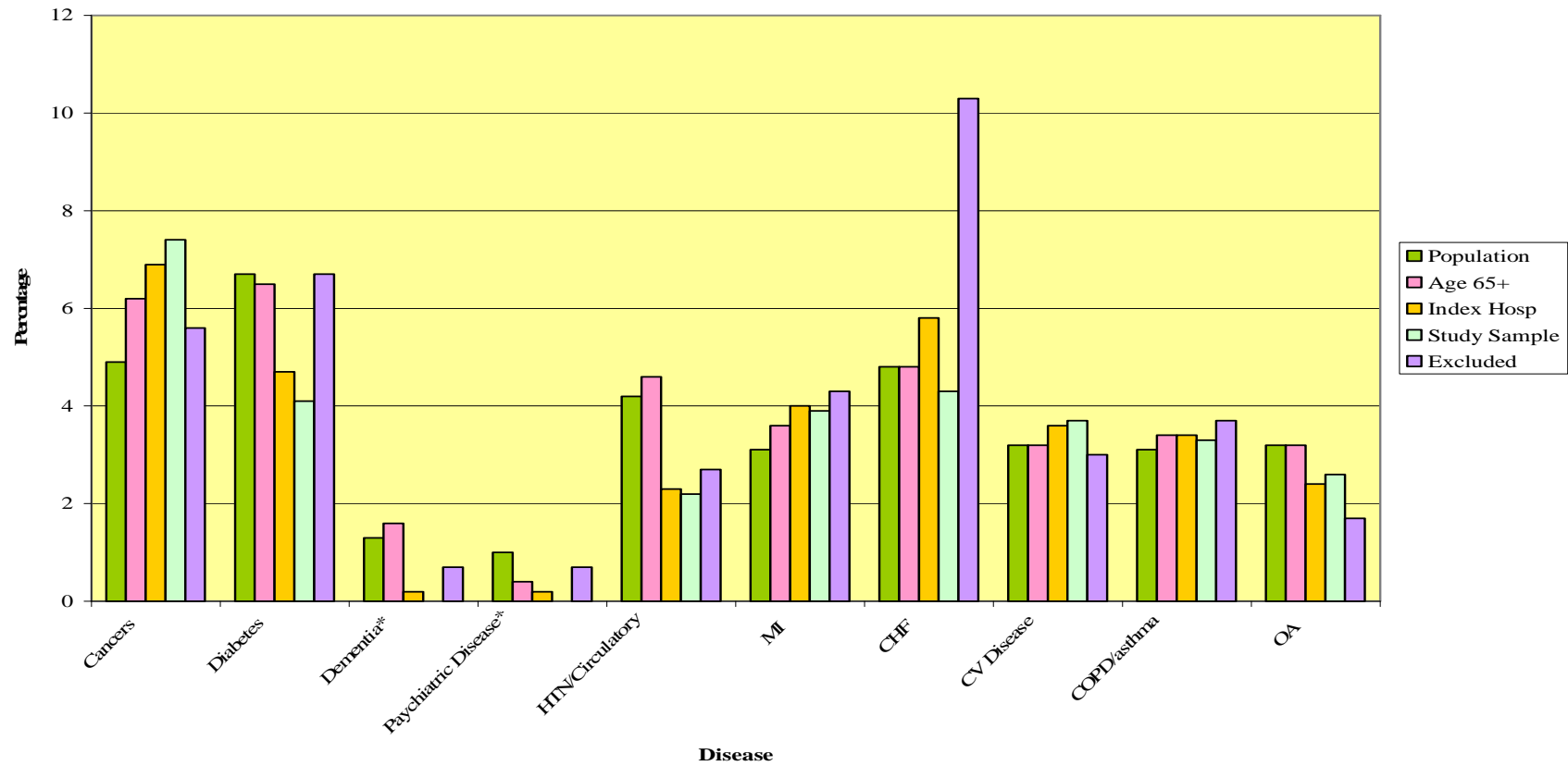
community. The remaining 554 patients were admitted in some other manner to home health care. Of the 535 people who were initially discharged from institutions (rehabilitation facility, skilled nursing facility or nursing home) other than a hospital in the previous 2 weeks, 20% (n = 110) were calculated to be recertifications of care, leaving 425 patients (15% of the population) entering home health care after prolonged rehabilitation stays. These patients would not have been included in the sample by definition.

Compared to the final study sample (Table 4.2), the complete dataset patients were younger (mean age 74.9 vs. 78.9), slightly healthier (Charlson Comorbidity Index score > 3), had fewer surgical wounds (31% vs. 50%), had higher hospital readmission rates (37% vs. 20%), and had longer lengths of stay in home health care (154 days vs. 35 days). The long length of stay and the lower percentage of surgical wounds indicated that these patients likely had multiple home care recertifications for continued care of chronic problems. The complete dataset had lower rates of cancer and heart disease as the primary diagnosis, but higher rates of diabetes, dementia, psychiatric disease, hypertension, and arthritis than the final study sample (Figure 4.1).

Table 4.2. Comparison of the samples drawn for the propensity analysis.

Parameter	Step 1 Population (All Ages) N = 2772	Step 2 Sample (≥ Age 65) n = 2277	Step 3 Sample (Hosp) n = 1212	Study Sample n = 911	Excluded n = 301
Start of Care Episode	74.4%	75.4%	88.0%	92.6%	88.3%
Recertification Episode	25.5%	24.9%	11.7%	7.2%	11.7%
Mean Age in Years	74.9	80.2	79.2	78.9	80.0
Caucasian	98%	98%	99%	99%	99%
Female	64%	65%	62%	61%	63%
Lives Alone	38%	40%	33%	31%	38%
Lives with Spouse	42%	41%	49%	51%	43%
Needs ADL Help	56%	56%	60%	61%	59%
Needs IADL Help	92%	93%	97%	97%	96%
Needs Oral Med Help	98%	98%	99%	99%	99%
Cognitively Intact	73%	72%	75%	75%	75%
Depressed	21%	19%	16%	16%	17%
Memory Deficit	8%	8%	7%	7%	10%
Impaired Decisions	8%	8%	7%	7%	7%
CCI Score > 3	4%	4%	5%	5.1%	3.3%
Life Exp. < 6 mo.	6%	6%	6%	6%	6%
Surgical Wound	31%	31%	46%	50%	34%
Readmission Rate	37%	34%	29%	20%	29%
Med Related Rate	0.6%	0.6%	0.4%	0.4%	0.3%
HHC < 30 Days	48%	49%	62%	68%	62%
Readmit in < 30 Days	33%	34%	30%	23%	30%
LOS in HHC	154 days	145 days	56 days	35 days	119 days
Death	1.5%	1.8%	1.2%	1.5%	0.3%

Figure 4.1. Comparison of primary disease diagnosis rate in population versus samples.



*Study sample did not include this disease category

HTN = hypertension; MI = myocardial infarction; CHF = congestive heart failure; CV = cardiovascular;
 COPD = chronic obstructive pulmonary disease; OA = osteoarthritis

Step 2: Developing the Age 65 and Over Sample

As the inclusion criteria only included those age 65 and older, all patients under age 65 on first day of 2004 were removed from the dataset in the initial step (n = 2,277). In table 4.1, 45% of the age 65 and over sample (n=990) had no index hospitalization. There were 656 patients (28.5%) in the 65 and older sample entering home care without any type of institutional stay. However, a number of patients had inpatient stays in settings other than in the hospital (21.5%). Of the 485 patients with these other institutional stays, 151 (6.6%) had both an index hospitalization and a subsequent short stay in a rehabilitation setting in the previous two weeks before admission to home care, so would be eligible for the study sample. Nearly 15% (n = 334) did not have a hospitalization in the previous two weeks, but came from a skilled nursing facility, rehabilitation unit, or a nursing home indicating that they likely had a prolonged rehabilitation. These patients would not have been eligible for the study due to exclusion criteria.

It was felt that perhaps patients from the rehabilitation setting or the transitional care unit were sicker than those who remained in the final sample because they were over the two week window for hospitalization. However, only 2.8% of these excluded patients from the rehabilitation setting had Charlson Comorbidity Index Scores of greater than 3, compared to the final study sample rate of 5.1% of patients with Charlson Comorbidity Index scores of greater than three (Table 4.2). Thus, the patients who were excluded because they came from the rehabilitation setting seem to be healthier than the final study sample. Yet only 38% of these excluded patients had surgical wounds (a rather indirect way of determining if a patient is healthy enough to survive a surgical procedure)

compared to the 50% of final study sample. This suggested perhaps medical instability rather than surgery, accounted for the prolonged stay in rehabilitation. Medically unstable patients would be expected to have diseases such as congestive heart failure, chronic obstructive pulmonary disease, and diabetes. Seventeen percent of these patients in rehabilitation settings were recertifications, meaning that they likely were in the home health care system chronically. Excluding patients with lengthier institutional stays helped control for the confounding effect of long term care provision on the subjects.

The sample of patients age 65 and older mirrors the complete dataset in almost all respects except age (Table 4.2), with the age 65 and older sample being five years older on average than those in the complete dataset (80.2 years vs. 74.9 years). This age 65 plus group seems to be representative of the population of home care patients in all areas except age.

Step 3: Excluded Patients

Because the endpoint for this study was readmission to the hospital, all patients without an initial hospitalization precipitating admission into HHC were excluded from the OASIS data set before the data sets were merged. In addition, only the first episode of care occurring in 2004 was evaluated, with the episodes of care being completed by December 26, 2006. The patients age 65 and older who did not have an index hospitalization (n = 1048) and those with multiple episodes of care (n = 17) were thus removed from the sample leaving 1,212 patients who were age 65 and older, having their first episode of care in 2004 within two weeks after an initial hospitalization. The characteristics of the remaining 1,212 patients who had initial hospitalizations are shown

in Table 4.2. Two areas difference are obvious when the hospitalized patients are culled from the age 65 and over group. The sample of patients with an index hospitalization (n = 1,212) had significantly shorter episodes of care in home health care (indicating fewer recertifications) and had higher rates of surgery, likely indicating a healthier group of people than age 65 plus sample. However, Figure 4.1 demonstrates little difference in the primary diagnoses between those who had index hospitalizations and the larger group of those ages 65 and older.

When the final exclusion process was completed, 301 additional patients were excluded from the sample with an index hospitalization (n= 1,212). It is apparent, and was validated by the propensity analysis, that these excluded patients were significantly different from the study sample and warranted a separate evaluation which was beyond the scope of this study. No episodes of care were allowed to carry over from 2003 into 2004 because these patients would not have begun their episode of care in 2004 according to the inclusion criteria. The 181 patients who had episodes of care which carried over from 2003 or earlier were thus removed from the sample. Next, the 15 patients who had open cases beyond 2006 were also removed from the sample. Finally, OASIS records were then merged with the medication records to determine which patients had a complete OASIS (start and end assessment representing one episode of care) and a medication record. The 105 patients who did not have a medication record, had a medication record but no corresponding complete OASIS record, or those who had no medications listed in their medication record were removed from the sample in the final step of the exclusion process. This step, in particular, illuminates the issue of data being collected for reasons other than the purpose of

secondary analysis. These patients may have had records that stated that “the family sets up and dispenses the medications” or similar notes that the nursing staff used to help clarify an order.

After these 301 patients were removed, 911 patients remained who fit the inclusion criteria for the final study sample. Although all 911 patients came from the hospital, a number of patients (13.4 %, n = 122) also had short stays in a rehabilitation location (rehabilitation unit, skilled nursing facility, or nursing home) in the previous two weeks before admission to the home health care.

The 301 excluded patients (Table 4.2) were slightly older, more likely to live alone, had slightly higher levels of memory deficit, less likely to have surgery, had much higher readmission rates (29% vs. 20%), but were in home health care longer (119 days vs. 35 days), and more likely to be readmitted to the hospital in fewer than 30 days than the final study sample. These excluded patients also had much higher rates of diabetes and congestive heart failure as a primary diagnosis (Figure 4.1). These two diseases are likely to cause the home health care patient a prolonged stay in the transitional care unit and also would cause the patient to have multiple recertifications, thus significantly increasing the length of stay in home health care.

The final analytic data set included 911 patients and excluded in total 1,861 patients. Included patients were age 65 and older, in their first episode of care in 2004, had complete records, and had an index hospitalization in the previous two weeks. Overall, few patients were lost to death. The death rate of 1.5% in the final study sample was the same as the death rate of the original population. Death was included in the

discharge calculations of those who were not hospitalized. Unfortunately, the death rate in the hospitalized group was not able to be determined with accuracy.

Descriptive Analysis

Characteristics of the study sample, excluding medication pattern characteristics, are described in this section. In addition, the difference in characteristics between readmitted patients and those who were not readmitted is examined.

Demographics

The demographic characteristics of the sample are presented in Table 4.3. The mean age of HHC patients for this study was 78.9 years, patients were predominately Caucasian, and expected to live longer than six months (93.7%). There were more females in the sample (61%), and half (50.7%) were age 75-84, with the remainder of the sample divided between the oldest-old (age 85+), and the young-old (age 65-74). A third of the HHC patients lived alone (30.6%), however, almost half were living with their spouses (48.2%). Only 1.8% lived with paid help. The remainder of patients either lived with other family members or friends (19.4%).

Table 4.3. Selected demographic characteristics of home health care patients (n = 911).

Demographic Characteristic	Mean \pm SD	Range	Number	Percent
Age	78.9 \pm 7.4	65-106		
Age 65-74			260	28.5%
Age 75-84			462	50.7%
Age 85+			189	20.7%
Life Expectancy < 6 Months			67	6.3%
Female			556	61.0%
Caucasian			898	98.6%
Lives Alone			279	30.6%
Lives with Spouse			439	48.2%
Lives with Paid Help			16	1.8%

Caregiving Assistance, Functional Status and Cognition

Caregiving, functional and cognitive status are outlined in Table 4.4. Most HHC patients relied on informal (unpaid) supports of one kind or another. Over one third (38.2%) depended on primary caregiving by their spouses, while 27.2% had help from children. Fewer sought help from people who were not in their immediate family, including relatives, friends, and paid help (12.3%). Although most patients needed help managing their independent activities of daily living, less than one half needed assistance with ADLs. Three quarters of the patients were assessed to comprehend and follow directions. For those who had cognitive deficits, 6.5% suffered from memory loss and

6.5% also suffered from impaired decision making; it is likely that there was considerable overlap in these two categories as these categories were not mutually exclusive.

Table 4.4. Caregiving, function, and cognitive characteristics of home health care patients.

Characteristics	Number (n = 911)	Percent
Caregivers Used Other Than HHC	900	98.8%
Spouse	348	38.2%
Child(ren)	248	27.2%
Other Family Member	56	6.1%
Friend or Neighbor	17	1.9%
Paid Help	39	4.3%
ADL Help Needed (n=705)	425	46.7%
IADL Help Needed (n=705)	674	74.0%
Oriented/Comprehends/Follows Directions	686	75.3%
Depressed Mood	149	16.4%
Memory Deficit	59	6.5%
Impaired Decision Making	59	6.5%

Health Status

Table 4.5 provides information about the health status of the patients. These HHC patients had a low level of comorbidity, with a Charlson Comorbidity Index (CCI) score of three or more indicating relatively severe comorbidity (Nunez et al., 2004; Testa et al.

2009). Half of the sample was presumed to have had surgery due to the presence of a surgical wound. Twenty seven percent of patients were incontinent of urine.

Approximately 20% had at least one risk factor (smoking, alcohol use, obesity, and recreational drug use). Few patients had medical diagnoses (CHF, diabetes, and depression).

Table 4.5. Comorbidity, medical, and health conditions of HHC patients (n = 911).

Variables	Number	Percent
Low Level Charlson Comorbidity Index (CCI \leq 1)	639	70.1%
Moderate Level of Comorbidity (CCI 2-3)	224	24.6%
High Level of Comorbidity (CCI > 3)	48	5.3%
Pressure Ulcer Present	47	5.2%
Surgical Wound Present	451	49.5%
UTI Treatment in Last 2 Wks	82	9.0%
Incontinent of Urine	246	27.0%
Congestive Heart Failure Primary Diagnosis	39	4.3%
Diabetes Primary Diagnosis	37	4.1%
Any Risk Factor Present*	181	19.9%

*Risk Factors Include: Smoking, Alcohol, Obesity, Recreational Drug Use.

Hospital Readmission and HHC Length of Service

A large majority of HHC patients experienced changes in their medical regimen (inpatient stay, medical or treatment changes) in the previous two weeks (Table 4.6). The overall readmission rate was 20.4%, with 16% of the entire sample being readmitted within 30 days of the start of the episode of care. Whether readmitted or not, the length of service was less than thirty days for 68% of the patients; however, given some rather severe outliers, the mean HHC episode length was almost 40 days.

Table 4.6. Hospital readmissions and length of HHC service for HHC patients (n = 911).

Variables	Mean \pm SD	Range	Number	Percent
Regimen Change in Last 14 Days			847	93.0%
Any Emergent Care Since Admit			182	20.0%
Hospital Readmission			186	20.4%
Hospital Readmit Related to Meds			46	5.0%
In HHC < 30 Days			618	67.8%
Hospitalized within 30 Days of Admission to HHC			143	23%
HHC Episode Length (in days)	39.4 \pm 72.2	1-838		

Differences between Those Not Readmitted and Those Who Are Readmitted

The sample of 911 HHC patients was also evaluated to determine if there were statistically significant differences between those who were readmitted (n = 186) and the 725 patients who were not readmitted to the hospital (Table 4.7). Chi-square statistics were used for dichotomous variables, while *t*-tests for independent samples were used for continuous variables. Patients who were not readmitted were significantly different from those who were readmitted in all dimensions except gender, ethnicity, living alone, living with spouse, urinary incontinence, the need for ADL assistance, the percentage having regimen changes, and the mean episode length. Particularly noteworthy differences were in the level of comorbidity, depressed mood, impaired decision making, and use of emergent care. Figure 4.2 illustrates the difference in the primary diagnosis for admission to home care between those who were readmitted and those who were not readmitted. Those who were readmitted had much higher rates of cancer, diabetes, and congestive heart disease, consistent with higher comorbidity and comorbidity scores greater than three. When age was broken down by category, significant differences appeared between the non-readmitted and readmitted groups, as well, with fewer youngest-old and oldest-old being readmitted.

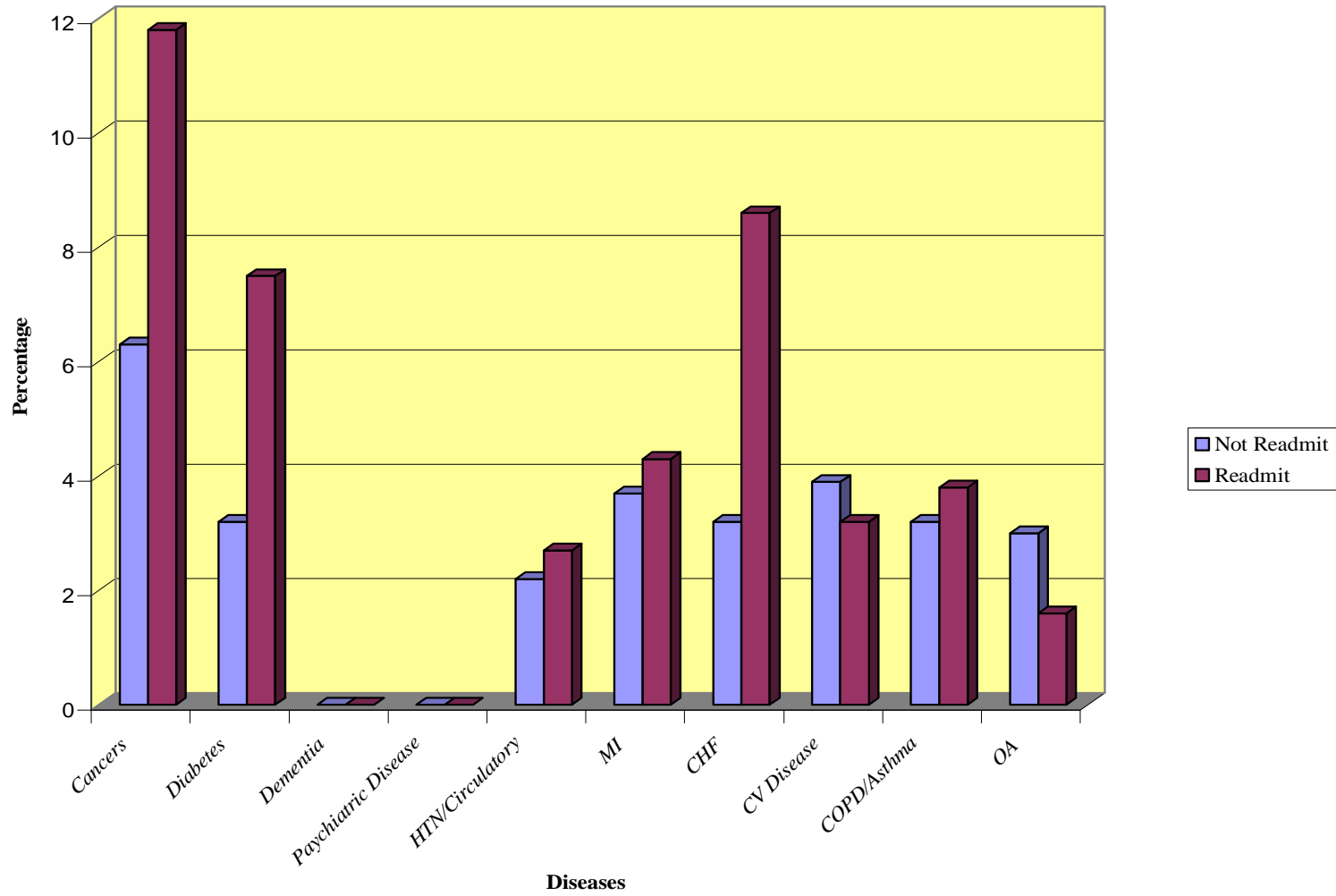
Table 4.7. Comparison of subject characteristics for patients who were readmitted versus those who were not readmitted when receiving HHC (n = 911).

Variables	Not Readmitted n = 725 (79.6%)	Readmitted n = 186 (20.4%)
<i>Demographic Variables</i>		
Mean Age in Years	78.8	79.0***
Age 65-74	211 (29.1%)	49 (26.3%)*
Age 75-84	361 (49.8%)	101 (54.3%)*
Age 85+	153 (21.1%)	36 (19.4%)*
Female	447 (61.7%)	109 (58.6%)
Caucasian	716 (98.8%)	182 (97.8%)
Living Alone	232 (32.0%)	47 (25.3%)
Lives with Spouse	373 (51.5%)	94 (50.5%)
Spouse as Caregiver	280 (38.6%)	68 (36.6%)
Child(ren) as Caregiver	195 (26.9%)	53 (28.5%)
Paid Help as Caregiver	31 (4.3%)	8 (4.3%)
<i>Physical Health Status Variables</i>		
Charlson Index Score ≥ 3	65 (9.0%)	41 (22.0%)*
% With Life Expectancy < 6 Months	35 (4.8%)	22 (11.8%)*
% Death	14 (2.0%)	Unknown
% With CHF Primary Diagnosis	23 (3.2%)	16 (8.6%)*
% With Diabetes Primary Diagnosis	23 (3.2%)	14 (7.5%)*
% With Pressure Ulcer	31 (4.3%)	16 (8.6%)*
% With Surgical Wound	373 (51.4%)	78 (41.9%)*

Table 4.7 (continued)

Variable	Not Readmitted	Readmitted
% With UTI in Last 2 Wks	58 (8%)	24 (12.9%)**
% With Urinary Incontinence	189 (26.1%)	57 (30.6%)
<i>Cognitive and Functional Status Variables</i>		
% Needing Help With ADLs	329 (45.4%)	96 (51.6%)
% Cognitively Intact	554 (76.5%)	131 (70.4%)
% With Depressed Mood	101 (13.9%)	48 (25.8%)***
% With Memory Deficit	39 (5.4%)	20 (10.8%)**
% With Impaired Decision Making	35 (4.8%)	24 (12.9%)***
<i>Transition Variables</i>		
% Having Regimen Change in Last 14 Days	674 (93.0%)	173 (93.0%)
% Using Emergent Care Since Admit to HHC	43 (5.9%)	139 (74.7%)***
% Sample in HHC < 30 Days	475 (65.5%)	143 (76.9%)**
% Readmitted within 30 days	N/A	143 (76.9%)
Mean Episode Length (in days)	38.6	32.9
* p < .05		
** p < .01		
*** p < .001		

Figure 4.2. Comparison of primary diagnosis disease categories for those not readmitted to those who were readmitted.



*Aim One: Descriptive Analysis of Medication Variables**Medication Use Patterns*

The prevalence and characteristics of polypharmacy, potentially inappropriate medication use, and medication regimen complexity for home health care patients age 65 and over are presented in Table 4.8. Home care patients were taking many medications (mean = 11.1) when returning home from the hospital. Most medications were prescribed (mean = 10.3), and consumed via an oral route (mean = 9.7). Given that no inappropriate medications should be used, the potentially inappropriate medication (PIM) score was high (mean PIM score = 3.5) indicating a significant risk of adverse events per subject. The Medication Regimen Complexity Index (MRCI) is a weighted score to evaluate additional actions needed to take medications and assumes daily dosing of oral medications as the simplest regimen. Therefore, medication regimens, as measured by the MRCI score, appear to be very complex (mean score 35.4). Over half (54%) of HHC patients have nine or more medications in their medication regimen, which is a conservative definition for polypharmacy. Eighty-eight percent of patients had at least one PIM in their regimen, and three fourths of the patients had moderate to high medication regimen complexity, defined as an MRCI score greater than twenty. In the judgment of the home health care nurse, all but six patients (99.3%) needed help to manage their oral medications.

Table 4.8. Medication measures for HHC patients (n = 911).

Variables (n = 911)	Mean \pm SD	Range	# Patients	% Patients
Number of Medications	11.1 \pm 5.9	1-40		
PIM Score	3.5 \pm 2.7	0-17.5		
MRCI Score	35.4 \pm 22.4	2-149		
Number of Prescribed Meds	10.3 \pm 5.4	0-36		
Number of PRN Meds	1.6 \pm 1.8	0-13		
Number of PO Meds	9.7 \pm 4.9	0-39		
Number with > 9 Meds			493	54.1%
Had at Least One PIM			805	88.4%
MRCI Score > 20			682	74.9%
Needs Help to Manage Oral Meds			90.5	99.3%

In Table 4.9, differences in the medication related variables for the HHC patients who were not readmitted are compared to patients who were readmitted. Independent *t*-tests were used to determine statistically significant differences for continuous variables, and chi-square tests used to determine statistical significance for categorical variables. Although the mean was significantly different between the patients who were not readmitted and those who were readmitted for each of the medication related variables, this was not the case when the *percentage* of cases was examined in each category. In those who were readmitted, the rate of polypharmacy was nearly 1.5 times that of those

who were not readmitted (73.7% versus 49.1%). Although not as dramatic, significant differences existed in the percentage of those patients who had high MRCI scores was also seen between those who were not readmitted (72.3%) and those who were readmitted (84.9%). However, the difference between patients who had one or more PIM in their regimens was not significant between the group who was not readmitted and the group who was readmitted. Again in both groups nearly all of the patients needed help to manage their oral medications.

Table 4.9. Comparison of medication characteristics for those without readmission versus those with readmission episode (n = 911).

Medication Parameter	Not Readmitted n = 725 (79.6%)	Readmitted n = 186 (20.4%)
Mean Number of Medications	10.4	13.9***
Mean PIM Score	3.4	4.3***
Mean MRCI Score	32.5	46.9***
% With > 9 Medications	356 (49.1%)	137 (73.7%)***
% With 1 or More PIM	634 (87.4%)	171 (91.9%)
% With MRCI > 20	524 (72.3%)	158 (84.9%)***

*** p < .001

Correlation Analysis

An intermediate step, correlation analysis, was undertaken prior to the factor analysis, logistic regression, and SEM to evaluate the degree of correlation between the variables, and in preparation to complete aims two and three. Correlation analyses were used to determine covariates that should be considered for inclusion into the predictive model. Correlation coefficients measure the strength of a linear relationship. The null hypothesis for statistical testing is that the two variables do not have a linear relationship i.e. they are independent of each other. If a correlation does not reach statistical significance, the relationship is likely not a linear relationship. Non-linear relationships violate the assumptions for many modeling procedures (Howell, 2007). Squaring the correlation coefficient will allow an estimation of how much of the variability in a second variable is accounted for by the first variable as opposed to other factors such as measurement error or non-measured variables (Howell, 2007). A weak correlation ($r < .3$) between variables lessens the chance of confounding relationships, and demonstrates independence of the covariates, meaning the covariates are not measuring the same concept. Weak correlations can also be due to restrictions in the range of the data (truncated data) or by having heterogeneous samples in which data points lie far from the regression line (Howell, 2007).

Correlation analyses are also used to determine how closely related the variables in a mediating model are to one another. In this case, it is desirable for the predictors and outcome to have strong relationships, but the mediators should not be so highly correlated to one another that they are essentially measuring the same dimension(s) of the concept in question. If the mediators are highly correlated, the model will not be a well fitted model

because of redundancy in the variables chosen. In that case, the interpretation of the model is in jeopardy. Typically, variables having a 0.7 or greater correlation are considered to be highly correlated and there is a significant amount of shared variance between the two variables (Rummel, 2001).

Six sets of correlation analyses were completed. Because the relationship of the covariates listed in the black box of the analytic model to the main predictor (Charlson Comorbidity Index [CCI]) and the outcome of readmission was unknown at the outset of the study, the analysis for each covariate against each other and against both CCI and readmission was examined. Each analysis evaluated a different block of variables: 1) demographic and functional status variables, 2) physical illness variables, and 3) behavioral status variables.

Table 4.10 demonstrates that none of the demographic and functional status variables were so highly correlated to merit eliminating them from the modeling process except for ADLs and IADLs ($r = .919$), although many of the variables did have correlations that reached significance ($p < .05$, two-tailed test) providing evidence that the relationship is a linear relationship. These variables included comorbidity and life expectancy with readmission; gender with comorbidity; primary caregiver and life expectancy with age; living situation and primary caregiver with gender; primary caregiver, ADLs, and IADLs with life expectancy; and ADLs and IADLs with primary caregiver. Although these relationships are weak as demonstrated by the actual correlation value, nonetheless these variables have a relationship that should be considered in both the logistic regression and structural equation modeling. If the logistic regression modeling process demonstrates that both the ADL and IADL variables should

remain in the SEM model, these variables would then be modeled with a covariance structure. The relationship between comorbidity and readmission may prove to be problematic in the SEM process as the relationship, although significant, is not particularly strong ($r=.196$). This lack of a strong correlation may be related to truncation of the comorbidity data imposed by the only having 11 fields to measure comorbidity, or it may be related to the overall good health of the sample patients.

Table 4.10. Correlation between demographic covariates and readmission.

		Readmission	Comorbidity	Age	Gender	Living Situation	Primary Caregiver	ADL Help Needed	IADL Help Needed	Regimen Change in Last 2 Wks
	Pearson Correlation									
Comorbidity	Pearson Correlation	.196 **								
	Sig. (2-tailed)	.000								
	N	911								
Age	Pearson Correlation	.008	-.009							
	Sig. (2-tailed)	.818	.776							
	N	911	911							
Gender	Pearson Correlation	-.025	-.113 **	.055						
	Sig. (2-tailed)	.447	.001	.096						
	N	911	911	911						
Living Situation	Pearson Correlation	.079 *	.028	.003	-.068 *					
	Sig. (2-tailed)	.018	.404	.938	.039					
	N	910	910	910	910					
Primary Caregiver	Pearson Correlation	.041	.009	.170 **	.070 *	.157 **				
	Sig. (2-tailed)	.221	.782	.000	.034	.000				
	N	911	911	911	911	910				
ADL Help Needed	Pearson Correlation	.006	-.045	-.024	.044	-.146 **	-.519 **			
	Sig. (2-tailed)	.859	.177	.474	.185	.000	.000			
	N	911	911	911	911	910	911			
IADL Help Needed	Pearson Correlation	-.011	-.045	-.019	.053	-.216 **	-.522 **	.919 **		
	Sig. (2-tailed)	.745	.174	.570	.112	.000	.000	.000		
	N	911	911	911	911	910	911	911		
Regimen Change in Last 2 Wks	Pearson Correlation	.001	-.013	.054	-.026	-.038	.016	-.064	-.039	
	Sig. (2-tailed)	.983	.693	.106	.435	.248	.627	.052	.238	
	N	911	911	911	911	910	911	911	911	
Life Expectancy	Pearson Correlation	.117 **	.207 **	.101 **	-.035	.089 **	.058	-.043	-.057	.036
	Sig. (2-tailed)	.000	.000	.002	.288	.007	.081	.196	.087	.284
	N	911	911	911	911	910	911	911	911	911

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

Table 4.11 shows that all of the illness covariates were independent of each other, but weakly related to readmission. Although correlations did not exceed 0.2, a number of pairs of variables had statistically significant correlations indicating that these relationships should be explored further in the logistic regression modeling. If these variables are used in the structural equation modeling, these variable pairs need not be modeled with covariance relationships due to the weakness of the correlations. Relationships such as pressure ulcers, surgical wounds, urinary incontinence and comorbidity with CHF are examples of these statistically significant variable pairs with low correlations. These statistically significant but low correlations suggest that although there is a linear (predictive) relationship, the relationship is quite weak (data points are far from the regression line).

Table 4.11. Correlation between physical illness covariates and readmission.

		Readmission	Age	Any Risk Factor Present	CHF	Diabetes	Pressure Ulcer	Surgical Wound	UTI Treated in Last 2 Wks	Urinary Incontinence
	Pearson Correlation									
Age	Pearson Correlation	.008								
	Sig. (2-tailed)	.818								
	N	911								
Any Risk Factor Present	Pearson Correlation	.000	-.209 **							
	Sig. (2-tailed)	.993	.000							
	N	911	911							
CHF	Pearson Correlation	.108 **	.090 **	.058						
	Sig. (2-tailed)	.001	.007	.081						
	N	911	911	911						
Diabetes	Pearson Correlation	.089 **	-.061	.093 **	-.044					
	Sig. (2-tailed)	.007	.067	.005	.189					
	N	911	911	911	911					
Pressure Ulcer	Pearson Correlation	.079 *	.009	-.017	.073 *	-.023				
	Sig. (2-tailed)	.017	.778	.616	.027	.491				
	N	911	911	911	911	911				
Surgical Wound	Pearson Correlation	-.077 *	-.262 **	.013	-.188 **	-.070 *	-.042			
	Sig. (2-tailed)	.021	.000	.691	.000	.034	.201			
	N	911	911	911	911	911	911			
UTI Treated in Last 2 Wks	Pearson Correlation	.069 *	.077 *	.026	-.010	.032	.048	-.120 **		
	Sig. (2-tailed)	.037	.021	.433	.771	.328	.148	.000		
	N	911	911	911	911	911	911	911		
Urinary Incontinence	Pearson Correlation	.026	.113 **	.050	.079 *	-.036	.149 **	-.115 **	.221 **	
	Sig. (2-tailed)	.430	.001	.135	.017	.271	.000	.001	.000	
	N	911	911	911	911	911	911	911	911	
Comorbidity	Pearson Correlation	.196 **	-.009	.015	.080 *	.019	.070 *	-.080 *	-.010	-.037
	Sig. (2-tailed)	.000	.776	.654	.015	.563	.035	.015	.760	.259
	N	911	911	911	911	911	911	911	911	911

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

Table 4.12 also demonstrates that none of the behavioral covariates are so highly correlated to be of concern that the variable pairs are measuring the same dimension except for memory deficits and impaired decision making with orientation and impaired decision making with memory deficits. These variable pairs are both statistically significant and are moderately correlated. If the results of the logistic regression modeling indicate that these variables should still be included in the structural equation modeling process, covariance between these variable pairs should be indicated in the model using double headed arrows. These relationships illustrate the difficulty in deciding how to model variables that are correlated, but not so strongly to eliminate one variable from a pair of variables.

Table 4.12. Correlation between behavioral covariates and readmission.

		Readmission	Age	Regimen Change in Last 2 Wks	Any Risk Factor Present	Orientation	Memory Deficit	Impaired Decision Making	Depressive Feelings Reported/Observed
	Pearson Correlation								
Age	Pearson Correlation	.008							
	Sig. (2-tailed)	.818							
	N	911							
Regimen Change in Last 2 Wks	Pearson Correlation	.001	.054						
	Sig. (2-tailed)	.983	.106						
	N	911	911						
Any Risk Factor Present	Pearson Correlation	.000	-.209 **	.040					
	Sig. (2-tailed)	.993	.000	.228					
	N	911	911	911					
Orientation	Pearson Correlation	.057	.204 **	.018	-.081 *				
	Sig. (2-tailed)	.084	.000	.588	.014				
	N	911	911	911	911				
Memory Deficit	Pearson Correlation	.088 **	.094 **	.020	-.041	.377 **			
	Sig. (2-tailed)	.008	.005	.546	.215	.000			
	N	910	910	910	910	910			
Impaired Decision Making	Pearson Correlation	.132 **	.093 **	.020	-.008	.377 **	.366 **		
	Sig. (2-tailed)	.000	.005	.546	.821	.000	.000		
	N	910	910	910	910	910	910		
Depressive Feelings Reported/Observed	Pearson Correlation	.129 **	-.037	-.053	-.004	.118 **	.089 **	.185 **	
	Sig. (2-tailed)	.000	.264	.112	.892	.000	.008	.000	
	N	911	911	911	911	911	910	910	
Comorbidity	Pearson Correlation	.196 **	-.009	-.013	.015	-.012	.028	.006	.051
	Sig. (2-tailed)	.000	.776	.693	.654	.720	.407	.849	.126
	N	911	911	911	911	911	910	910	911

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

On the one hand a moderate relationship is desirable to establish a relationship that is being considered for modeling, while on the other hand, if two variables are being considered as predictors for the same outcome, this relationship should be as low as possible as covariance confounds the ability to determine the independent contribution of the variable to the predictive relationship. Variables with this moderate relationship should be carefully modeled and consideration should be given to reasons what dimension these types of variables represent and their combined and unique contributions to the relationship.

In the second set of analyses, the relationships between the predictor variables, age, and the outcome were examined. Age was included in this analysis because of the equivocal findings regarding the relationship of age to medication use patterns. It was found that many of the medication variables (Table 4.13) were significantly and highly correlated to one another. However, for the purpose of this study, the most important relationship was between polypharmacy and medication regimen complexity because these variables were hypothesized as predictors of admissions in the models developed in Chapter 3. Generally, one of the pair of variables should be removed from models when the correlation exceeds 0.7, however since the hypothesized models include all three potential medication mediators, both the polypharmacy and medication regimen complexity variables were retained in the modeling process. Due to the potential for confounding during the modeling process, the relationship between polypharmacy and medication regimen complexity was further explored in the structural equation modeling (SEM) described later in this chapter. SEM elucidates the unique contribution to the

variance of the outcome from each of the variables modeled even if the variables are highly correlated.

The remainder of the medication variables in Table 4.13, with the exceptions of PIM and age, were not considered for the modeling process, so the high correlations between these variables were not of interest. In this study, age was not correlated to any of the medication variables except for medication regimen complexity, but this was not a high enough correlation to merit eliminating the age variable from the modeling process.

Three remaining analyses were evaluated after the logistic regression model was developed and were used to determine which variables should be retained for SEM. These correlation analyses will be discussed in conjunction with the logistic regression findings.

In conclusion, through exploring the first aim, a high level of polypharmacy, potentially inappropriate medication use (PIM), and medication regimen complexity in HHC patients was found. In addition, HHC patients who were readmitted to the hospital had significantly higher levels of polypharmacy, PIM, and medication regimen complexity as indicated by mean scores on measures for these variables. However, the absolute number of PIM medications between those who were not readmitted and those who were readmitted was not significantly different. This implies that those who were readmitted, although having the same number of PIMs in their regimens, may have had riskier PIMs in their regimens.

Table 4.13. Correlation between medication related covariates and readmission.

		Readmission	Age	PP Score	PIM Score	MRCI Score	Needs Help to Manage Oral Medications	Number of Oral Route Medications	Number of Prescribed Medications
	Pearson Correlation								
Age	Pearson Correlation	.008							
	Sig. (2-tailed)	.818							
Polypharmacy	Pearson Correlation	.234 **	-.049						
	Sig. (2-tailed)	.000	.139						
	N	911	911						
PIM Score	Pearson Correlation	.135 **	-.025	.593 **					
	Sig. (2-tailed)	.000	.453	.000					
	N	911	911	911					
MRCI Score	Pearson Correlation	.261 **	-.072 *	.894 **	.530 **				
	Sig. (2-tailed)	.000	.031	.000	.000				
	N	911	911	911	911				
Needs Help to Manage Oral Medications	Pearson Correlation	-.026	-.007	-.033	.016	-.084 *			
	Sig. (2-tailed)	.432	.836	.326	.625	.011			
	N	911	911	911	911	911			
Number of Oral Route Medications	Pearson Correlation	.201 **	-.038	.949 **	.605 **	.792 **	.006		
	Sig. (2-tailed)	.000	.255	.000	.000	.000	.851		
	N	911	911	911	911	911	911		
Number of Prescribed Medications	Pearson Correlation	.248 **	-.063	.975 **	.598 **	.900 **	-.038	.911 **	
	Sig. (2-tailed)	.000	.057	.000	.000	.000	.250	.000	
	N	911	911	911	911	911	911	911	
Number of PRN Medications	Pearson Correlation	.125 **	-.052	.462 **	.345 **	.520 **	-.071 *	.412 **	.459 **
	Sig. (2-tailed)	.000	.117	.000	.000	.000	.033	.000	.000
	N	911	911	911	911	911	911	911	911

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

In the correlation analysis, statistically significant relationships were found between comorbidity, medication variables, and readmission to the hospital, thus helping to establish the mediation model. Individually, although each of the medication variables was related to readmission at a statistically significant level, the correlations were low level correlations. Medication regimen complexity just met the threshold for a desirable moderate correlation ($r > .5$). It is likely that only this variable will prove significant in a reduced model in the logistic regression modeling process. The medication variables were more highly correlated with each other than with the outcome of readmission. That level of covariance needs to be accounted for in the structural equation modeling process. Highly correlated variables that are exogenous should be modeled with covariance pathways and those that are endogenous are likely to be eliminated in model fitting. Polypharmacy and medication regimen complexity exemplify this issue. These variables were so highly correlated with each other, that the relationship will confound the modeling process, if a multivariate modeling process is used, rather than a structural equation modeling process. It is expected that one or more of the redundant medication variables will be eliminated in the model fitting process.

In exploring the first aim, a high level of polypharmacy, potentially inappropriate medication use (PIM), and medication regimen complexity in HHC patients was found. In addition, HHC patients who were readmitted to the hospital had significantly higher levels of polypharmacy, PIM, and medication regimen complexity as indicated by mean scores on measures for these variables. However, the absolute number of PIM medications between those who were not readmitted and those who were readmitted was not significantly different. This implies that those who were readmitted, although having

the same number of PIMs in their regimens, may have had riskier PIMs in their regimens. Finally, polypharmacy and medication regimen complexity were highly correlated with each other, which may confound the modeling process.

Aim Two: Factor Analysis of High Risk Medication Regimens

Factor analysis was implemented to address the research question derived from aim 2, “*Can a construct of high risk medication regimens be created from the operational definitions of polypharmacy, potentially inappropriate medication use, and medication regimen complexity?*” Factor analysis, using the SPSS program, was completed to determine if a newly constructed factor (variable), high risk medication regimens, was composed of one, two, or three of the proposed medication indicator variables, or in the words of Byrne (2010), the variable relationships were tested to see if the concept of high risk medication regimens is multi-dimensional. The proposed factor (in this case called high risk medication regimens) represents the shared variance between the indicator variables (polypharmacy, PIM, and medication regimen complexity). In other words, factor analysis allows the researcher to assess what dimensions in a set of measured indicator variables are shared between the variables and essentially allows the researcher to cluster these dimensions together into one variable in order to reduce the number of variables being used for modeling (Garson, 2010a). In essence, factor analysis clusters similar traits or dimensions together and these clusters of traits or factors define the boundaries of a newly constructed variable or factor. In this analysis, each factor chosen for analysis represents a different dimension and the goal of this analysis was to verify that all three variables are really measuring one factor (dimension), the riskiness of the medication regimen.

Eigenvalues, according to Garson (2010, Factor Analysis), are a ratio of the individual factor variance to the total variance accounted for by the factors being tested and indicate the relative importance the factor contributes to the total variance of the constructed variable. Using the Kaiser rule (Garson, 2010a), eigenvalues over one indicate separate dimensions. If more than one factor had an eigenvalue over one, then those factors are considered to be measuring different dimensions and those factor groupings would be distinctly different from one another (Garson, 2010a). Typically, order of entry does not make a difference in eigenvalues (Thompson & Vidal-Brown, 2001).

A principal axis factoring method, used in theory confirmation or for causal modeling (Garson, 2010a), was used to determine the eigenvalues of the factors. Principal axis factoring, rather than principal components analysis, was used to extract the factors for modeling. Principal axis factoring accounts for the shared covariance between factors contributing to the newly constructed variable and unlike principal components analysis, excludes the unique variance accounted for by the individual factors (Garson, 2010a).

Rotating the factor matrix, if there is more than one factor used to construct the new variable, allows the researcher a better understanding of the variance. Essentially, rotating the matrix helps the researcher determine best fit to the regression line vector when there is more than one cluster. According to Garson (2010, Factor Analysis), rotating the matrix using the varimax rotation, would ensure that the maximum variance between the factors had been extracted and that the factors are clustered in three dimensional space in the most efficient fashion.

Table 4.14A shows the results of the factor analysis using Kaiser's rule. This table has three factors. The total variance explained, shows the initial solution to the factor analysis in the left half of the table and the final solution in the right half of the table. Factor one had an eigenvalue over one (2.359), and explained 77% of the variance in the newly constructed variable high risk medication regimens. In comparison, the eigenvalue attached to factor two was much smaller (.539), and explained only 18% of the variance in the dimension. The final factor had an eigenvalue of .103, thus explaining little of the variance in high risk medication regimens. Factors two and three should be eliminated based on the Kaiser's Rule because both eigenvalues are less than one. When the final solution uses only one factor, 71% of the variance in high risk medication regimens is explained.

Table 4.14A. Results from factor analysis demonstrating a one factor model.

Total Variance Explained						
Factor	Initial Eigenvalues			Extraction Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	2.359	78.620	78.620	2.150	71.655	71.655
2	.539	17.957	96.577			
3	.103	3.423	100.000			

Extraction Method: Principal Axis Factoring.

Therefore, a one factor model (Table 4.14A) explaining 71% of the variance in high risk medication regimens was a reasonable representation of the concept of high risk

medication regimens. The communality (Table 4.14B) is the percent of variance explained by all the factors together and is interpreted as the reliability of the factors in representing the new variable (Garson, 2010a). In this case, the dimension of riskiness of the regimen is best captured by factor one, and least well by factor two. In essence, factor one is the most reliable indicator of high risk medication regimens, followed by factor three. The factor matrix (Table 4.14C) shows the factor loadings. Factors with loadings above .7 indicate the percent of variance in a particular dimension explained by the factor (Garson, 2010a). For example, factor one explains 99% of the variance in the dimension of riskiness of medication regimens, while factor two and factor three explain 60% and 90% of the variance respectively. Essentially, both factors one and three are much better at explaining the variance in high risk medication regimens and both are nearly equal in reliably measuring the dimension of riskiness in medication regimens.

Table 4.14B Communality results demonstrating that medication count is the most effective factor.

Communalities		
	Initial	Extraction
Factor One	.818	.995
Factor Two	.352	.352
Factor Three	.799	.802

Extraction Method: Principal Axis Factoring

Table 4.14C. Factor matrix with percentage of variance in high risk medication regimens accounted for by the factors analyzed.

	1 Factor Solution
Factor One	.998
Factor Two	.594
Factor Three	.896

Extraction Method: Principal Axis Factoring
One factor extracted. 18 iterations required

A second analysis (not shown), using a single factor probability method with principal axis factoring rather than using the Kaiser's rule to determine the number of factors, verified that the number of factors representing the dimension of high risk medication regimens. A one factor solution was again substantiated and the relationship of the factors was the same, although the factor loadings were less than when using Kaiser's rule to determine the loadings.

Aim Three: High Risk Medications and Hospital Readmissions

Logistic Regression Modeling

Once the factor analysis was concluded, logistic regression modeling was also completed in preparation for developing the SEM used to accomplish the research question derived from aim three, "*How much do high risk medication regimens increase the risk of readmission in home health care patients age 65 and over?*" Completing logistic regression modeling assists the investigator to determine which variables are significant and should be included in the final SEM and which variables should be eliminated. The results of logistic regression provided an odds ratio (beta estimate) based

on the odds (number of patients readmitted/number of patients) of being readmitted versus not readmitted to the hospital.

The odds ratio (OR) is:

$$\frac{\text{odds of being readmitted/not having a high risk medication regimen}}{\text{odds of being readmitted/having a high risk medication regimen}},$$

and is interpreted as the increase (if positive) or decrease (if negative) in the odds of being readmitted when the value of the predictor variable increases by one unit. The advantage of logistic regression, according to Howell (2007), is there is no assumption about the population distribution. Logistic regression does assume at least enough outcomes (five outcomes) for the expected cell frequency in the contingency tables and that the observations cannot be in both categories i.e. are independent (Howell, 2007).

The simultaneous model, which is also the starting point for the backward elimination method, is shown in Table 4.15. These variables were tested for inclusion into the logistic regression model and only episode length (odds ratio [OR] = .24, $p = .003$) and emergent care in the previous two weeks (OR = 60.1, $p < .001$), as well as comorbidity, were significant in a reduced model (not pictured). Upon further consideration, episode length was dropped from the model as determination of episode length occurs after the outcome and therefore, the assumption regarding placement within the path would be violated.

Table 4.15. Variables used in logistic regression modeling.

	Variables in the Equation				Odds Ratio	95.0% C.I. for Odds Ratio	
	Parameter Estimate	S.E.	Wald	Sig.		Lower	Upper
	Comorbidity	.200	.082	5.910		.015	1.221
Polypharmacy	.002	.050	.002	.961	1.002	.910	1.105
PIM	.002	.055	.001	.975	1.002	.899	1.116
MRCI Score	.014	.012	1.341	.247	1.014	.990	1.039
Age	-.012	.019	.382	.537	.988	.952	1.026
Life Expectancy < 6 Months	.272	.473	.330	.566	1.313	.519	3.320
Female	.182	.281	.422	.516	1.200	.692	2.081
Caucasian	.667	.883	.571	.450	1.949	.345	10.995
Lives With:							
Spouse	.310	.440	.496	.481	1.364	.575	3.232
Other Family	.399	.425	.881	.348	1.490	.648	3.424
Friend	-17.941	10192.970	.000	1.000	.000	.000	.
Paid Help	.824	1.171	.495	.482	2.279	.230	22.604
Spouse & Family	-.395	.800	.244	.621	.674	.141	3.229
Primary Caregivers:							
Spouse	1.129	1.548	.532	.466	3.092	.149	64.215
Child(ren)	1.555	1.463	1.129	.288	4.735	.269	83.354
Other Family Member	.682	1.520	.201	.654	1.977	.100	38.899
Friend/Neighbor	2.984	1.656	3.249	.071	19.769	.771	507.207
Paid Help	.422	1.011	.174	.676	1.525	.210	11.062
ADL Help Needed	-1.070	1.420	.567	.451	.343	.021	5.549
IADL Help Needed	-.372	.909	.167	.683	.689	.116	4.098
Help with Oral Medication Management Needed	-1.714	1.337	1.644	.200	.180	.013	2.474
Cognitively Impaired	-.189	.345	.301	.583	.828	.421	1.626
Depressive Symptoms	.210	.335	.394	.530	1.234	.640	2.381
Memory Impairment	.025	.506	.002	.960	1.026	.381	2.764
Impaired Decision Making	.819	.511	2.569	.109	2.269	.833	6.181
Pressure Ulcers	.755	.512	2.177	.140	2.128	.780	5.805
Surgical Wounds	-.063	.278	.051	.821	.939	.545	1.619
UTI Tx in Last 2 Weeks	-.012	.426	.001	.977	.988	.428	2.276
Urinary Incontinence	-.188	.298	.400	.527	.828	.462	1.484
Catheter to Contain Leakage	-.579	.586	.976	.323	.561	.178	1.767
CHF	.898	.525	2.920	.088	2.454	.876	6.869
Diabetes	.913	.624	2.141	.143	2.491	.734	8.456
Regimen Change in Last 2 Weeks	.114	.514	.049	.825	1.120	.409	3.066
Emergent Care in Last 2 Weeks	3.834	.274	196.018	.000	46.240	27.035	79.087
HHC Episode Length	-1.259	.334	14.256	.000	.284	.148	.546
Constant	-.507	2.334	.047	.828	.602		

A second logistic regression (Table 4.16A) was run without length of stay in home care as part of the regression. In this run, pressure ulcers, comorbidity, and emergent care use in the previous two weeks were statistically significant. However, it was determined that there was almost a 1:1 correspondence between emergent care use and readmission. Emergent care use was also very close to the cut off value to assess whether two variables are measuring the same concept ($r = .6$). Given the high correlation and the potential for confounding due to the level of missing data in this particular variable, it was felt that this variable was too unreliable to include in the modeling process. Even if the emergent care use variable was deemed reliable, this variable likely would act as a proxy for readmission. Since the outcome variable of readmission, as a concept, should not be measured twice in the model, emergent care use was dropped as a predictor. However, it is important to note that those who have used emergent care use in the previous two weeks are 40 times ($p < .001$) more likely to be readmitted to the hospital than those who have not used emergent care.

Table 4.16A. Original reduced logistic regression model.

Variables in the Equation							
	Parameter Estimate	S.E.	Wald	Sig.	Odds Ratio	95.0% C.I. for Odds Ratio	
						Lower	Upper
Comorbidity	.198	.072	7.621	.006	1.218	1.059	1.402
Polypharmacy	.005	.045	.013	.911	1.005	.920	1.098
PIM	-.005	.051	.008	.927	.995	.900	1.101
MRCI Score	.016	.011	2.036	.154	1.016	.994	1.039
Pressure Ulcer	.893	.458	3.811	.051	2.443	.996	5.990
Emergency Care Any Venue in Last 2 Weeks	3.697	.239	239.136	.000	40.319	25.236	64.417
Constant	-3.573	.293	149.181	.000	.028		

Thus, the logistic regression was run a third time using the maximum likelihood ratio, with forward selection and backward elimination methods producing the same results in the choice of significant variables (Table 4.16B). Of the predictor variables, only the CCI (CCI Wald statistic = 15.855, $p < .001$, OR = 1.24) and MRCI (MRCI Wald statistic = 4.247, $p = .039$, OR 1.017) scores increased the odds of being readmitted and were significant predictors in the initial modeling. However, the remaining medication variables (polypharmacy and PIM) were not found to be predictors of readmission in the reduced logistic regression model. Significant covariates associated with an increased risk of readmission in the reduced logistic regression model (excluding episode length and emergent care) included a diagnosis of congestive heart failure (Wald statistic 5.055, $p = .025$, OR = 2.24), impaired decision-making (Wald statistic 9.106, $p = .036$, OR = 2.12), and symptoms of depression (Wald statistic 5.853, $p = .003$, OR = 2.50). Based on the Wald statistic, removing comorbidity from the model would have the largest effect on the predictive ability, followed, in order, by impaired decision making, depressive symptoms, CHF, and MRCI score.

Table 4.16B. Final reduced logistic regression model.

Variables in the Equation							
	Parameter Estimate	S.E.	Wald	Sig.	Odds Ratio	95.0% C.I. for Odds Ratio	
						Lower	Upper
Comorbidity	.215	.054	15.855	.000	1.239	1.115	1.377
Polypharmacy	.016	.032	.252	.616	1.016	.954	1.082
PIM	.005	.038	.020	.887	1.005	.933	1.083
MRCI Score	.016	.008	4.247	.039	1.017	1.001	1.032
Depressive Symptoms	.524	.217	5.853	.016	1.689	1.105	2.581
Impaired Decision Making	.915	.303	9.106	.003	2.497	1.378	4.524
CHF	.808	.359	5.055	.025	2.244	1.109	4.539
Constant	-2.709	.209	168.546	.000	.067		

Overall model statistics:

Chi-square: 98.787, df 7; $p < .001$

Nagelkerle R Squared: 0.152

Model Fit (Hosmer/Lemeshow): Chi-square: 9.523, df 8, $p = .300$

The actual fit of the model was good as demonstrated in a significant chi-square omnibus test (chi-square = 98.8, $df = 7$, $p < .001$). The omnibus chi-square predicts whether the model with the predictors differs significantly in predictive capability for the outcome variable than just with the intercept alone (Garson, 2010b).

The Hosmer-Lemeshow statistic, which should *not* be significant, demonstrates that the predictive model is not significantly different than what the observed data shows (Garson, 2010b).

In the logistic regression model, 15.2% of the variance in readmission is explained by these predictors and covariates; the remaining variance is either covariates not measured or considered for the modeling process, or is due to error.

The overall model (Table 4.16C) predicted those patients not being readmitted and those being readmitted correctly in 79.9% of the cases. Above the fifty percent cut off level (chance), comorbidity alone, correctly predicted 3.8% of those who were hospitalized. However, adding in the medication related predictors, increased the percentage correctly predicted to be readmitted by almost a threefold factor to 9.7%. Using all the significant covariates in addition to comorbidity and the medication related variables increased the percent correctly predicted over chance to 14.5%.

Table 4.16C. Correctly predicted classification of readmission above chance.

Patients Correctly Predicted	Not Hospitalized	Hospitalized
Null Model (no predictors)	100%	0%
Comorbidity Alone	100%	3.8%
Comorbidity + Predictor variables	97.0%	9.7%
All Covariates	98.7%	14.5%

Overall Model: 79.9% at cut point of .50

Table 4.17 shows the predictors that were significant when comorbidity was the outcome of interest. The step-wise elimination process was completed to determine whether some of the covariates were related to comorbidity and should also be included in the SEM modeling. The three significant covariates remaining from the full model included life expectancy less than six months, female gender and Caucasian ethnicity. Therefore, these variables were included in the SEM modeling.

Life expectancy was highly predictive of comorbidity; those with a life expectancy of less than six months were almost four times as likely to have higher comorbidity. Being female or Caucasian had a protective effect on being readmitted, with being female decreasing the odds of being readmitted to almost half those of males, and being Caucasian reducing the odds of being readmitted to three fourths of those patients who were not Caucasian.

Table 4.17. Predictors of comorbidity.

	Variables in the Equation						
	Parameter Estimate	S.E.	Wald	Sig.	Odds Ratio	95.0% C.I. for Odds Ratio	
						Lower	Upper
Life Expectancy	1.271	.314	16.352	.000	3.566	1.926	6.604
Female	-.543	.211	6.638	.010	.581	.385	.878
Caucasian	-1.312	.630	4.331	.037	.269	.078	.926
Constant	-.562	.636	.780	.377	.570		

Correlation Analysis Revisited

The second set of correlation analyses were completed to establish whether any of the pre-determined covariates should be modeled with covariance structures in the path analysis, or if the covariates were only related to just the outcome variable rather than to each other.

Table 4.18 illustrates the relationship of the covariates predicting comorbidity, as well as, the relationship of comorbidity to the potential medication variables. Although all of the medication variables were significantly related to comorbidity, none of the variable relationships were strong enough to be considered as likely confounding relationships. Both gender and ethnicity carried a negative sign indicating that being female or Caucasian was less likely to correlate with higher comorbidity. The most important finding from this analysis was that the predictors of comorbidity were independent of one another and will not co-vary with one another.

Table 4.18. Correlations of variables related to comorbidity.

		Readmitted	Comorbidity	Polypharmacy	PIM	MRCI Score	Life Expectancy	Female
	Pearson Correlation							
Comorbidity	Pearson Correlation	.196**						
	Sig. (2-tailed)	.000						
	N	911						
Polypharmacy	Pearson Correlation	.234**	.203**					
	Sig. (2-tailed)	.000	.000					
	N	911	911					
PIM	Pearson Correlation	.135**	.028	.593**				
	Sig. (2-tailed)	.000	.401	.000				
	N	911	911	911				
MRCI Score	Pearson Correlation	.261**	.252**	.894**	.530**			
	Sig. (2-tailed)	.000	.000	.000	.000			
	N	911	911	911	911			
Life Expectancy	Pearson Correlation	.117**	.207**	.065	.079*	.127**		
	Sig. (2-tailed)	.000	.000	.051	.017	.000		
	N	911	911	911	911	911		
Female	Pearson Correlation	-.025	-.113**	-.052	-.030	-.073*	-.035	
	Sig. (2-tailed)	.447	.001	.117	.367	.029	.288	
	N	911	911	911	911	911	911	
Caucasian	Pearson Correlation	-.031	-.052	.023	.051	-.005	-.007	-.020
	Sig. (2-tailed)	.352	.117	.484	.124	.874	.830	.542
	N	911	911	911	911	911	911	911

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

Table 4.19 depicts the relationships between readmission, CCI, the medication variables, and the covariates. Three important findings are of note. Congestive heart failure (CHF) was independent of the other covariates for predicting readmission. Impaired decision making shared covariance with depressive feelings, and should have the covariance indicated in the SEM modeling. Finally, CHF was correlated with the polypharmacy and the MRCI score, while, depressive feelings was correlated with all three medication predictors. Although they share covariance, when assessed with binary logistic regression, the amount of variance accounted for in each of the medication related variables by these two predictors, although statistically significant, was of little practical importance. For example R-squared for CHF with both polypharmacy and MRCI score was .11. In addition, although CHF also shares some covariance with comorbidity, the amount is small in all cases and therefore, will not be accounted for in the SEM.

A final correlation analysis (Table 4.20) was conducted to determine if predictors of comorbidity were related to predictors of readmission. In this analysis, it was demonstrated that gender and ethnicity were not correlated to any of the other covariates, while life expectancy was related to impaired decision making and depressive symptoms. Impaired decision making was again shown to be related to depressive symptoms. Each of these significant correlations was represented in the SEM by a covariance arrow.

Table 4.19. Correlations of variables related to readmission.

		Readmission	Comorbidity	Polypharmacy	PIM Score	MRCI Score	CHF	Impaired Decision Making
	Pearson Correlation							
Comorbidity	Pearson Correlation	.196**						
	Sig. (2-tailed)	.000						
	N	911						
Polypharmacy	Pearson Correlation	.234**	.203**					
	Sig. (2-tailed)	.000	.000					
	N	911	911					
PIM Score	Pearson Correlation	.135**	.028	.593**				
	Sig. (2-tailed)	.000	.401	.000				
	N	911	911	911				
MRCI Score	Pearson Correlation	.261**	.252**	.894**	.530**			
	Sig. (2-tailed)	.000	.000	.000	.000			
	N	911	911	911	911			
CHF	Pearson Correlation	.108**	.080*	.114**	.012	.110**		
	Sig. (2-tailed)	.001	.015	.001	.715	.001		
	N	911	911	911	911	911		
Impaired Decision Making	Pearson Correlation	.132**	.006	.031	.053	.064	.010	
	Sig. (2-tailed)	.000	.849	.354	.110	.055	.754	
	N	910	910	910	910	910	910	
Depressive Feelings Reported/Observed	Pearson Correlation	.129**	.051	.125**	.138**	.120**	-.020	.185**
	Sig. (2-tailed)	.000	.126	.000	.000	.000	.542	.000
	N	911	911	911	911	911	911	910

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

Table 4.20. Correlations between covariates used in SEM.

		Life Expectancy	Female	Caucasian	Impaired Decision Making	CHF
	Pearson Correlation					
Female	Pearson Correlation	-.035				
	Sig. (2-tailed)	.288				
	N	911				
Caucasian	Pearson Correlation	-.007	-.020			
	Sig. (2-tailed)	.830	.542			
	N	911	911			
Impaired Decision Making	Pearson Correlation	.135**	-.036	.032		
	Sig. (2-tailed)	.000	.272	.340		
	N	910	910	910		
CHF	Pearson Correlation	.035	-.031	.025	.010	
	Sig. (2-tailed)	.292	.347	.443	.754	
	N	911	911	911	910	
Depressive Symptoms	Pearson Correlation	.070*	-.036	-.022	.185**	-.020
	Sig. (2-tailed)	.036	.276	.510	.000	.542
	N	911	911	911	910	911

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

Structural Equation Modeling (SEM)

SEM Procedure Description

Structural equation modeling (considered to be a form of path analysis) was performed on the analytic models presented in chapter 3 (Figure 4.2 – 4.4). Garson (2009, SEM) explains path modeling as the following process. Path arrows are drawn between the predictor variables to outcome variables and represent the standardized beta coefficients associated with the direct effect of one variable on the outcome variable in the path. In models with multiple causal variables, these paths represent partial regression coefficients which control for the effect of prior variables in the path. Structural equation modeling is able to model covariance structures, and can easily handle latent variables with many indicators (Garson, 2009b).

Those variables with only outgoing arrows are considered exogenous variables. In the model these variables do not have a “cause”. Endogenous variables are those with both incoming arrows and outgoing arrows, indicating both the predictive nature and the outcome nature of the variable (Garson, 2009b). These variables have a residual error term (disturbance term) associated with the variable that is composed of both measurement error and the effect of unmeasured variables in a particular model (Garson, 2009b). Double headed arrows for the path reflect variables that are correlated. SEM calculates all regression coefficients simultaneously (Garson, 2009b).

Once the paths are calculated, models can be compared using various “goodness of fit” indices, such as those listed in Table 4.21 (p. 219). “Fit” is the ability of the model to reproduce what is happening in the data. Good fit does not imply validity of the model.

The goal of path analysis is to mathematically describe a model and have that model “fit” the data being used. In path analysis, the null hypothesis is that the model (factor loadings, variances, covariances, and error variances) have been correctly specified and that the model fits perfectly to the population as represented by the sample being tested (Byrne, 2010). The hope is *not* to reject the null hypothesis, meaning that a non-significant value for the chi-square statistic, represented by CMIN statistic (chi-square minimum discrepancy), indicates a good fitting model (Byrne, 2010; Garson, 2009b). When evaluating models, higher probabilities indicate closer fitting (increasingly perfect fitting) models for most indices.

Byrne (2010) describes models as being on a continuum from being independent, with each variable representing a factor perfectly and without shared covariance between factors, to the saturated model where data points and estimated parameters are equal. The independence model is the null model and is a restricted model because no variables can co-vary. Models being tested should lie somewhere between these two endpoints on the continuum. A good fitting model should be parsimonious (having the least number of parameters while still adequately describing the data), should adequately describe the data, be specified accurately, and be replicable (Byrne, 2010).

Model fitting is a reiterative process. Once the model is chosen based on the goodness of fit, interpreting the paths may proceed. Garson (2009, SEM) notes that even though the model may be an overall good fit, portions of the model may be ill fitting, with insignificant individual paths, indicating further modification of the model should be made in an attempt to develop a more parsimonious model. Once post hoc analysis of the model is completed, the goodness of fit indices and paths are again re-evaluated to

determine whether the subsequent model is an improvement over the original model proposed (Garson, 2009b).

Assumptions Underlying SEM

SEM is a more forgiving process than path analysis, which must meet the assumptions of multivariate normality, rather than just normality of the individual variables. Compared to path modeling, fewer assumptions must be met before using SEM (Garson, 2009b). Assumptions include:

- Models must have enough structural equations to be able to solve for the unknown variables. This is akin to having enough data points to draw conclusions.
- Models must include all of the significant causal variables. Changing one variable changes the whole model.
- Appropriate correlations must be calculated given the data i.e. biserial for interval and dichotomous variables, Pearson for two interval variables.
- The sample size must be large enough; 10-20 times the number of parameters being tested (Garson, 2009b; Byrne, 2010).
- Samples cannot be modified between testing different models.

Researchers traditionally have used the minimum discrepancy (CMIN), which is a chi-square statistic, to evaluate the overall fit of the model. This test statistic is used to evaluate the null hypothesis that all the covariance residuals are zero. However, both Byrne (2010) and Garson (2009, SEM) discuss problems with this goodness of fit test. Byrne notes that large sample sizes with few degrees of freedom will often yield falsely

non-significant overall model fit and large chi-square statistics. Garson notes that the chi-square is a very conservative statistic and researchers may choose to reject the finding of a significant chi-square, especially if other, more specific measures, demonstrate a good fit. This is true in cases where the model is not especially complex, or has few degrees of freedom relative to the sample size, as the CMIN factors in the complexity of the model. Typically the CMIN statistic requires 75-200 cases to be a valid measure. A significant chi-square is also likely in cases where non-interval level data are used in developing the model, as the chi-square is particularly sensitive to violations of multivariate normality of the data (Garson, 2009b). Chi-square is also extremely sensitive to highly kurtotic data (Garson, 2009b).

According to Garson (2009b), in situations when the CMIN is significant, a normed chi-square (chi-square/degrees of freedom or $CMIN/df$), which takes into account the degrees of freedom, may be more useful as a test of fit. Most researchers believe a normed value should have a 3:1 or a 2:1 ratio to be considered a good fit. However, some researchers let that value increase to 5:1 and still consider the model a good fit (Garson, 2009b). Due to the issues with the omnibus tests, researchers have developed a number of other goodness of fit indices which address specific issues. These tests generally fall into four categories: 1) those that are information theory goodness of fit indices used to compare models against one another, 2) non-centrality goodness of fit measures that test the hypothesis that chi-square is greater than zero, 3) goodness of fit tests which usually test the developed model against the null model (independence model), and 4) tests that evaluate the parsimony of the model (Byrne, 2010; Garson, 2009b).

The basic information theory goodness of index is the Akaike Information Criterion (AIC). The AIC is used to evaluate the discrepancy between the covariance matrix of the model and that of the actual data. It carries a penalty for unnecessarily complex models. The AIC is used to compare models to each other, with the lower AIC (best if close to zero) the better fitting model (Garson, 2009b). Other information theory indices are adjusted for smaller sample sizes or carry larger penalties for increased model complexity (Byrne, 2010). An example would be the expected cross-validation index (ECVI) which is similar to the AIC in evaluating the discrepancies between the observed and implied model matrices, but penalizes for degrees of freedom (Garson, 2009b).

The comparative fit index (CFI) is a non-centrality index that assesses the fit of the developed model against the independence model. It is not much affected by sample size (Garson, 2009b). For that reason, the CFI has superseded the normed fit index (NFI), which has been the default index for a number of years (Byrne, 2010). However, smaller samples and increased model complexity both affect the NFI (Byrne, 2010). Values for the CFI should be above .90 to be considered a good fit (Garson, 2009b).

Similar to the idea that significance may be found just because the sample is extremely large, complex models often demonstrate overall better fit, just because there are a larger number of estimated parameters (Garson, 2009b). The parsimony indices address this issue by penalizing models that are unnecessarily complex (Garson, 2009b). The parsimony comparative fit index (PCFI) is one commonly used measure to evaluate parsimony; the lower the number, the better the fit (Garson, 2009b).

However, the most useful index, and one of the oldest indices, is the RMSEA, the root mean square error of approximation (Byrne, 2010). The RMSEA normalizes the data

and therefore is not so affected by sample size (Garson, 2009b). Garson (2009b) suggests the RMSEA retains popularity as it does not require a null model as a comparator, it is based on a chi-square distribution (allows for non-normality of the data), and corrects for non-parsimonious models. Good fit is suggested by p values of $\leq .05$, with adequate fit at $p \leq .08$ (Garson, 2009b). An associated statistic, PCLOSE, assesses how close the REMSEA is to the .05 cut off. Values greater than .05 indicate a poor fitting model (Garson, 2009b).

As indicated by the above discussion, an ongoing issue with many of the fit indices is the sample size effect on the test statistic. Hoelter's Critical N attempts to rectify this issue by addressing whether the sample size is large enough to truly specify a good fitting model. This statistic addresses the chi square (CMIN) statistic and specifies how small a sample size must be for the result to be no longer significant, with values > 200 having an adequate sample size to represent the sample in the model building process (Byrne, 2010; Garson, 2009b).

Modeling Results

Six model variations (3 full models and 3 reduced models) were tested to identify a good fitting model. The models tested are depicted in Figures 4.3 - 4.9 and are labeled by how they appear visually in the path diagram. In the full models, the relationships between comorbidity, the medication variables, and readmission were developed based on the findings from the literature review. The three reduced models were based on reiterations of the modeling process as well as a combination of the logistic regression and the literature review. The covariate pathways did not differ between models and were based on findings from the literature, correlation analyses, and logistic regression. No

matter the model, these pathways remained significant throughout all the model iterations, and therefore were able to be held constant across models. This allowed the researcher to compare the main portion of the model without changes in the covariate pathways affecting the fit statistics. The models will be discussed in the order of development, with the original models from Chapter 3 discussed first followed by a discussion of the reduced models.

The comparison of model results is shown in Table 4.21. In addition to the omnibus hypothesis indices ($CMIN$, p , and $CMIN/df$), four indices recommended by Garson (2009, SEM) were evaluated, as well as the Hoelter index for assessing the adequacy of the sample size, in order to specify a good fitting model. As none of the models proposed in Chapter 3 were feasible when evaluating the omnibus fit indices, the RMSEA and $CMIN/df$ were used to determine if a model was even viable. Comparisons of the remaining fit statistics assisted in determining which remaining model was the best fitting model.

Based on the omnibus test with the associated p value (Table 4.21), the models proposed in Chapter 3 (Figures 3.2, 3.3, and 3.4) had insignificant chi-square statistics, and therefore, if only the omnibus test was considered as the fit index, none of the models would be a good fitting model. This is likely the result of highly kurtotic categorical data, and the fact that these are simple models with few degrees of freedom. The chi-square is very sensitive to both of these issues. However, aside from the Mediating Model (Figure 4.4), the $CMIN/df$ ratios were all near a 2:1 ratio. This normed chi-square ($CMIN/df$), which is not sensitive to the above issues, does indicate that model depicted in Figures

4.5- 4.9 are reasonably good fitting models. However, other parameters were used to assess goodness of fit of the models to ensure that this was indeed the case.

The r-squared was also evaluated for the outcome of readmission. All models showed an r-squared of 10% of the variance being explained by the particular model. However, the r-squared is not a particularly reliable indicator of good model fit as many of the other model fit indices varied substantially while the r-squared did not. Therefore, this particular statistic, although informative in demonstrating how little variance was actually explained by the model, was not helpful in determining the model fit in this exploratory research.

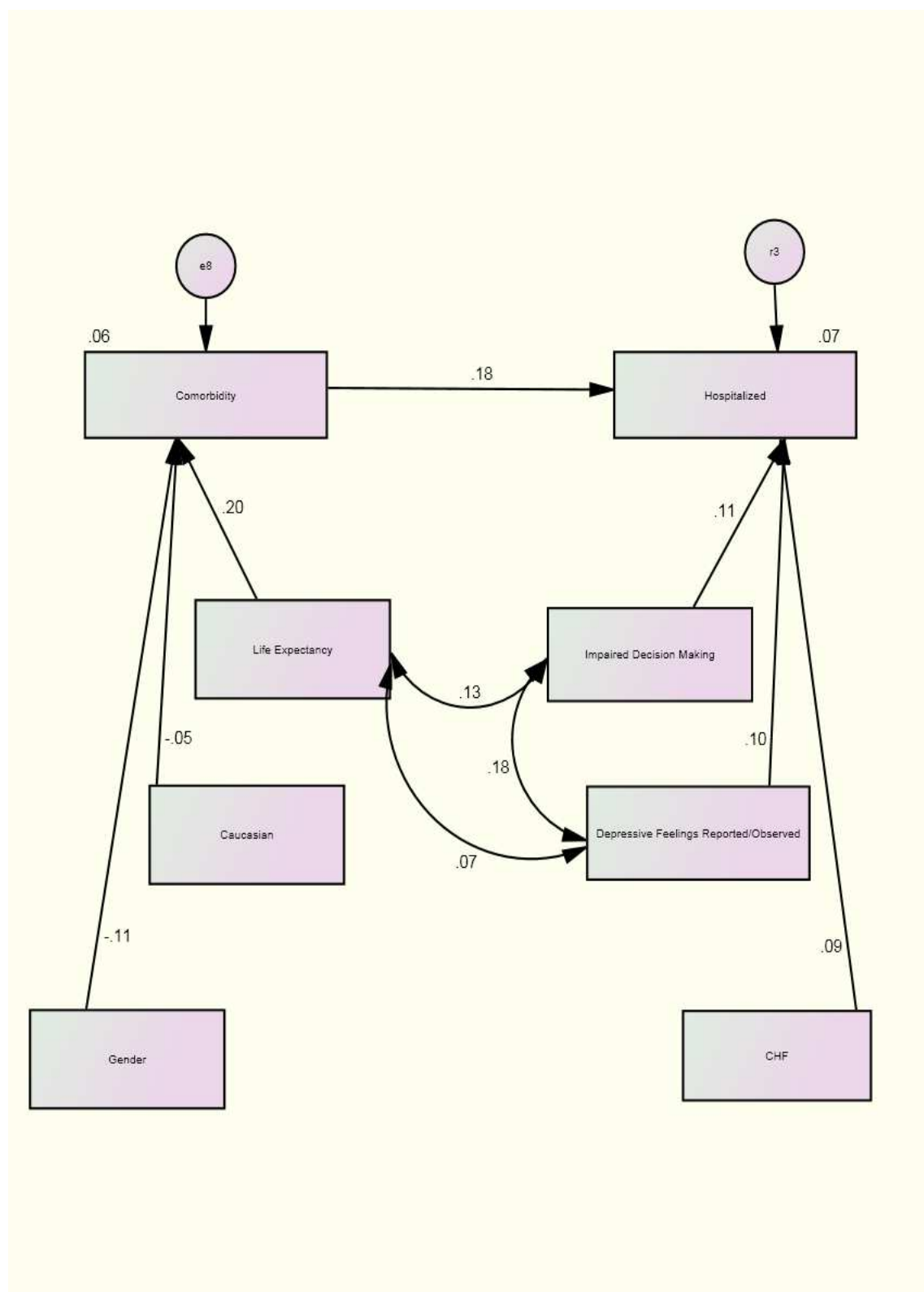
Table 4.21. Comparison of structural equation model fit indices.

Models	CCI Figure 4.3	Mediating Figure 4.4	HRMR Figure 4.5	Waterfall Figure 4.6	2 Pathway Figure 4.7	1 Pathway Figure 4.8	MRCI Figure 4.9
CMIN	18.49	1910.208	42.85	117.36	64.55	88.05	44.54
(<i>p</i> value)	(.424)	(.000)	(.010)	(.000)	(.000)	(.000)	(.007)
CMIN/ <i>df</i>	1.03	48.98	1.79	2.93	2.08	2.75	1.86
CFI	1.00	.13	.92	.96	.98	.97	.92
PCFI	.50	.08	.49	.58	.55	.56	.49
RMSEA	.005	.23	.03	.05	.03	.04	.03
(CI)	(.00-.03)	(.22-.24)	(.01-.04)	(.04-.06)	(.02-.05)	(.03-.06)	(.02-.05)
AIC	70.49	1986.21	102.85	191.36	132.55	154.05	104.54
Hoelter	1422	26	774	433	635	478	745
<i>r</i> ² Hospitalized	.071	.095	.096	.098	.101	.098	.101

Suggested values: CMIN < 2; *p* value > .05; CMIN/*df* = 3:1 ratio or 2:1 ratio; CFI = .90; PCFI-lower is better; RMSEA < .05; AIC-lower is better; Hoelter > 200

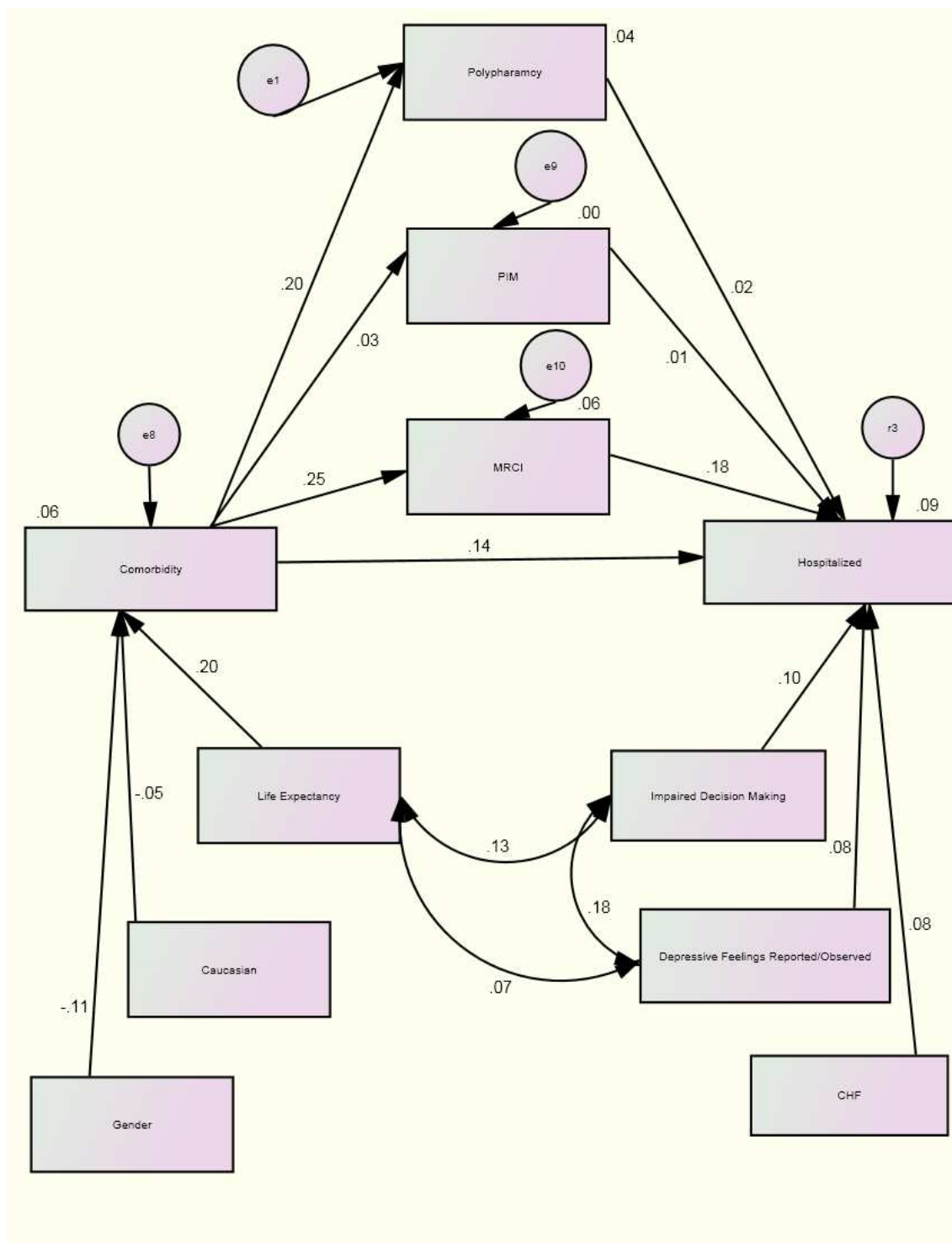
The Comorbidity (CCI) Model. This baseline model (Figure 4.3) depicts the focal relationship before the proposed medication related variables are added into the model. This is the model to which the other models will be compared. Hoelter's Critical N reveals that sample size is adequate for the model specification. Based on the CMIN value of 18.49 (< 2 is the best fitting model), this model is not a particularly good fitting model, although it does meet the desirable non-significance criterion. The poorer fit as indicated by the CMIN is most likely related to the sensitivity of the CMIN statistic to the kurtosis and lack of multivariate normality in the data. However, examining the CMIN/df statistic reveals a reasonably good fitting model as a statistic approaching "1" is the most desirable. The model is parsimonious as indicated by the PCFI statistic. The remaining fit indices also all indicate a reasonable fitting model.

Figure 4.3. The Comorbidity Model.



The Mediating Model. All models had sample sizes adequate to accurately model the data except for the Mediating Model (Figure 4.4). The Mediating Model had an inadequate sample size to accurately model the number of parameters in the model. Therefore, the Mediating Model demonstrated significant issues with the chi-square statistic. This statistic was so large relative to the degrees of freedom, that the goodness of fit statistics was severely affected by the discrepancy. Although this model was the original model proposed in Chapter 3, the model was dropped from consideration of model fit as the Hoelter index was only 26, indicating a model that had too many degrees of freedom for the sample size evaluated. Therefore, based on both the CMIN/*df* and other fit statistics, this model does not warrant discussion other than as the basis for further model development.

Figure 4.4. The Mediating Model.



The High Risk Medication Model. The factor analysis process demonstrated that a new variable, named high risk medication regimens could be formed based on the combination of polypharmacy, potentially inappropriate medication use, and medication regimen complexity. The next model tested (described in Chapter 3), included this new variable as the mediating variable (Figure 4.5).

Excluding the Comorbidity and the Mediating Models, the remaining models' CMIN statistics all were significant. The null hypothesis in SEM indicates that the model has been specified correctly. So a statistically significant finding, in essence, means that the model has not been specified correctly. The CMIN statistic was lowest for this model, of all the models proposed as alternatives to the Comorbidity Model. As the CMIN statistic is affected by the non-normality of the data, the significant CMIN statistic for the HRMR Model was likely the result of the influence of the kurtotic PIM medication data in the high risk medication regimen variable. Therefore, the alternative fit indices were used to assess model fit for the remaining models. All the remaining models had RMSEAs of .05 or less indicating a good model fit. The HRMR Model was a distinct improvement in both model fit and parsimony ($CMIN/df = 1.79$, $RMSEA = .029$, $PCFI = .492$) compared to the Mediating Model. These fit statistics were well within the parameters for good model fit suggested by Garson (2009, SEM).

The path coefficients in High Risk Medication Regimen Model are all significant (Table 4.22), indicating that no paths should be deleted from the model, and that the model was indeed the most parsimonious model of the models tested. However, the fit statistics for this model were not as good as the fit statistics for the Comorbidity Model.

Figure 4.5. The High Risk Medication Regimen Model.

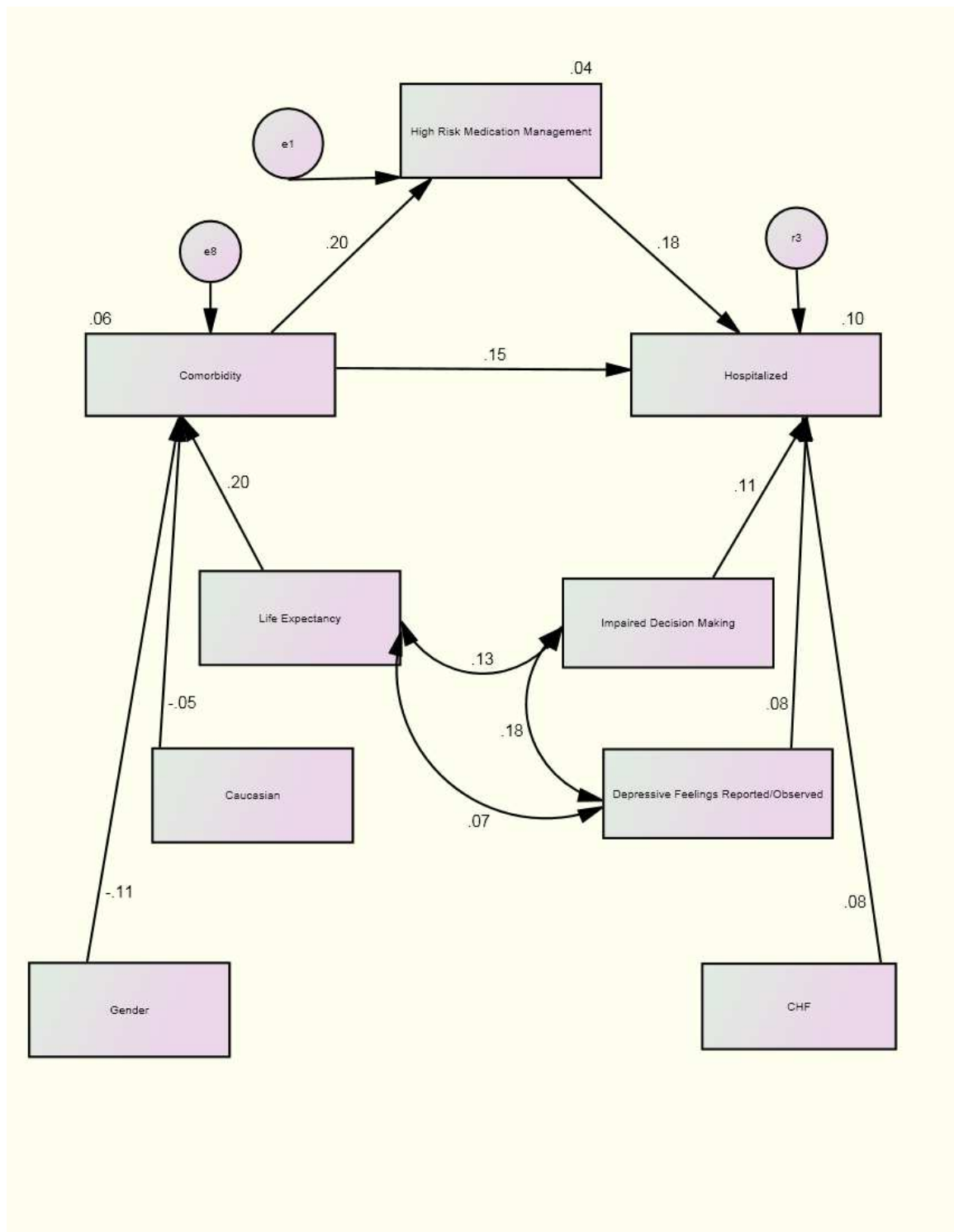


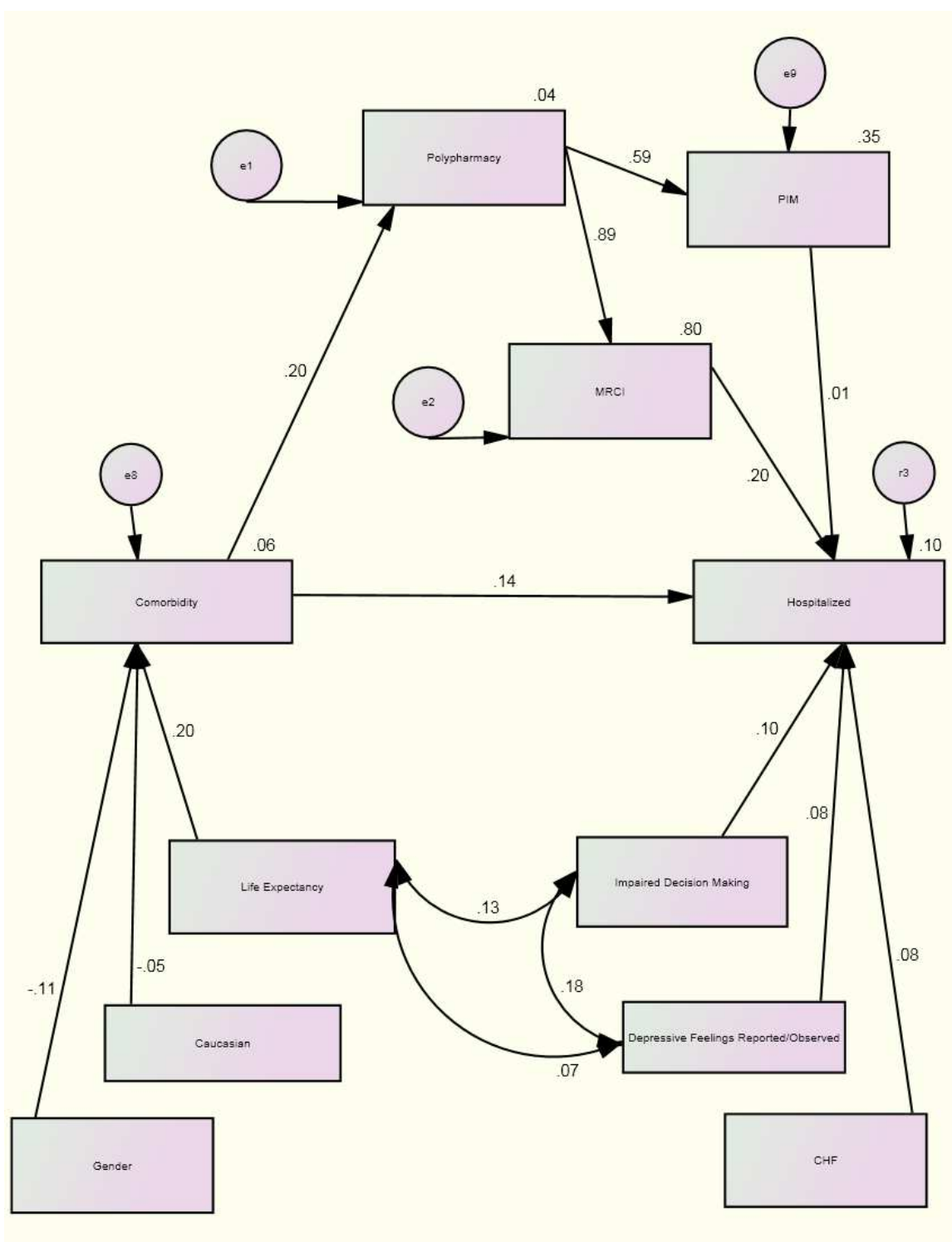
Table 4.22. Unstandardized regression coefficients for HRMR model.

			Estimate	S.E.	C.R.	P
Comorbidity	<---	Gender	-.322	.097	-3.240	***
Comorbidity	<---	Life Expectancy	1.237	.196	6.312	***
Comorbidity	<---	Caucasian	-.654	.400	-1.631	.102
HRMR	<---	Comorbidity	.138	.022	6.304	***
Readmission	<---	Comorbidity	.041	.009	4.617	***
Readmission	<---	HRMR	.074	.013	5.637	***
Readmission	<---	Impaired Decision Making	.180	.052	3.439	***
Readmission	<---	Depression	.088	.035	2.495	.013
Readmission	<---	CHF	.151	.063	2.399	.016

The Waterfall Model. The Waterfall Model was developed to account for the covariance between polypharmacy, PIM and medication regimen complexity. Although the Waterfall Model (Figure 4.6) had a RMSEA of .046, this model was not the most parsimonious model (fewest parameters possible) as indicated by the PCFI of .584, nor was it the best fitting model as indicated by the AIC (191.362) which was higher than the AIC of the HRMR model depicted in Figure 4.6. The CFI, which tests against the independence model, was the second highest of all the original models tested at .964. However, since the CMIN/*df*, the PCFI, and the AIC were higher than in the HRMR

model, this model was removed from contention as the best fitting model of the alternatives to the Comorbidity Model.

Figure 4.6. The Waterfall Model.



Post Hoc Analysis

During the post hoc analysis, three alternative models were developed based on the literature review, the logistic regression findings, evaluation of both the Mediating Model (Figure 4.4) and the Waterfall Model in Figure 4.6. These models were reduced models developed by reiterative process of evaluating the parameter estimates for significance. Both the Two Pathway Model (Figure 4.7) and the One Pathway Model (Figure 4.8) were developed based on the finding that polypharmacy was associated with both PIM and medication regimen complexity. This was clearly demonstrated in the reiterative modeling process which showed both PIM pathways (comorbidity to PIM, and PIM to readmission) in the Mediating Model to be insignificant, as was the polypharmacy to readmission pathway. These were expected findings as the correlation analysis demonstrated high correlations between these variables and the logistic regression modeling demonstrated that both of these variables were insignificant in the final logistic regression model. Therefore, all three pathways were modified or removed in subsequent model specification. Since the models were developed based on the initial modeling results and are really variations on a theme, the models will be compared to one another.

The One and Two Pathway Models. The Two Pathway Model in Figure 4.7 was developed when PIM and the associated pathways, as well as the polypharmacy to readmission pathway, were entirely removed from the model. Polypharmacy was instead connected to readmission through MRCI instead of directly to readmission. This model had the highest CFI (.981) of all the models tested, indicating the fit was the least close to the independence model, in which there is no relationship of the variables to each other. Although the Two Pathway Model improved the fit indices over the Waterfall Model, it

was theorized that model parsimony could be further improved by eliminating the separate pathway to MRCI. Subsequently, a One Pathway Model, shown in Figure 4.8, was developed where both polypharmacy and MRCI were in the same pathway. The Two Pathway and One Pathway models have a subtle, but important difference in how polypharmacy is modeled. In the Two Pathway Model (Figure 4.7), both polypharmacy and MRCI each were predicted by the CCI; in essence polypharmacy becomes a sub-mediating pathway for MRCI to readmission in the One Pathway Model (Figure 4.8). However, in the One Pathway Model all fit indices except CFI (.968), increased slightly over the Two Pathway Model. Therefore, the One Pathway Model was also dropped from consideration for well fitting models.

The Medication Regimen Complexity Index (MRCI) Model. Finally, given that in the logistic regression modeling, only MRCI was a significant medication related variable, a model was evaluated that included only MRCI scores as a mediating variable (Figure 4.9).

Of all the models evaluated, this model was the second best fitting model with a RMSEA of .034, CMIN/df of 1.86, and an AIC of 104.54. If only basing the decision on the RMSEA, then the HRMR model and the MRCI models would essentially be equivalent. However, based on all the fit indices considered as a group, the HRMR model was slightly superior to the MRCI model. Unfortunately, the model statistics for the MRCI model (not shown) revealed that the outcome of readmission was not a significant parameter in the model, thus the contribution of the predictors to the outcome could not be evaluated accurately. Therefore, further evaluation of this model was warranted.

Figure 4.7. The Two Pathway Model.

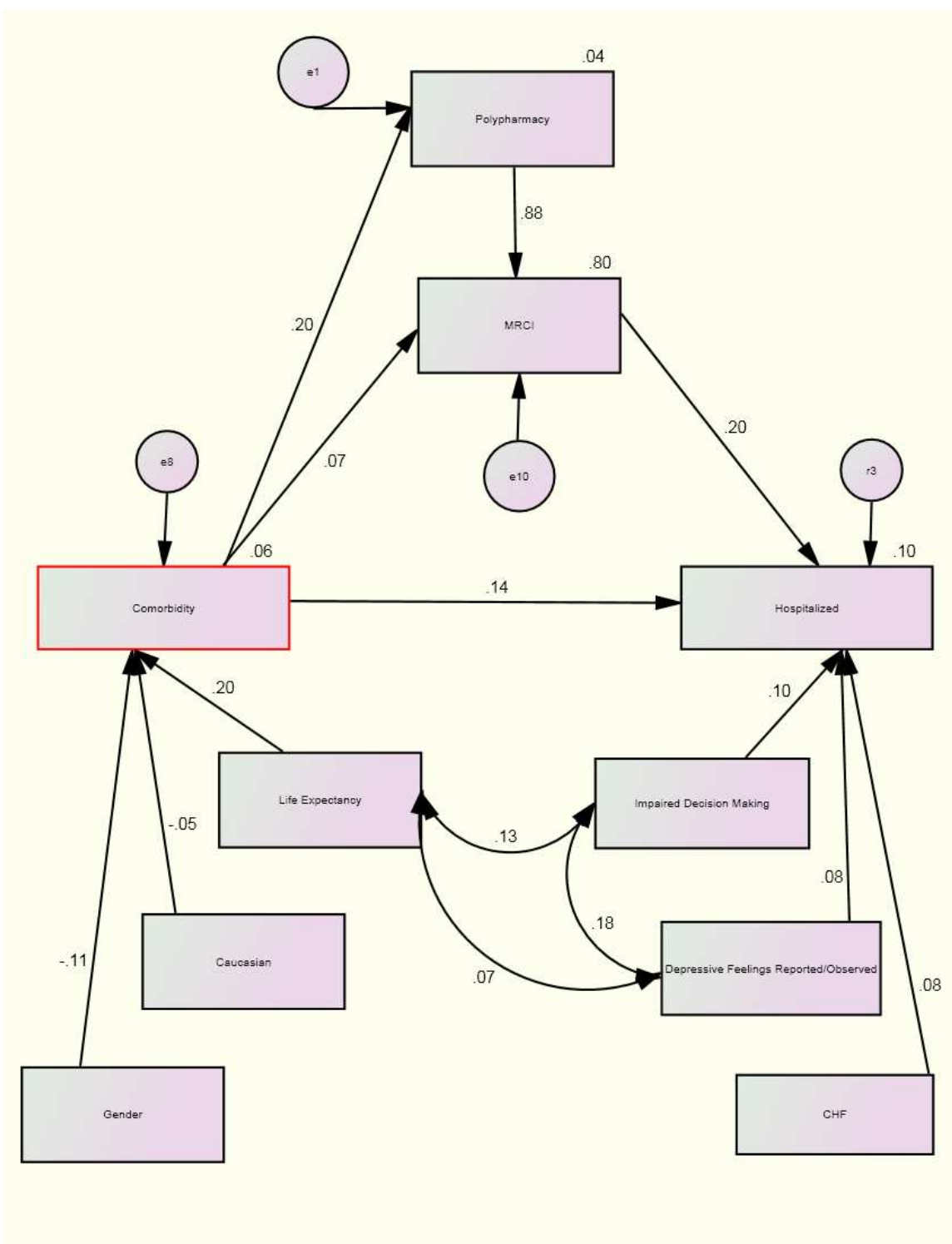


Figure 4.8. The One Pathway Model.

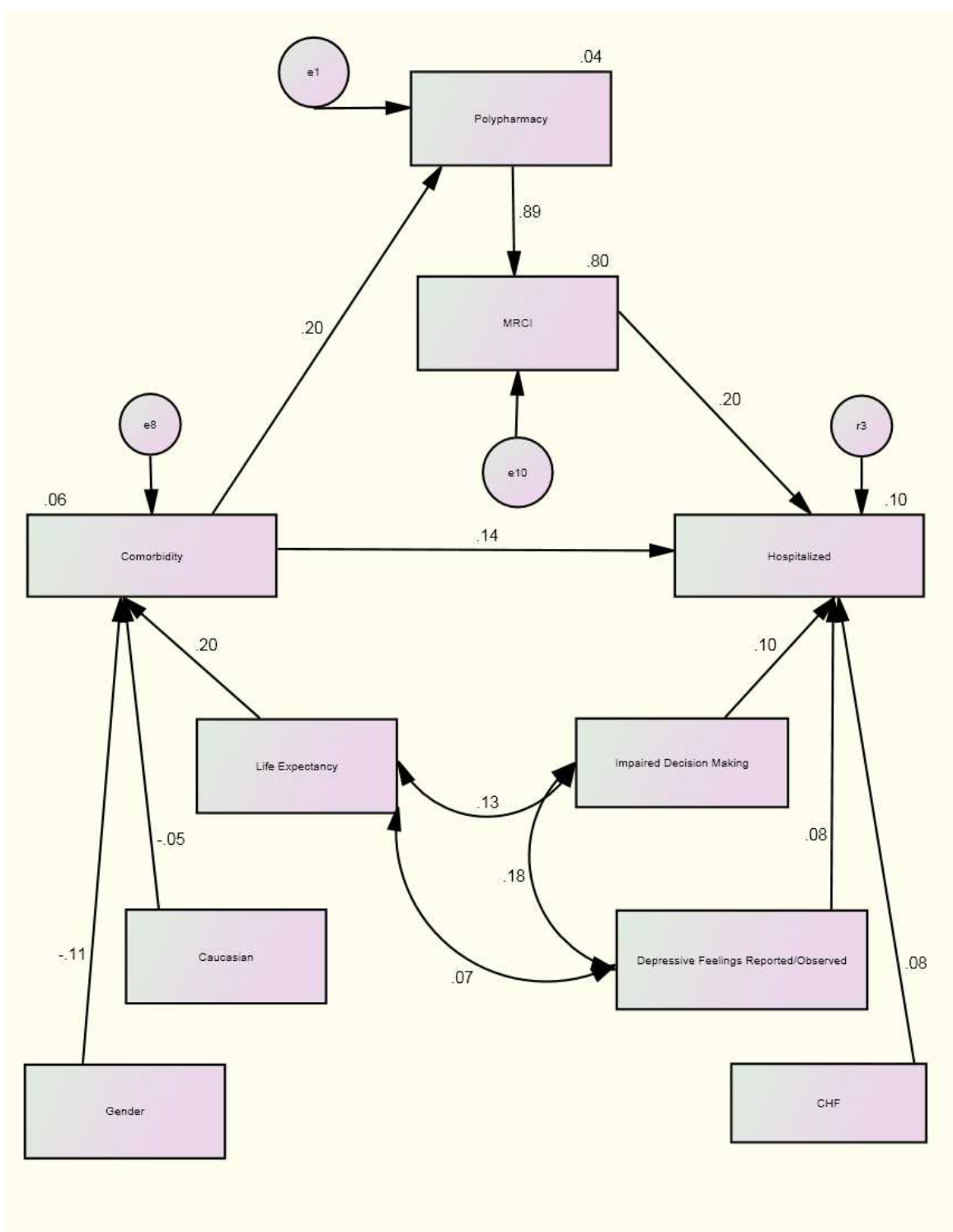
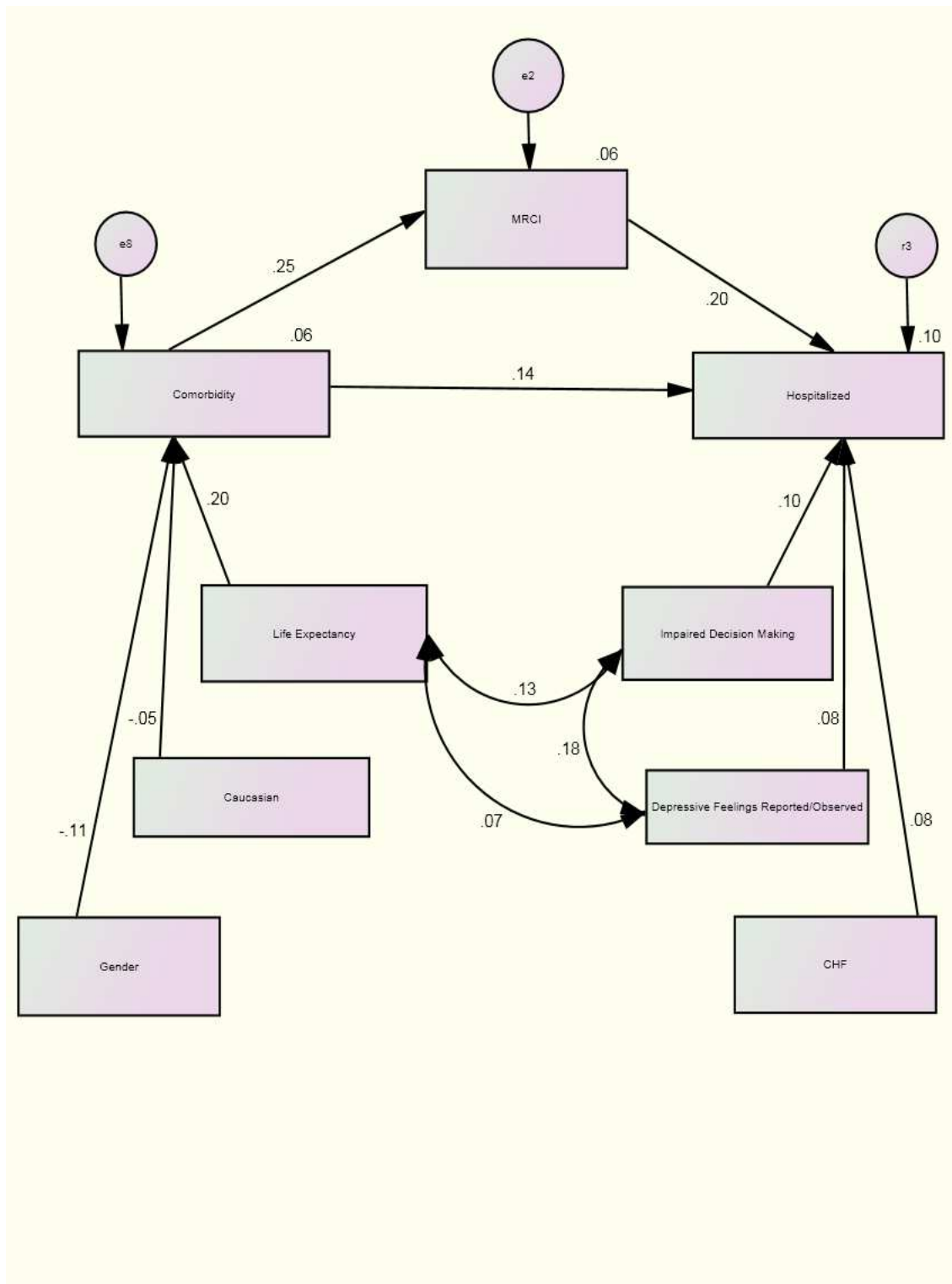


Figure 4.9. The Medication Regimen Complexity Index Model.



The Polypharmacy Model. A final model was tested (not shown) based on the literature findings that polypharmacy alone could be just as predictive for adverse drug events as some of the more complex measures. Therefore polypharmacy was substituted for MRCI as a parameter in the MRCI model picture in Figure 4.9. However, this model could not be evaluated, as the CMIN could not be calculated by the AMOS program, thus no other test statistics would be available.

In conclusion, the HRMR model (Figure 4.5), as hypothesized, was the best fitting of the model alternatives to the Comorbidity Model. Nonetheless, the Comorbidity Model remains the best fitting model, although it is less predictive of readmission (at 7.1%) than the HRMR model (9.6%, Table 4.23). However, with this particular data set, model fit indices only relay part of the story. The remainder of the interpretation is in the path coefficients.

Table 4.23. Squared multiple correlations for the HRMR Model.

	Estimate
Comorbidity	.056
HRMR	.042
Readmission	.096

Interpretation of the High Risk Medication Regimen (HRMR) Model

Given that the focus of this study is whether the HRMR model is viable, only the HRMR path coefficients are examined in detail. The best fitting model is the Comorbidity Model, although the CMIN statistic is not ideal (< 2). Despite the HRMR

model being a poorer fitting model than the Comorbidity Model, likely due to kurtotic data, high risk medication regimens play an important role in prediction of readmission as evidenced by the path coefficients and the predictive power of the model.

Each of the models is depicted in figures 4.3-4.9 with standardized regression coefficients for the pathways. This allows the investigator to compare the relative weights of the independent variables within the model (Garson, 2009b). Since this is a single sample, reporting standardized estimates is acceptable. The regression weights are interpreted as weights in standard units comparable to one another no matter the measure. However, if there were multiple samples with unequal variance, the unstandardized coefficients would be reported rather than the standardized coefficients (Garson, 2009b). The unstandardized coefficients (Table 4.22, p. 227) give information about the relative weight of each of the pathways, and are interpretable as weights in the units used to measure the scores (Garson, 2009b).

Table 4.22 depicts the unstandardized parameter estimates of the HRMR model (Figure 4.3). For example, in Table 4.22, the life expectancy to comorbidity pathway has the highest estimate, i.e. it is the strongest predictor of comorbidity of the three predictors of comorbidity (gender, life expectancy and ethnicity). In this instance, it is interpreted as when life expectancy increases by one unit, the comorbidity score increases by 1.237 units. On the other hand, ethnicity and comorbidity have an inverse relationship; when ethnicity increases by one unit, the comorbidity score decreases by .654 units.

Neither comorbidity, nor HRMR, is very strong predictors of readmission. In this model, the strongest predictor of readmission is actually impaired decision making, which for every one unit increase, readmission increases by .18 units. For every unit of

increase in comorbidity, readmission increases by .041 units, while readmission increases by .074 units for every unit increase in HRMR. Therefore, in this model HRMR is a slightly stronger predictor of readmission than is comorbidity. These two pathway estimates have quite low standard errors, suggesting that these estimates are quite reliable. The critical ratio (CR) for HRMR is determined by dividing the regression weight estimate by the estimate of its standard error ($.074/.013 = 5.637$). If the assumptions for modeling are met, the critical ratio has a normal distribution (AMOS, Version 18). The critical ratio states that the regression weight is 5.637 standard errors above zero, far into the tail of the distribution, and would naturally have a p -value of $< .001$.

Table 4.24 give the variance associated with the exogenous variables. As shown, there is quite a bit of error in the measurement of both comorbidity and in high risk medication regimens accounting for a large part of their variance. Either these variables are measured poorly or there are additional factors not accounted for in the measurement of these variables. Therefore, the conclusions drawn from this particular model must be cautiously drawn.

Table 4.24. Variance associated with exogenous variables.

	Variance	S.E.	C.R.	P
Gender	.238	.011	21.331	***
Life Expectancy	.059	.003	21.331	***
Ethnicity	.014	.001	21.331	***
CHF	.041	.002	21.331	***
Error associated with Comorbidity	2.046	.096	21.331	***
Error associated with HRMR	.953	.045	21.331	***
Impaired Decision Making	.061	.003	21.320	***
Depression	.137	.006	21.331	***
Error associated with Readmission	.145	.007	21.331	***

Effects Decomposition

Effect decomposition using the standardized regression weights was calculated to further assess the answer to the third research question: Do high risk medication regimens increase the risk of readmission in home health care patients age 65 and over? Table 4.25 depicts the standardized regression weights for the HRMR model. The path with the most direct influence on readmission was that from HRMR to readmission (beta = .184, $p < .001$) versus that from comorbidity to readmission (beta = .149, $p < .001$). For example,

the standardized regression weight for the HRMR to readmission pathway can be interpreted thusly: when the HRMR score increases by 1 standard deviation, readmission increases by .184 standard deviations. However, the indirect effect must also be calculated for comorbidity and reflects the effect of the predictor variable on the outcome accounting for the effect of intervening variables (Garson, 2009b). The indirect effect was calculated by multiplying the path coefficients for each of the paths from the predictor to the outcome variable and then adding the sum of those products (Garson, 2009b). The indirect effect of comorbidity (as measured by the CCI) on readmission is: $CCI \rightarrow HRMR \rightarrow Readmission = [.204 \times .184] = .037$.

The total causal effect equals the direct effect of comorbidity on readmission plus the indirect effect of the comorbidity variable on the outcome (Garson, 2009b), or $[.149 + .037 = .186]$. The total causal effect holds all variables but the intervening variables constant. Thus, the total causal effect of comorbidity on readmission is equal to that of high risk medication regimens; thus if this model were accurate, both factors carry equal weight in assessing the risk of readmission.

Table 4.25. Standardized regression weights for the HRMR Model.

Pathway Between Parameters			Estimate
CCI	<---	Gender	-.107
CCI	<---	Life Expectancy	.203
CCI	<---	Ethnicity	-.053
HRMR	<---	CCI	.204
Readmission	<---	CCI	.149
Readmission	<---	HRMR	.184
Readmission	<---	Impaired Decision Making	.110
Readmission	<---	Depression	.081
Readmission	<---	CHF	.076

Assessing Mediation

The final operation on the SEM model assessed for mediation. The HRMR Model was compared to the Comorbidity Model to assess how the focal relationship of comorbidity to re-hospitalization changes with the addition of the high risk medication regimen variable. The Comorbidity Model version yielded a standardized pathway coefficient of 0.18 for the comorbidity to readmission pathway. When the mediating variable of high risk medication regimens is added to the model, the path coefficient drops to 0.15. Therefore, because the focal relationship was reduced, but not extinguished when the high risk medication variable was added to the model, partial mediation did indeed exist. Assuming that all variables were specified correctly in the model, twenty

percent of the effect of comorbidity on readmission was calculated to be due to high risk medication regimens.

The calculation of this effect is:

$$\frac{|a| - |a'|}{|a|} = \frac{.18 - .15}{.15} = \frac{.03}{.15} = .20$$

Conclusion

In this chapter, the sample was described, medication variables were explored, summative factor analysis was performed to determine if a concept of high risk medication management could be developed, and correlation and logistic regression analyses were completed to determine the relationship of covariates used in the structural equation modeling process. Five models were tested against the Comorbidity Model to assess whether various combinations of medication related variables were independently predictive of readmission, and one model was tested to see if a constructed variable of high risk medication regimens predicted readmission. The HRMR Model was tested against the Comorbidity Model to assess whether a mediating relationship existed between comorbidity and readmission.

This chapter described the sample used in the study as being predominantly Caucasian, slightly over half being female, in their later 70's who are relatively healthy with little cognitive dysfunction. While half the sample needed help with ADLs, nearly three quarters of the sample needed IADL help, and almost all needed help with

medication management. Almost everyone in the sample had at least one PIM, the number of medications in their regimens was quite high, and the regimens were quite complex. Those who were admitted to the hospital were statistically significantly more likely to be older, sicker, cognitively impaired, depressed, having more medications, PIM and complexity in their medication regimens, and more likely to have been seen in the emergency room in the previous two weeks.

Correlation analysis showed a high correlation between polypharmacy and medication complexity, but not high enough to eliminate one of the variables from the model. High risk medication regimens were found to be composed of the three variables proposed, polypharmacy, PIM, and medication regimen complexity, affirmatively answering research question two. Logistic regression revealed that predictors of readmission included comorbidity, medication regimen complexity, CHF, depression, and impaired decision making. These variables were then used in the structural equation modeling process. The Comorbidity Model was found to be the best fitting model, although it predicted only 7.1% of readmissions. When compared to the Comorbidity Model, the HRMR Model was a poorer fitting model (likely due to kurtosis of the medication data), although the alternative fit indices still indicated a reasonable fit. The model found to be the most parsimonious, while at the same time the best fitting model of the alternative models to the Comorbidity Model, was the model that used high risk medication regimens as a mediator between comorbidity and readmission. However, the error associated with measuring the exogenous variables is high and thus leaves the findings open to question. Given the error in measurement, the findings affirm that both comorbidity and high risk medication regimens both play a role in predicting

readmissions. This model also demonstrates that high risk medication regimens are a potential mediating variable in the causal pathway between comorbidity and readmission. The next chapter will consist of a discussion of these results, the limitations and strengths of this study, and implications and suggestions for future study of this topic.

CHAPTER V

DISCUSSION

This study is based on the premise that medication use must be carefully balanced to improve outcomes and prevent side effects. Decreasing medication mismanagement which results in inappropriate prescribing is so essential to improving the outcomes of care that consequently, many national initiatives focus on medication regimen management including initiatives from the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), the Agency for Healthcare Research and Quality (AHRQ), the Institute of Medicine (IOM), National Institute on Aging (NIA), and the Centers for Medicare and Medicaid Services (CMS). As the potential for errors and adverse outcomes is so high, this study was based on the premise that health care providers not only balance the risks and benefits of medications prescribed, but do so on some unnamed metric that likely consists of some combination of number of medications, whether the medications impose an undue risk on the age group for which they are prescribing, and whether the regimen is too complex for the patient and their support person(s) to manage correctly. An assumption is made that high risk medication regimens are composed of these contributing factors. Also grounding this study was a second assumption that high risk medication regimens are, in fact, partially responsible for readmissions to the hospital.

Based on an extensive literature review, it was found that few researchers have examined the link between hospital readmissions and high risk medication regimens of community dwelling elders. Although the relationship of number of medications to adverse events (the precursors to readmission) had been firmly established, the

relationship of inappropriate medication prescribing to adverse events is less clear.

The relationship between medication regimen complexity and adverse events, to date, has not been established. Little research has been exclusively focused on the older adult population and most research that exists in this area usually includes a broad range of age groups. Institutional settings have been examined most closely for issues regarding medication management, but little is known about the transition points between settings, nor much about those in a non-institutional settings.

This study was designed to examine the gaps in the literature regarding older adults in a community setting using transition services, such as home health care. In particular, a new definition of high risk medication regimens, composed of polypharmacy, potentially inappropriate medications (PIM), and medication regimen complexity, was developed and tested for the impact of this new concept on readmission of older adults to the hospital from home care. Analysis of OASIS data and medication records from 911 adults age 65 and over from 15 Medicare certified home health care agencies primarily located in the Midwest was used in this exploratory study to evaluate three aims:

Aim 1: To describe the medication regimens of older adult home health care clients in terms of polypharmacy, potentially inappropriate medication use and medication regimen complexity.

Aim 2: To determine what combination of factors (polypharmacy, potentially inappropriate medications, medication regimen complexity) compose the concept of high risk medication regimens.

Aim 3: When combined with other potential risk factors, to evaluate the extent to which high risk medication regimens, as a mediating variable between comorbidity and hospital readmission, account for variance in hospital readmission.

A conceptual framework was developed to guide the study as there were no appropriate frameworks found in the literature. Based on the literature review, two analytic frameworks, with variations on the proposed mediation pathways, were developed for evaluation. In one of these analytic frameworks it was hypothesized that the medication variables were intrinsically linked with each other to form a concept of high risk medication regimens in which the whole (the concept of high risk medication regimens) is more than the sum of the parts (polypharmacy, PIM, medication regimen complexity). Another analytic framework was developed based on the theory that each medication variable contributed to hospital readmission independently of each other.

A number of analytic methods were used in this study to answer the research questions stemming from the study aims including descriptive analysis, correlation analysis, factor analysis, logistic regression, and structural equation modeling. The results from this study demonstrate that not only are older adults in home health care prescribed many medications on their admission to home health care from the hospital, but often there is use of medications, whether prescribed or over the counter (OTC), deemed inappropriate for this age group. Older adults' regimens are exceedingly difficult to manage, requiring the help of others to assist in using regimens correctly. In addition, it was found that high risk medication regimens are indeed composed of polypharmacy, PIM, and medication regimen complexity. High risk medication regimens account for a

significant amount of variance in readmission in this population in addition to the variance accounted for by comorbidity. Finally, it was demonstrated that partial mediation for the influence of comorbidity occurs through high risk medication regimens.

In the following sections, the study results for each aim are discussed in the light of previous findings from the literature, and conclusions are drawn about the nature of the findings. Both limitations and strengths of the study design are described. The study findings are linked to the guiding conceptual framework and theoretical background of the study. Implications for future study, policy, and clinical practice are discussed, including future study designs using this type of data.

Sample Demographics

The literature on home health care (HHC) patients is relatively sparse compared to literature on patients in other settings such as in hospitals or in nursing homes. HHC patients are difficult to study because they have such heterogeneous characteristics. Patients enter home health care from any number of settings including hospitals, from the community, from long term care, or from rehabilitation settings. Newborns to patients older than 100 years old are represented among their ranks. Patients with profound, lifelong disabilities are among home health care patients, as are those who are usually healthy, but are temporarily incapacitated by surgery. Previous studies have not differentiated between patients who entered home health care from any setting, and those who were admitted from the hospital. Nor have studies necessarily ensured a homogeneous sample either in age, insurance coverage, or in conditions. Although these studies may have had samples broadly representative of home health care patients, the conclusions drawn might not be applicable to other age groups or types of illnesses. It is

unknown whether being in home health care benefited these patients. Controlling for the effect of home health care could have been done by comparing the findings from this sample to a similar sample from a different setting such as the ambulatory care venue. However, the scope of this study precluded doing this. Given that a second non-home health care sample was not available, it was assumed that both hospitalized and non-hospitalized patients were equally affected by the presence of home health care, although within the home health care clientele, patients who are severely cognitively or functionally impaired may be more intensely monitored. Unfortunately, number of home health visits was not part of this data set to check this assumption.

Because the patients in this study were age 65 and over and therefore most likely Medicare eligible, the influence of age (and associated differences in likely number and types of illnesses) is minimized, as well as disparities that differences in insurance coverage causes. However, these patients may have carried lifelong illnesses into their elderly years or the accumulated insult from lack of insurance over their lifetime, thus may still make this a very heterogeneous sample in which individuals are quite different from one another based on their history of insurance coverage. However, by narrowing the inclusion parameters to specific subsets of patients, a more homogenous sample is studied and the opportunity for confounding is greatly reduced.

Choice of Sample

The results from this study elucidate the characteristics of older adult home health care patients who have been discharged specifically from a hospital setting. Although the agencies sampled were not randomly chosen, the agencies were representative of different types of ownership and size. Furthermore, 100% of the

patients seen in these agencies in 2004 were used to select the original sample for this study, thus all Medicare eligible patients age 65 years and older admitted in 2004 to these agencies were eligible for inclusion in this study. In addition, the study sample reflects the population in most parameters other than age (slightly older), readmission rate (lower), and length of stay in home health care (much shorter). Therefore, these results should be readily generalizable to similar home health care populations in the Midwest.

A propensity analysis was used to narrow the original sample to the patients of interest: those age 65 and over, admitted to home health care from the hospital for the first episode of care in 2004. Based on the results of the propensity analysis, patients admitted to home health care from the hospital versus other inpatient or community settings, were statistically significantly different in terms of age, comorbidities, and length of stay in HHC. These differences in age, comorbidities, and length of stay in home health care may have confounded the findings from previous studies and may prevent generalizing findings from previous studies to this specific group of patients admitted to home health care from the hospital. Ensuring that the sample was relatively homogeneous helped to control for extraneous factors (type of episode, episode start date, children/young adults) that might confound the results. Thus, the differences between the readmitted patients versus those not readmitted were likely to be the result of the factors under study rather than confounding factors.

Description of Sample

A number of covariates were chosen to be evaluated in addition to the predictor variables. Variable choice was limited due to the nature of the study (secondary data analysis), however, many of the variables previously studied for predictive capability for

hospital readmission in home health care were able to be included as covariates.

Additionally, other variables were chosen based on findings pertinent to the ambulatory care literature. The variables studied and associated findings are described below.

Age. This sample of patients was similar in age (mean age = 78.9 years) to other studies using Medicare eligible patients (Cannon et al., 2006; Flaherty et al., 2000; Fortinsky et al. 2006; Madigan et al., 2001). Similar to other studies using home care patients, the sample was predominately Caucasian (98.6%) and 61% female (Cannon et al., 2006; Flaherty et al., 2000; Fortinsky et al. 2006; Madigan et al., 2001), with almost one third living alone (Madigan et al. 2001; Rosati & Huang, 2007). This was in keeping with the demographics of the home health care population described by the Centers for Medicare and Medicaid Services (NAHC, 2008).

Cognitive Status. Given the literature on the rates of dementia development in the 65-85 year old age group (Alzheimer's Association, 2010), most patients retained executive function (75%). A small percentage of patients (6.5%) had impaired decision-making and/or memory deficits. Nonetheless, despite the high level of cognitive function, almost all patients needed help managing their medication regimens safely. Given that these issues were addressed very specifically in the OASIS assessment, it was likely that these data were accurate. Little information was available about cognition in the HHC population, so this is important information regarding the cognitive function of those in home health care

Comorbidity. Although there are a number of older studies examining the relationship of comorbidity to hospital readmission in the HHC setting (Anderson et al., 1999; Flaherty et al., 2000; Madigan et al., 2001; Martens & Mellor, 1997), this

relationship has not frequently been studied since the implementation of the Balanced Budget Act in 1997 which so dramatically changed the delivery of home health care (Anderson, Clarke, Helms, & Foreman, 2005; Chrischilles et al., 2007). Although Rosati and Huang (2007) found that four or more diseases increased the risk of re-hospitalization in HHC patients, no other recent studies specifically evaluated this relationship in home health care, so this study adds new information to the knowledge base regarding this issue.

There was little comorbidity in this sample, despite the higher age of the sample. Although these patients may have had exacerbations of existing illnesses or new onset of illness at admission to HHC, overall, their degree of comorbidity is not as high as would be expected given their recent hospitalizations and age. The average Charlson Comorbidity Index (CCI) score of 1.1 (range 0-10) is quite low and 88% of subjects had CCI scores of less than three. Although Sheeran, Beyers, and Bruce (2010) did use the Charlson Comorbidity Index to assess their subjects, the score was higher (mean 2.77) in their depressed patients. However, Coleman et al. (2004) found the average Charlson Comorbidity Index score to be 1.3 in the samples derived from Medicare Current Beneficiary Study for those ages 65 and over discharged from an acute care hospital during the years 1997-1998. It is difficult to compare the level of comorbidity in this sample to other studies as few studies in HHC evaluate a global risk score, but rather examine disease categories (Anderson et al., 2005, Fortinsky et al., 2006; Rosati & Huang, 2007) or count number of chronic conditions (Li et al., 2004; Rosati & Huang, 2007).

This low level of comorbidity might be affected by methods of data collection. Systematic bias likely was introduced by not including the primary diagnosis in the Charlson Comorbidity Index Score. Therefore, the scores would be lower for the entire sample, thus decreasing the effect of comorbidity on readmission and increasing measurement error. In addition, only diagnoses related to the HHC admission are recorded, thus underlying, but stable diseases and inactive diagnoses, may not be adequately identified on the OASIS assessment, which may again decrease the effect of comorbidity on readmission and increase the effect of high risk medication regimens.

Some questions allow for more accurate data collection on specific conditions, for example depression. In this instance, a separate, specific query on depressive symptoms appears in the OASIS items, but multiple answers can be marked. Having a specific assessment question for this condition, rather than identifying the presence of depression in the OASIS items for medical conditions (MO230), primary diagnosis (M0230), or in other diagnoses (MO 240), allows for more accurate data collection. Therefore, the effect of some covariates may be magnified.

Low comorbidity scores may also be a function of the Deyo modification of the Charlson Comorbidity Index. In this instrument, only 17 diseases are identified as opposed to the Elixhauser Index, which is designed to identify many more diseases. Finally, the exclusions included those who were not hospitalized in the last two weeks. Therefore, systematic sampling bias may have occurred, as it is probable that those patients who were the sickest upon discharge from the hospital, may have spent time in long term care, rehabilitation, or transitional care, and were not included the sample examined.

Although low comorbidity scores are troubling, there are eleven fields excluding the primary diagnosis, from which to collect comorbidity information. It is likely most fields were completed given that this document is also the basis for billing of the services rendered in home health care. Given that number of fields, it is probable that many of the common diseases contributing to the Charlson Comorbidity Index score will be identified. In addition, it is likely that home health care patients *are* harder patients. Patients who are severely functionally dependent or cognitively impaired are liable to have already been placed in long term care prior to hospitalization and would not be in this population. Those who are marginally healthy may not make it back to their former living situation or may be enrolled in hospice, making them ineligible for home health care.

Given that 50% of the subjects had surgical wounds, low comorbidity scores might also be expected, as surgical candidates, in general, are healthier, especially if procedures are elective. The number of surgical cases is consistent with low rates of congestive heart failure and diabetes as the primary diagnosis in this sample as well. The rates of diabetes in this sample were similar to that found by Coleman et al. (2004). Unlike Coleman et al. who found 13-16% rates of congestive heart failure, in the present study, a 4% rate of congestive heart failure was found in this sample for the primary diagnosis. It is likely that higher rates of congestive heart failure and diabetes occurred in this sample, but if listed as a secondary diagnosis, these diseases would not have been included in these rates. Patients with diabetes or CHF might be more likely to be admitted to a higher intensity environment or to hospice directly after the index hospitalization

causing a selection bias. However, systematic bias is unlikely given the low comorbidity in the population before the sample specification occurred.

The presence of depressive symptoms (16.4%), is less than what Sheeran et al. (2010) found in the home care setting (16% meeting major depression DSM criteria, 8% meeting minor depression criteria) but in keeping with the 13.4% rate found in HHC clients by Hybels and Blazer (2003). Depending on how the researcher treats the responses, (dichotomously or categorically), the rates of depressive symptoms (or other behavioral issues) might vary. In this instance, the lower rates found in this study may be related to collapsing the responses.

An unexpected finding was that those who had the least comorbidity, were re-hospitalized most frequently. Perhaps, those who were the most ill were electing not to be re-hospitalized, but instead chose palliative care in the home setting. However, this finding could also indicate a sampling issue. For example, those with surgical complications stayed in the hospital for a longer period of time and then were admitted to a transitional care or a rehabilitation unit and thus were not among those chosen for the sample because they had not been hospitalized in the previous two weeks. Since this finding was at odds with previous literature (Rosati & Huang, 2007) the finding deserves further investigation.

Risk Factors. Risk factors such as smoking, obesity, and substance abuse were prevalent in this sample (19.9% had at least one or four risk factors) despite age, numerous medications, and chronic health conditions, perhaps indicating how hard it is to apply current medical findings to breaking old habits. No studies were found that examined risk factors as predictors of hospitalization in HHC clients.

Caregiving Help. Given the low level of comorbidity, it was expected that the need for help with activities of daily living (ADLs) and independent activities of daily living (IADLs) would be low. In spite of low CCI scores, however, there is significant need for ADL help (46.7% of subjects needed ADL help) and for IADL help (74% needed IADL help); however this percentage of patient needing help is lower than that found in other studies. Li et al. (2004) found that in their sample of HHC patients with CHF, 70% of their sample needed help with ADLs and 96% of their sample needed IADL help. Anderson et al. (2005) found a higher number of people who could care for themselves (40%). Again, this may indicate a problem with how data is collected regarding diseases or this may reflect that in this age group surgical recovery greatly increases the need for ADL help. Although almost 40% relied on their spouse to fulfill primary caregiving functions, children were also serving as caregivers in 27% of cases. This finding is at odds with the Anderson et al. (2005) study in which 22.4% of patients designated spouses and 22.4% of patients designated children as primary caregivers. It appears that despite the availability of HHC, families continue to provide a significant amount of care.

Length of Stay in HHC and Hospital Readmission. The average length of stay in HHC in this sample is seven days shorter than the national average of 46.4 days (Home Health Interactive, 2009), although the national average includes people under age 65. Nonetheless, this relatively short stay is in keeping with other studies in home care (Murkofsky, Phillips, McCarthy, Davis, & Hamel, 2003).

Even when accounting for the change in length of stay in HHC before and after the Balanced Budget Act of 1997, the length of stay for this sample is shorter than in

other studies (Martens, 2000). The length of stay in HHC may be shortened because half of this sample had surgeries (as evidenced by the presence of a surgical wound), thus needing HHC to be resettled in their home again. High levels of cognitive function coupled with lower comorbidity may have also accounted for shorter episodes of care and the short lengths of stay in home care. Many studies in home health care also took place before the Balanced Budget Act of 1997, so newer studies may more accurately reflect the length of stay. Finally, both lengths of length of stay, as well as comorbidity, may be positively affected in the Midwest given the health maintenance organization (HMO) penetration in the mid-section of the country.

Literature that addresses adult learning and motivation suggests that it takes at minimum three weeks for behaviors to become habits (Lally, van Jaarsveld, Potts, & Wardle, 2009). The short stay in home health care is a particular concern given the complexity of medication regimens and the fact that most patients who are hospitalized experience a regimen change upon discharge and new habits have yet to form. The frequency of regimen change in the post-discharge period reinforces the theory that these patients are at very high risk for errors in dispensing their medication regimens following hospital discharge as they are just getting used to the new regimens. Although an intense service level is important early in the HHC episode, perhaps additional attention should be provided in the form of follow up by a health care provider, either in person, by phone, or by e-mail, six to eight weeks after admission to HHC because of both the short length of stay in HHC and the steep learning curve regarding regimen changes instituted in the hospitalization. The lack of attention to follow up is a missed opportunity for intervention to prevent hospital readmissions.

In this sample, the overall hospital readmission rate of 20.4% is similar to the 18.9% readmission rate in HHC found by Fortinsky et al. (2006), and the 19.9% rate cited by Rosati and Huang (2007), but is slightly lower than the 24.4% rate found by Madigan et al. (2001). The difference in the definition, i.e. using any hospitalization rather than just re-hospitalization, may account for a rate much lower than the 29% rate cited by CMS (2009a). Unlike the Jencks et al. (2009) finding that 20% of all Medicare beneficiaries were re-hospitalized within thirty days, 23% of this sample were readmitted in this time frame, a concerning percentage, given monitoring by home health care personnel. The readmission rate and the emergent care rates are almost identical, perhaps related to the fact that if emergent care is sought between visits from the HHC staff, the patient is probably ill enough to be admitted to the hospital. Anderson et al., (2005) found that the mean length of stay in HHC before readmission was 11.7 days, while Sheeran et al. (2010) found that for non-depressed patients the length of stay in HHC before readmission was 19.4 days.

Differences between Those Readmitted and Those Who Are Not Readmitted

There were significant differences between the readmitted group and those who were discharged to other settings. What distinguished the non-readmitted group from the readmitted group was that the latter group was sicker (mean CCI score .99 vs. 1.7), had more complex medication regimens (MRCI score 32.4 vs. 46.9) with higher levels of both polypharmacy (mean number of medications 10.4 vs. 13.9) and PIM (mean PIM score 3.4 vs. 4.3), were depressed (13.9% vs. 51.6%), had memory impairment (5.4% vs. 10.8%), and/or impaired decision making (4.8% vs. 12.9%), and had shorter life expectancies (4.8% vs. 11.8% under 6 months). This profile of readmitted patients is

consistent with findings from other research (Li et al., 2004; Fortinsky et al., 2006; Madigan et al., 2001; Rosati & Huang, 2007; Sheeran et al., 2010).

Age and Other Demographic Variables. Although statistically significantly different, the mean age is, in practical terms, the same between those who are not readmitted (78.8 years) and those who are readmitted (79.0 years). Age was not correlated significantly with any of the predictor variables, except medication regimen complexity, and with few of the other covariates except for surgery, mental status variables, and continence status. However, when age was broken down into categories, significant differences appeared between those who were hospitalized and those who were not, with the oldest-old being hospitalized at much lower rates than younger age groups despite similar life expectancies. This finding is consistent with modeling done by CMS (Nuccio, Goodrich, & Hittle, 2008). This may indicate some bias towards aggressive intervention in younger age groups. It appears that the medical condition, rather than having surgery, puts patients at higher risk of readmission, which is also consistent with previous findings (Nuccio et al., 2008). There were no differences in gender, the rate of living alone, or who was providing informal care among those readmitted or those not readmitted.

Comorbidity. Those who were readmitted had higher comorbidity scores (almost double those who were not readmitted), had shorter life expectancies (11.8% vs. 4.8%), and had almost double the rates of CHF (8.6% vs. 3.2%), diabetes (7.5% vs. 3.2%), pressure ulcers (8.6% vs. 4.3%), and had one third more urinary tract infections than those who were not admitted (12.9% vs. 8%).

Cognition and Functional Status. Functionally, almost the same percentage of patients needed help in the readmitted group as those in the non-readmitted group (51.6% vs. 45.4%), but in terms of depression and cognitive status, there were significant differences between the groups. Those who were re-hospitalized had almost double the rate of depression than those who were not re-hospitalized (25.8% vs. 13.9%). Memory deficit rates in those readmitted were double that of those who were not readmitted (10.8% vs. 5.4%), while those with impaired decision making were three times more prevalent among the readmitted group than in the non-readmitted group (12.9% vs. 4.8%).

Readmission Rates and Regimen Change. Although only 23% of the entire sample was readmitted to the hospital within four weeks of being admitted to HHC, 77% of those readmitted were in HHC less than 30 days suggesting that these patients were medically unstable. Perhaps the readmitted patients were discharged from the hospital in either too unstable of a condition, had regimens too complicated to handle when they were on their own at home, or did not have adequate support to manage at home. Nonetheless, the rate of regimen change between those who are readmitted and those who are not, is exactly the same, suggesting that regimen change is not the reason for readmission, but perhaps rather the level of comorbidity, the level of regimen complexity, or some interaction between the levels of comorbidity and regimen complexity.

Similar to other studies (Fortinsky et al., 2006; Madigan et al., 2001; Rosati & Huang, 2007), emergent care use was dramatically higher in the readmitted group than in the non-readmitted group (74.7% vs. 5.9%), again suggesting that this group was a more labile group in terms of their health status. A higher percentage of the readmitted group

was in HHC less than 30 days than those who were not readmitted (76.9% vs. 65.5%). Mean episode length for HHC patients was not statistically significantly shorter in the readmitted group (32.9 days) versus the non-readmitted group (38.6 days), although, a week shorter stay in HHC would be clinically significant.

Findings from the Correlation Analysis

In the correlation analysis, non-medication related covariates, for the most part, were independent of each other allowing for use in the logistic modeling process. As expected based on the literature review, comorbidity, life expectancy, and living situation were significantly related to readmission, but none so highly correlated that confounding would be an issue. Based on the relationship between comorbidity and readmission, it was plausible that CHF, diabetes, pressure ulcers, surgical wounds, and urinary tract infections were correlated with both comorbidity and readmission. Again, although the correlations were statistically significant, they were low level correlations. Unlike other literature (Anpalahan & Gibson, 2008; Rosati & Huang, 2007), urinary incontinence was not found to be significantly correlated to readmission. Memory deficits, impaired decision making, and reporting depressive feelings were also significantly related to readmission, although the correlations were low. Given that these covariates were not highly correlated to each other or to the outcome of readmission, all were able to be used in the logistic regression analysis. Of the proposed mediating medication variables, only polypharmacy and medication regimen complexity were significantly related to comorbidity, but the correlation was low ($r < .3$). PIM was not related to comorbidity at all, but included in the modeling process due to its significant relationship with readmission. All the medication related variables had significant, but low level

correlations with readmission allowing the use of the variables to predict readmission.

Polypharmacy and PIM had a moderate correlation ($r = .59$), as did PIM and medication regimen complexity ($r = .53$) implying stronger relationships that should be modeled in the SEM.

In summary, the overall sample patients averaged 78.9 years old were predominantly white, and slightly over half were females. About half of the patients lived with a spouse, but a little over one third lived alone. There were significant caregiving demands placed on both spouses and children. Nearly half of the sample required assistance with activities of daily living, while 75% required assistance with independent activities of daily living. Half of the sample had surgical wounds on admission to HHC, yet overall, there were low levels of comorbidity. Almost all needed help with managing oral medications despite 75% of patients having no cognitive deficits of any kind. This may be the result of the high levels of polypharmacy, inappropriate medication use, medication regimen complexity or a simple problem like a lack of manual dexterity.

Almost all (93%) patients experienced a change in treatment regimens, and of the 20% of patients readmitted to the hospital, only 16% of patients who returned to the hospital were readmitted in less than 30 days. This finding suggests that although readmission rates are high, it is not likely that these patients were readmitted due to being released from the hospital too quickly. Rather, other factors are operating that account for the readmissions. On average, patients received HHC about 6 weeks, leaving these patients a short time to not only heal and recover their functioning, but also to adjust to treatment changes.

Examination of those who were re-hospitalized versus those who were not revealed that those who were readmitted were older, sicker, with shorter life expectancies, and less likely to have had surgery, but more likely to have CHF, diabetes, pressure ulcers, a urinary tract infection in the previous two weeks, cognitive deficits, or depression. They were far more likely to have used emergent care in the previous two weeks and were far less likely to complete a 30 day stay in HHC. As a group, the readmitted patients were no more likely than the non-readmitted patients to have a regimen change in the previous two weeks, again pointing to other factors accounting for readmission to the hospital.

Significant Findings and the Relationship to Existing Literature

Medication Regimens of HHC Clients

In aim one, the medication regimens were examined in detail. Previous studies have not evaluated the medication regimens in home health care in such detail, but rather have tended just to assess the number of medications in use or evaluated whether patients were able to self manage the prescribed medication regimen. These findings are the first comprehensive evaluation of the nature of medication regimens in HHC and will give future researchers a baseline to which to compare their studies. The following section details the use of polypharmacy, potentially inappropriate medications (PIM) and medication regimen complexity as defined previously (Dierich, 2009, unpublished). The triangulation of three measures should capture the entire spectrum of medication management issues faced in home health care.

Polypharmacy. The number of medications used (mean = 11) when counting all medications (not just prescribed medications) surpasses that of nursing home use (Dwyer,

Han, Woodwell, & Rechensteiner, 2010), and is higher than studies in HHC which have counted only prescribed medications. Previous studies have cited between 5.5 - 6 medications used on average in HHC patients (Cannon et al., 2006; Gray et al., 1999; Meredith et al., 2001). It is important to remember that this study counts unique medicines in the regimen during an entire episode of care rather than at one point in time. In this study, it was not possible to narrow down the dates of usage beyond evaluating the first episode of care, so given the length of the first episode, there may have been several changes made to the regimen during that time period. Both discontinued and new medications might be counted in the regimen with serious over-estimation in all medication related variables as a result. However, given the rapidity of discharge and the geriatric principle of “start low and go slow,” it is likely that most medications counted were prescribed on admission to HHC. It was expected that little change occurred in the regimen, other than dosage adjustment, given such short episodes of care. However, regimen changes such as dose adjustments, timing changes, or starting or stopping medications were able to be captured within the episode through the Medication Regimen Complexity Score. Even with the potential for miscounting, the difference in the amount of unique, prescribed medications in an episode of care is very significant between the readmitted and non-readmitted groups.

For the most part, medications were prescribed medications, and there was little PRN medication use or over-the-counter (OTC) medication use (mean 1.6 medications per patient), unlike previous findings in the literature (Yoon & Horne, 2001). Since the nurses collecting the information were actually in the home, the amount of OTC use would appear to be an accurate assessment as opposed to relying on patient report.

However, given the data set, it was difficult to determine OTC use in medications like Tylenol or Mylanta, as these drugs often had a prescribed frequency, making them adjudicated as a prescription drug. In this case, if the medication had a frequency attached, it was considered prescribed. Based on these issues, it appears that careful definition in counting does make a difference in the results.

PIM. PIM use was much higher in this sample than in other studies (Cannon et al., 2006; Flaherty et al., 2000; Hajir et al., 2005; Hanlon et al., 2000; Rossi et al., 2007), with 88.4% of patients having at least one PIM in their regimen as compared to most studies with PIM rates of 20% to 59%. The difference between this study and previous studies is likely due to the use of the 2003 revision of the Beers' criteria (Fick et al., 2003) and the fact that this was a HHC setting where counts are likely to be more accurate as the nurse is observing the medications in the home.

The number of patients with at least one PIM in their regimen was significantly different between the readmitted (91.9%) and non-readmitted groups (87.4%). The actual PIM scores were also statistically significant between the readmitted and non-readmitted groups (4.3 vs. 3.4). While there were differences between the readmitted and non-readmitted groups in the descriptive analysis, PIM was not associated with readmission in either the logistic regression model or in the structural equation model (SEM) and therefore was not a predictor of readmission. The relationship between PIM and re-hospitalization is a new relationship, not previously explored in the literature. The high rate of at least one PIM being prescribed (88.4%) is especially alarming, given that PIM is calculated, for the most part, on prescribed medications. Over-the-counter medications,

which frequently contain PIM compounds, were not counted in this study for PIM as the Beers' criteria only examines prescribed medications.

It is clear that providers in this study, similar to other studies, continue to use medications from the well known Beers' criteria despite research verifying that these medications are strongly correlated with adverse events (Fincke et al., 2005; Fu et al., 2007; Hanlon et al., 2002). The high levels of prescribed medications coupled with high PIM use in this population, may signify the need for additional training of providers in geriatric prescribing principles. It may also mean that prescribers are aware of the risks associated with these medications, but feel that the HHC patient is closely enough monitored to warrant the use of riskier medications.

Medication Regimen Complexity. George et al. (2004; 2006) give little guidance regarding what would be considered a high level of medication regimen complexity. For this study, a score of 20 was selected as a marker of high medication regimen complexity. With a score of 20, the regimen would have considerable steps in preparation or many changes in regimen to attain a score that high. Most patients (74.9%) had scores of at least 20 on the Medication Regimen Complexity Index. Those who were readmitted had a statistically significantly higher score than those who were not readmitted (mean = 46.9 versus mean = 32.5) lending strength to the premise of the study that medication regimens are, in part, responsible for increased readmission rates. Other than tool development studies (Conn et al., 1991; George et al., 2004; George et al., 2006) there is little known about this concept in the literature, therefore, all the findings about this variable add to the knowledge base.

Other new information discovered in this study includes the significant correlation of polypharmacy to medication regimen complexity. This relationship has been theorized by investigators, but not previously studied in other research. Correlation analyses examining the medication related variables revealed that polypharmacy, PIM, and medication regimen complexity were all related to both comorbidity and to re-hospitalization, thus supporting the evolution of a mediation model. In the correlation analyses, polypharmacy was significantly related to both PIM and the Medication Regimen Complexity Index (MRCI) score. This was not surprising, as many authors (Aspinall, Sevick, Donahue, Maher, & Hanlon, 2007; Barkin, Barkin, & Barkin, 2007; De Smet et al., 2007; Elliott et al., 2007; Field et al., 2007; Williams et al., 2004; Wu et al., 2008) have suggested these relationships. However, the polypharmacy-MRCI relationship was strong enough to consider dropping one of these two variables in the modeling process. While this relationship is intuitive and has been mentioned in the literature, no authors have specifically studied this relationship. The PIM-MRCI relationship, which also has not been studied, was also statistically significant, but not to the degree to warrant dropping one of the variables from the modeling process.

It is uncertain why these variables would be related other than through a confounding or mediating relationship with polypharmacy. However, since the odds of PIM increase as the level of polypharmacy increases, polypharmacy is a potential moderating variable in the relationship of PIM to re-hospitalization. In the case of the MRCI score, medication regimen complexity may be mediating the relationship between polypharmacy and readmission, as the MRCI score itself is based, in part, on a weighted score of the routes used, and the number of times a medication regimen is changed.

Therefore, it is likely to capture polypharmacy as a concept. Since relationships involving medication regimen complexity and other medication related variables have never been studied, this information adds to the existing body of knowledge not only in HHC, but in medication related factors in general.

Medication Management Help. Although medication management was not part of aim one, this was explored in the descriptive analysis. In particular, oral medication management help was evaluated in light of the findings about medication regimen complexity. Given that MRCI uses oral medications as the reference group for scoring, only accounts for prescribed medications, and scores extra points for PRN medications, it is not surprising to see that both number of oral medications, prescribed medications, and PRN medications are all strongly correlated with MRCI. An unexpected finding was that the MRCI score was statistically significant, and negatively correlated with needing help to manage the medication regimen (Pearson correlation coefficient = -0.84). This means that as the complexity score increases, the need for help managing medications decreases, which is not a likely scenario. It can also mean that as the need for help managing medications increases, there is likely to be a lower MRCI score. It is probable that providers only prescribe the most complex regimens to those who are cognitively intact enough to handle the regimen, and prescribe less complex regimens to those who are less cognitively able to handle the regimen. It appears however, no matter the level of complexity, almost all patients needed help with their regimens. Therefore, it is more likely that as help to manage medications increases, then the provider simplifies the regimen.

Interestingly, neither polypharmacy nor PIM were significantly correlated with the need for medication management help. This suggests that the complexity of the regimen may be solely responsible for the need for help in medication management, rather than numbers of medications used. Although, medication management as a predictor has been studied (Cannon et al., 2006; Ellenbecker et al., 2004), there is no research examining medication management in relationship to polypharmacy, PIM, or medication regimen complexity. These relationships need further investigation.

Needing help with medication management seems to be a common finding in the literature (Alkema & Frey, 2006; Cannon et al., 2006; Ellenbecker et al., 2004; Foust, Naylor, Boling, & Cappuzzo, 2005; Meredith et al. 2002; Triller, Clause, & Domarew, 2002). Interestingly, age was not found to be correlated to with the need for help with medication management. Therefore, the need for help may be related to the number of medications needing to be managed, and to the level of medication complexity in HHC population. Help may also be needed because of the changes in the regimens and patients' unfamiliarity with the new regimen. Most probably, it is a combination of both regimen complexity and unfamiliarity, rather than cognitive deficits increasing the level of assistance needed with medication management. However, in this sample, since 93% of subjects in both the readmitted and the non-readmitted groups had regimen changes in the previous two weeks, it is more likely that complexity and number of medications are the reason help is needed, in keeping with original hypothesis driving this study, that more than just polypharmacy or medication regimen complexity alone make up high risk medication regimens. This indicates a need to evaluate the regimens being prescribed to patients and the burden it places on caregivers to manage this complex task.

Since medication regimens would not be expected to change much after discharge from HHC, this study should add to knowledge not only about older adults in HHC, but also by extrapolation, about older adults in the community. In this study, the medication regimens of home health care clients were found to have a high degree of polypharmacy, PIM use, and medication regimen complexity. Although, patients readmitted to the hospital experienced these conditions to a higher degree than those who were not readmitted, almost all patients required help to manage the medication regimens regardless of age or cognitive status, suggesting that medications may independently increase the risk of hospital readmission. Finally, there is a high degree of co-linearity between the medication variables. The strength of the relationship between polypharmacy and PIM, and the relationship between polypharmacy and medication regimen complexity strengthen the hypothesis that there is a mediating relationship between polypharmacy and both PIM and medication regimen complexity, and that together, these three variables may compose high risk medication regimens.

The Composition of High Risk Medication Regimens (HRMR)

Once the preliminary correlation analysis was completed, factor analysis was undertaken to assess whether a concept tentatively called high risk medication regimens could be composed of polypharmacy, PIM, and medication regimen complexity. It was expected that a two factor model would be the result of the confirmatory factor analysis, given that polypharmacy and medication regimen complexity were so highly correlated. However, only one factor had an eigenvalue that was over one, therefore one factor accounted for most of the variance in this new concept.

Previous literature had not considered all three of these factors in one study, let alone combined these factors to develop a new concept. Other studies done on one or two of these concepts (polypharmacy, PIM, or medication regimen complexity) may have had equivocal or negative findings because these factors may be part of a larger concept or have interactions not previously theorized. Additional factors no doubt are part of high risk medication regimens, but could not be studied given the data set. It is likely that a physician's knowledge of the patient's previous behavior and the patient's support system, as well as the patient's knowledge, ability, and beliefs about medications all play a role in high risk medication regimens. Collection and study of primary versus secondary data will help to test these relationships in the future.

Preliminary Steps for Model Building

To evaluate the extent that high risk medication regimens account for variance in re-hospitalization when combined with comorbidity and other potential risk factors, a structural equation modeling (SEM) approach was used. Because relationships had not been previously studied and it was not clear whether the relationships studied were indeed linear, SEM approach was chosen as underlying assumptions for SEM are more lenient. In addition, SEM can handle a latent variable such as high risk medication regimens, whereas neither the simpler logistic regression modeling nor path analysis can test latent variables. However, before setting up the SEM, logistic regression modeling was employed as a tool to determine which other covariates should be included in the model as exogenous variables.

Logistic Regression Modeling. Two logistic regression models were evaluated prior to developing the final logistic model. The first logistic modeling was run on all

predictors chosen for study. It was discovered that both emergent care and length of stay were the only significant predictors in this model. Length of stay determination occurs after the discharge from HHC, making it an illogical choice for a predictor. When length of stay was removed, emergent care became the only significant predictor along with pressure ulcers in the second model. Emergent care use was statistically significantly and highly correlated to readmission. Similar to previous studies, (Hastings et al., 2008), emergent care use strongly predicted readmission and increased the likelihood of readmission by a factor of forty. The item currently asks whether *any* emergent care was sought since the last OASIS assessment. If the OASIS item actually counted the number of emergent care visits during a specific period of time, perhaps this association would be less strong, as not all patients seeking emergent care are admitted to the hospital. However, no matter the venue for emergent care (urgent care, doctor's office, or emergency room), the portal of entry to the hospital is likely to be through emergency room for unplanned admissions, thus the high association. Given that there was nearly the same percentage in both the emergent care use and the readmission outcome, it was likely that both variables are measuring the same concept. However, because there were many missing values in this variable, and due to the strong correlation between emergent care and readmission, emergent care use was felt to be confounding the findings and therefore was not further evaluated.

In the final logistic regression model, in addition to comorbidity and medication regimen complexity as significant predictors, six other covariates (CHF, depression, impaired decision making, life expectancy, ethnicity, and gender) were found to be significant enough to include in the final models. Congestive heart failure (OR = 2.24),

impaired decision-making (OR = 2.12), and depressive symptoms (OR = 2.50) were found to increase the odds of hospital readmission. Both CHF and depression have been found to be consistently associated with hospitalization in previous studies (French, Bass, Bradham, Campbell, & Rubenstein, 2008; Li et al., 2004; Song, Lennie, & Moser, 2009; Zhang et al., 2009). Other covariates such as disability (Miller & Weissert, 2001), falls, wounds, urinary tract infections (Rosati & Huang, 2007), dyspnea, pressure ulcers, guarded prognosis (Fortinsky et al., 2006), social support (Li et al., 2004; Murphy et al., 2008) and age (Madigan et al., 2001) have been shown to be related to readmission in other studies, but were not shown to be predictive in this attempt at modeling. However, most of the results in the literature demonstrate a wide variety of findings related to readmission, indicating that researchers have not yet found the right combination of factors responsible for readmission or that perhaps interactions between variables are confounding the relationships. Impaired decision making is a variable that does not appear to have been studied in the past. This finding needs to be verified, but intuitively “fits” with the premise of the study regarding medication regimen complexity. It would seem that those who have impaired decision making likely would have more difficulty with complex medication regimens and therefore might be expected to be discharged to the hospital more frequently. This new finding gives researchers an opportunity to reevaluate predictors used in past studies in the HHC setting.

Female gender (OR = .58) and being Caucasian (OR = .27) decreased the likelihood of increased comorbidity, while life expectancy of less than six months (OR = 3.57) increased the odds of higher comorbidity. Decreased life expectancy is a covariate not found in many other studies, but when used has been found to associated with

increased comorbidity. Gender and ethnicity almost always are associated with both increased comorbidity and readmission (Howie-Esquivel & Dracup, 2007; Silverstein et al., 2008). However, the negative relationship between being female and increased comorbidity bears closer scrutiny in this setting because it is thought that females typically have more comorbidity throughout their life spans. Perhaps, in HHC, if females have higher comorbidity, they are admitted to assisted living facilities or long term care, rather than back to home because there is likely no one available to care for a female in the home. In essence, patients that do not appear in the data set cannot influence the outcome.

In the logistic regression modeling, impaired decision making was the strongest predictor of readmission to the hospital, followed by CHF, depressive symptomology, comorbidity, and lastly, MRCI score. Neither polypharmacy nor PIM were found to be predictive of readmission in logistic regression modeling. Although the medication variables have been studied in relationship to adverse events, which typically lead to readmission, readmission is typically not an endpoint for studies evaluating the medication related variables. Therefore, it was somewhat surprising that neither polypharmacy nor PIM were related to readmission, which is an adverse event, based on previous study findings that adverse outcomes positively associated with these variables (Flaherty et al., 2000; Fu et al., 2007; Hustey et al., 2007; Rosati & Huang, 2007). Although other adverse events could not be studied with any degree of accuracy given the data set, perhaps adverse events is a mediating or confounding variable for this relationship. These relationships between PIM, polypharmacy, and readmission bear further scrutiny.

Finally, the relationship of MRCI to readmission has never been studied, so this is an important new contribution to the literature. In previous studies (Conn et al., 1991; George et al., 2006), the attempt to link adverse events to MRCI has not been substantiated. This finding also bears increased scrutiny due to the relationship found.

Structural Equation Modeling (SEM)

Although the data met the assumptions for SEM, the data did violate the more stringent path modeling assumptions including that of multivariate normality, as opposed to individual variable normality. Therefore, a SEM procedure/program was used to elucidate the path coefficients. Despite using the SEM process, model development illustrated the pitfalls of using categorical data as predictors, as some of the data elements were highly kurtotic (peaked) making all models except the Comorbidity Model significant in the omnibus chi-square test, leading to an initial conclusion that none of the models were good fitting models. Therefore, other fit indices (CFI, PCFI, RMSEA, AIC) which were more robust regarding kurtosis and sample size, were used to evaluate model fit. In all, six models were tested to determine the best fitting model. Models were eliminated based on sample size being insufficient (Mediating Model), redundant pathways (Waterfall Model), as well as, evaluation of model fit indices (One Pathway, Two Pathway, and MRCI Models).

As these relationships had not previously been studied, six models were evaluated with SEM to determine a best fitting model. The models were developed based on a review of the literature, the logistic regression findings, as well as the findings from the factor analysis for this study. The base portion of the models (the relationships between the black box covariates, comorbidity, and rehospitalization) remained unchanged

throughout the modeling process. However, the upper portion of the model consisting of the comorbidity and medication predictors changed configurations based on the SEM reiterative process and relationships found in the literature.

The original two analytic models, the Mediating Model and the High Risk Medication Regimen Model (HRMR Model), developed in Chapter 3 based on the literature review, were used to develop a third model (Waterfall Model), which was then revised based on reiterations of SEM and the results of the correlation analysis into three versions of reduced models. The Waterfall Model (Figure 4.6) accounted for the covariance between the proposed mediating medication variables. However, this model was not as robust as other models tested, having a non-significant variable in PIM. On the other hand, polypharmacy and medication regimen complexity had a strong enough relationship that one of the variables was eliminated from the model or modeled in the pathway of another medication covariate to readmission. However, the One and Two Pathway Models, which eliminated non-significant variables (Figures 4.7, 4.8), again demonstrated a poorer model fit than either the Comorbidity Model or the HRMR Model. Eliminating both the non-significant PIM pathway and the redundant polypharmacy pathway in the MRCI model (Figure 4.9), depicted a model fit which was almost as good as the HRMR Model (Figure 4.5). Despite a reasonable fitting model in the HRMR model, the Comorbidity Model remained the best fitting model although this model is less predictive of readmission than the HRMR Model. Of the six models evaluated against the Comorbidity Model, the HRMR Model was the best fitting model, though the HRMR Model only accounted for about 10% of the variance in hospital readmission. Given the relatively poor fit indices of both the Comorbidity and HRMR models, and the

difficulty in measuring comorbidity in this sample, neither of these models may be very valid models. Nonetheless, the results from the modeling process are instructive in conceptualizing and operationalizing medication related variables and comorbidity in home health care data. The results also describe a potential pathway through which medication related variables influence readmission, and help to disentangle the effect of comorbidity and medication regimens on readmission.

The HRMR Model. Although this structural equation model had issues with measurement of the two predictors, the HRMR Model accounted for a respectable 10% of re-hospitalization. It remains unclear if this is a valid conclusion given the measurement error in the predictors of comorbidity and HRMR. However, the logistic regression modeling process clearly demonstrates the need to model medication factors separately from comorbidity factors. Researchers had not previously considered the relationship of medications to readmission; perhaps these factors should be considered in future predictive modeling. The findings suggest that high risk medication regimens might be an important part of the puzzle of covariates that contribute to hospital readmissions, at least in this population. The relationship between comorbidity, high risk medication regimens, and hospital readmission also needs to be substantiated in other settings such as in the community and long term care using more robust measures of both comorbidity and high risk medication regimens.

Although it was hypothesized that HRMR Model was a full mediation model, this was not found to be the case. However, partial mediation did occur and high risk medication regimens accounted for 20% of the effect of comorbidity on re-hospitalization. This has significant implications for how researchers should think about

how to structure research studies. Previously, researchers have not examined the effect of medication related variables on readmission, likely assuming that comorbidity fully accounted for the variance assumed by medication regimens. However, this study shows that high risk medication regimens are a risk factor in and of themselves and also mediate the effect of comorbidity. Older studies may need re-examination in light of these findings. It would be expected that further refinement of the model including the new variable should improve the predictive capabilities of future studies. Structural equation modeling, using both comorbidity and medication related variables, helped to untangle the contribution of each predictor variable to the outcome of hospital readmission.

The HRMR Model has not previously been proposed in the literature and now allows investigators to consider another link in the causal chain leading to readmission. Other incidental, but important new findings from the modeling process, included polypharmacy as a sub-mediator in the pathway between comorbidity and medication regimen complexity, and that much of the variance of medication complexity is explained by polypharmacy.

A Closer Examination of the Findings

The final model only fit the data moderately well, so further modification would be the next step in evaluating the HRMR Model. It is suspected that issues around measuring comorbidity may have accounted for some of the fit issues. In future studies, adding hospital discharge diagnoses and active medical problems may assist in more effectively operationalizing comorbidity. The lack of medication adherence factors and the lack of information about provider decision making regarding cost-benefit ratios

related to medication prescribing may also have had an effect on the fit of the model as both of these covairates could be assumed to contribute to the development of high risk medication regimens. Perhaps information about these concepts would add to the predictive ability of the model. Also, change over time was not evaluated in this study. Both comorbidity and the medication factors are ever evolving as patients either become well or more debilitated during the episode of care. Although two time points were measured to create the boundaries for inclusion and exclusion factors, change over time was not measured. Patients got sicker or became well, thus changing the regimen and trajectory of the illness, as well as, the probability of the outcome. A multiple measures design could be completed using this data set, but was beyond the scope of this study. However, this type of design would have improved the preciseness of the prediction and increased the richness of the findings.

Many outliers were in the data, thus affecting both the mean and the degree of influence a particular variable exerts. It is possible that the actual influence of the medication factors is decreased because of outliers in that data, or increased because of outliers in the covariate data. However, outliers were kept in the data despite the difficulty encountered when modeling, because the outliers were few in number and because outliers reflect the reality of HHC.

Binary measures of most of the covariates other than the predictor variables were used in this analysis. This type of measure loses much of the richness of the data. Finer measures of cognition, ADLs, and IADLs, and amount and type of caregiving help might have been more useful as predictor variables. However, many of the categories in the OASIS data overlap, making it difficult, if not impossible, to use the data as ordinal data.

In addition, a good measure of PIM has not been developed and tested, so it is possible that PIM might have more effect than demonstrated in this study. If that would be the case, perhaps the relationship between comorbidity and readmission would be lessened or extinguished entirely.

Finally, neither PIM nor the MRCI, was based on both prescribed and OTC medication as was the polypharmacy variable. This is likely to have provided polypharmacy more weight in the predictive modeling process. In future studies, a recommended change would be to count only prescribed medications for polypharmacy or to extend the PIM and MRCI measures to all medications used. Nonetheless, this model was indeed predictive of re-hospitalization, despite its simplicity. Further development of a latent model evaluating adherence and provider factors may prove to be more explanatory.

Linking This Study to Theory

This area of research has been viewed as atheoretical (Madigan et al., 2002). In the past, the line of inquiry has focused on linking polypharmacy and PIM to adverse events and subsequent increased utilization and cost of healthcare. However, only a few studies have examined medication related factors to these outcomes, and in these studies, only polypharmacy and PIM have been examined. Little was known about medication regimen complexity in relationship to re-hospitalization or other predictors. The link between polypharmacy and medication regimen complexity has been established with this study, as has the *lack* of a relationship between other predictors with PIM, or PIM with the outcome of hospital readmission. The findings of this study suggest that less time should be spent evaluating polypharmacy and PIM, and more effort focused on

studying high risk medication regimens as proposed by this author or medication regimen complexity as designed by George et al. (2004).

A new concept, high risk medication regimens, has been defined and tested for its influence on hospital readmission in this study. Theoretically, this concept has been mentioned in the literature, but has not been well studied, nor a multi-factorial model suggested for composition of this concept. At least three factors, polypharmacy, PIM, medication regimen complexity have been found to compose this concept. It remains for future investigators to evaluate other factors that could compose high risk medication regimens but which have not been examined in this study.

The high risk medication regimen was also evaluated for the influence it exerts on hospital readmission in a SEM. Typically, medications have been viewed as a function of comorbidities, that is, as comorbidity increases, medications are expected to increase, but an assumption underpinning many of these studies is that medications do not exert an influence greater than or equal to comorbidity or that medications and comorbidity are so highly correlated that their influences on outcomes cannot be separated. It was conjectured that high risk medication regimens were a mediator between comorbidity and hospital readmission. However, in this study, HRMR was not shown to be a full mediator, but partially mediated the effect of comorbidity on readmission and exerts an influence equal to comorbidity, and thus is an independent risk factor for hospital readmission. In future studies, the addition of the concept of high risk medication regimens to the constellation of predictors may improve predictive capability of models. A simpler and more robust way to measure this concept needs to be developed and tested. Questions remain regarding where in the recovery trajectory does the risk for readmission

related to high risk medication regimens occur. Further study is needed to not only refine the concept, but test the validity of this concept in other settings.

The medication concepts still remain difficult to define, and therefore, to measure. In particular, PIM as defined by the revised Beers' criteria, needs to be validated as a measurement tool and appropriate weighting attached to the medications. Nonetheless, evaluating whether a patient had PIM was relatively easy using the Beers' criteria with secondary data. The Beers' criteria should be pursued in the future as a viable option for measuring PIM. On the other hand, medication regimen complexity as measured by the George et al. (2004) tool was more cumbersome to use. The scoring process was quite lengthy and there was lack of clarity in the measures forcing the investigator to develop rules to be followed with scoring. In addition, there is no cut off for what makes a regimen "complex" or not. One final critique of the tool is that it clearly was developed to measure a point in time rather than an episode of care, again making it more difficult to score and perhaps changing the validity of the tool when used to measure changes in medications across time periods. With further refinement, this tool would seem capable to measure the concept of medication regimen complexity and merits further development.

The conceptual framework originally presented in Chapter 1 (Figure 5.1) seems to be a partially accurate representation of what is happening in reality. High risk medication regimens are indeed made up of at least the three factors proposed, polypharmacy, PIM, and medication regimen complexity. However, this model does not appear to be a strong contender for a mediation model and perhaps further refinement in measurement of the indicator variables and perhaps adding the ability to self manage medications would further strengthen the mediating relationship as well as the predictive

ability of high risk medication regimens. It is more likely that both comorbidity and high risk medication regimens are independent predictors of readmission to the hospital. Modifications to the conceptual model might include using a wagon wheel analogy, with the outcome of readmission at the center of the circle and comorbidity, high risk medication regimens, or other variables as predictors of the outcome (Figure 5.2).

In this model, the linear pathway has become circular with the predictor variables influencing each other as well as readmission as depicted with bidirectional arrows. This is a much more complex model and likely would include other variables such as adherence, the support persons, and provider prescribing patterns.

Figure 5.1. The original conceptual framework for predicting hospital readmission.

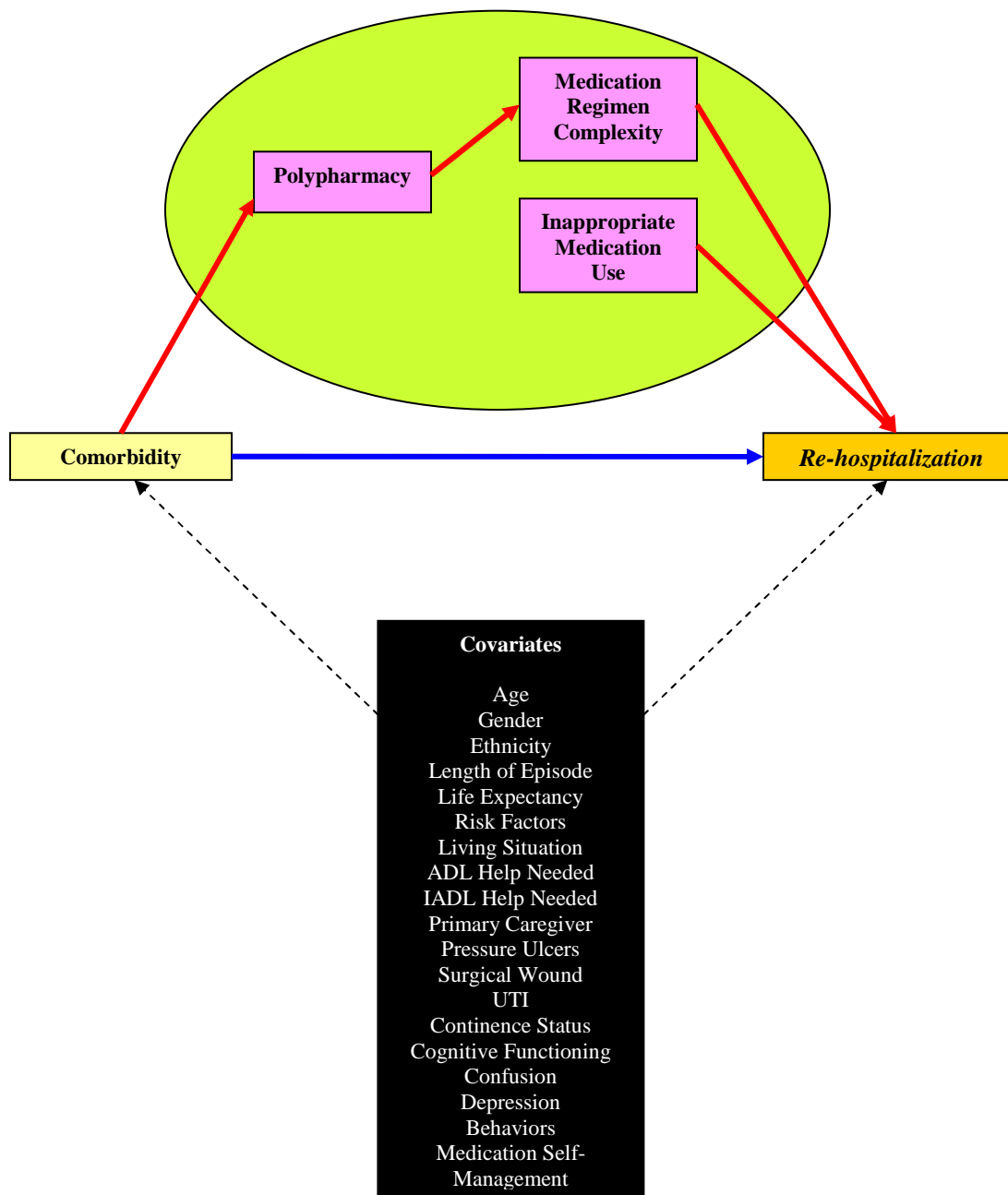
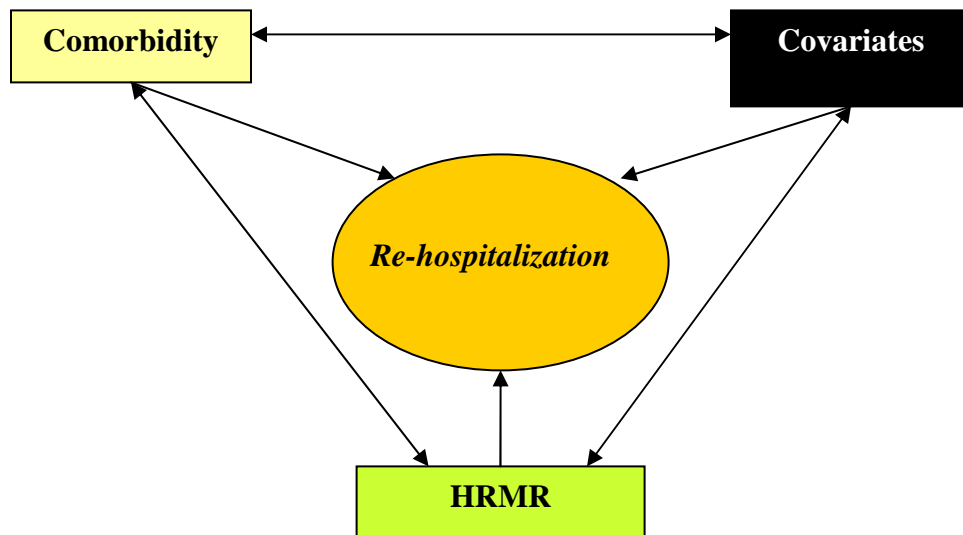


Figure 5.2. The revised conceptual framework for predicting hospital readmission.



In the clinical realm, these findings do not support the idea that polypharmacy alone may be a useful enough predictor to use for risk stratification. These findings have clarified a missing link for researchers who were not able to link polypharmacy, PIM, or medication regimen complexity individually to adverse outcomes. Perhaps, it is the synergistic interaction of these three indicator variables together that accounts for significant variance in hospital readmissions. The chain of events seems to be more complex than a direct link from the comorbidity predictor to the outcome.

Strengths and Limitations of this Study

There are many strengths to this study, but three design aspects are particularly important. The use of a conceptual framework grounds the study firmly in the literature, linking this study to a series of studies performed in the past and potential areas to be studied in the future. The analytic framework also is firmly based in the conceptual framework and allowed the investigator to methodically explore models based on both the modeling process as well as the literature review. The care and detail of the analytic design are important in allowing future researchers to either replicate or improve the study design. Finally, the analytic design using SEM to clarify the specific contributions of each variable to the model is important in exploring and disentangling the contributions of medication related variables from comorbidity variables. This finding allows future researchers to consider the contribution of medication related variables to outcomes separately from the contribution of comorbidity.

The specific definitions and discussion of how variables were operationalized also strengthened this study. A careful literature review revealed that the definitions of the predictor variables strongly influences how and what is counted, which in turn is likely to

impact the outcome of the study. The usefulness of several definitions was debunked and several new ways of operationalizing medication related variables were tested using a secondary data set. A critique of the usefulness and the shortcomings of these tools will make future research endeavors more reliably evaluated.

Another strength of this study was the use of secondary data across multiple sites and software vendors and the techniques used to merge two disparate data sets, the OASIS data and the medication records. Using secondary data analysis allows the examination of large volumes of data inexpensively. Few researchers have attempted to work with this combination of datasets in the past. Combining these datasets allowed for deeper exploration of important issues in HHC. It also allowed new variables to be studied in combination with variables that have been studied in the past. The use of the OASIS data set allows comparison of studies across time as it is a national data set that is relatively stable. Researchers should now be able to track changes in prescribing and use patterns over time in HHC.

The novelty of this study in several areas is a definite strength. This research identified medication use patterns in elderly HHC patients, two populations (the elderly and HHC patients) that are seldom studied. Findings from this study can readily be generalized to other HHC populations as this was a fairly representative sample, despite being a convenience sample. Additionally, no studies were found examining medication regimen complexity in this population, nor have the three medication related variables been studied together. Although high risk medication regimens have been discussed frequently in the literature, no researchers have actually operationalized regimens in this fashion or shown them to be related to readmission. Finally, little is known about

readmission to the hospital from HHC care, so this study provides initial findings for all these topics.

Other strengths of this study included:

- A study design that allowed for risk analysis free of confounding due to adherence, given that the patients are being monitored for proper medication consumption.
- The data and the design allowed following the cohort through time during their first episode of care.
- The use of the federally mandated OASIS data set allowed for standardization and comparison to other studies and, during future research with non-de-identified data, linkage to other federal data sets.
- The data preparation techniques proved useful in developing the medication record.
- The clinical expertise (geriatric nurse practitioner) allowed for creative research questions that are clinically important.

Limitations of this study included the usual issues in secondary data analysis such as 1) lack of control over data collection, 2) variables that may not be defined as precisely as the researcher would like, 3) data being outdated, and 4) data integrity issues (Nicoll & Beyea, 1999). With secondary data, researchers spend a significant amount of time in data preparation, resolving missing variable issues and attempting to understand the conditions under which the data were collected in order to understand what the variables actually mean. Specific to this medication database was a lack of forced choice in the data entry process which made data integrity and data preparation particularly difficult as

there are a variety of ways the names of medications were indicated, routes listed, and dosing amounts written.

Another issue was the measurement of comorbidity as this variable is crucial in defining the focal relationship. Some researchers advocate using a count of diseases as a predictor, and while this method was trialed for this analysis, it was not as predictive, despite using all the potential disease data available in the OASIS data set. The truncation of the diagnosis data in the OASIS database is a liability in evaluating comorbidity as well as not using the primary diagnosis in determining comorbidity. Truncation may have decreased the effect of comorbidity on readmission and perhaps obscured the strength of the focal relationship being tested.

However, with 11 fields in the dataset to identify comorbidity (depending on what fields are chosen for counting), it is probable that investigators will capture important diseases such as congestive heart failure, chronic obstructive pulmonary disease, cancers, diabetes, hypertension, renal or liver disease scored for the Charlson Comorbidity Index. These diseases have a significant impact on functional status, which is often the reason for admission to home health care in the first place. Given that the study sample closely reflected the population, which was a 100% sample from different sized agencies in various locations across the Midwest, it is unlikely sampling bias was operating. Instead, the home health care population, and this study sample which reflects the population, may indeed be a hardier group of patients. However, future researchers may wish to triangulate the data by using OASIS data, hospital discharge summaries, and administrative data collected for billing to ensure complete identification of comorbidity.

Another limitation of this study was the choice to collapse data into dichotomous categories for a large number of variables. Collapsing the variables was done in this setting primarily because many of the variables had choices such as “mark all that apply” (MO380-type of caregiver assistance) or the variable choices were items measuring distinctly different parameters (MO610-behaviors). Although collapsing categories into dichotomous variables is typically thought of as losing the richness of the data, in this instance, the dichotomization allowed more accurate representation of the data by demonstrating that either the patient did not have a condition or did have a condition. Fortunately, the OASIS data includes disparate categories within one variable, so a researcher can choose the variables to examine that have been shown to be most relevant in the literature search. In categories where no overlap occurred, or in variables that pertained to one item, levels of categorization were retained.

There were research issues with operationalization of the medication related variables. For example, PIM, as scored, is not known to have been tested for reliability or validity and it was beyond the scope of this study to appropriately weight the Beers’ criteria. In theory, the MRCI seemed to be an ideal measure of complexity, but in practice was cumbersome to apply, and because there were so many details to track, likely to have a poor inter-rater reliability if used in this type of data over a longer time period. Over-the-counter medications were not counted in either the PIM counts or the MRCI, so it is also likely that the contribution of polypharmacy, which included over-the-counter medications, may have been overestimated.

The simplicity of the model leaves many dimensions of high risk medications and the relationship of this concept to readmission unexplored. Prescribing practices,

adherence and support systems all have been theorized to influence medication regimen complexity and high risk medication regimens. These concepts are both difficult to conceptualize and operationalize, but need to be tested in future iterations of this model. Finally, because this study is not an experimental design, causal level conclusions cannot be drawn from these data.

Implications for Future Study and Translation to the Clinical Setting

Implications for Future Research.

This study was an exploratory study examining the potential to link the concept of high risk medication regimens and the components of high risk medication regimens to readmission to the hospital in HHC patients. While this study substantiated the linkage of these variables, further refinements to the model are needed. Several suggestions for future research studies could improve the research efficacy and the quality of data analyzed as well as the validity of the outcome of the study. In addition several potential areas for study could evolve from the discoveries made in this study.

Time would be saved and research efficacy would be vastly improved if all medication related data sets were entered into data bases that would automatically convert the medications to generic names and attach a National Drug Code (NDC) number or attach RXNorm nomenclature to the medications which uniquely describes the medication. The NDC allows the researchers to quickly and easily group medications by characteristics starting at manufacturer, type of drug, and dosage, form, and strength (United States Food and Drug Administration, 2010), while RXNorm is a standardized vocabulary produced by the National Library of Medicine for identification of drugs and drug delivery devices. RXNorm details the drugs by ingredients, dosage strength, and

physical form of the drug to allow communication across databases (National Library of Medicine, 2009). If one system of nomenclature for drugs could be determined for all electronic health record systems, it would be far simpler for clinicians and researchers to develop algorithms to automate information on PIM or medication regimen complexity. This informatics related task could greatly improve the quality of research, the accuracy of findings, and the speed of release of findings.

A great deal of progress could be made if a standardized method of measuring medication counts and PIM were developed, validated, and tested for reliability. In particular a valid, reliable, and weighted scoring metric for PIM would be valuable in assessing whether this concept impacts readmission far more greatly than this study reveals. Although the MRCI was useful in this study, design changes would improve the ease of use in large, electronic data sets. A problem with the MRCI was that it was developed to measure complexity at a particular point in time rather than over an episode of care. Therefore, the MRCI was difficult to tabulate, given the changes in medications over time. Clarity in the directions for scoring cases in which the medication regimens change over time would be helpful. Another improvement would be the determination of a cut off score for moderately or highly complex regimens, as the numbers at this point do not have a specific meaning attached to them as this is not an index in common usage. Changes in definition and standardization of measures would allow researchers to communicate their findings clearly, as well as allow comparability across studies. In addition, embedding algorithms measuring these concepts into the electronic health record would assist clinicians in identifying patients at higher risk for adverse events and assist researchers in their endeavors.

A number of future studies would extend the findings made from this study.

This study needs to be replicated with a larger, random sample to verify the findings.

After this study is verified, additional variables should be included in future modeling studies, including variables that account for change over time, adherence to the medication regimen, and the consideration of risk-benefit ratio that providers use as they decide what medications to prescribe. The addition of these variables would likely improve the explanatory power of the conceptual model and perhaps rebuild the model entirely. Should these findings be demonstrated again in a larger, random sample, findings from older studies might need to be reevaluated given that high risk medication regimens account for almost 10% of the variance in readmission to the hospital in this study. Replication studies not only need to be done in this population, but in other populations such as assisted living, long term care, and transitional care settings.

Two other types of studies may help elucidate the mechanisms by which inappropriate prescribing occurs, how PIM is managed by patients, and the nature of outcomes for patients subjected to PIM over prolonged time periods. Qualitative study of the metrics of how clinicians weigh the cost/benefit ratio of drug combinations would be useful to help in understanding where clinical knowledge gaps exist and the most efficacious way to address gaps in knowledge. Another qualitative study would be to evaluate the methods by which patients handle high risk medication regimens in order to understand what happens at the provider's office and what happens in the community. Finally, research with a trajectory focus would greatly improve the predictive capability of any models developed and also help determine the most appropriate points in time when interventions should be implemented. Improved predictive capability helps to target

the appropriate interventions to the appropriate population at the appropriate time, thus saving both time and money on the part of the patient, clinician, and the health care system as a whole. Given the number of hospitalizations and the degree of health care utilization directly related to medication mismanagement, interventions developed from accurate predictive models hold great promise in reducing the cost of health care and improving the quality of life for patients under our care.

Implications for Policy

Although the opportunity for policy change is great as the result of this study, only two policy issues will be discussed in this section. The first issue addresses the practical matter of doing research while the second addresses a policy change in the clinical realm. At the federal level, it is important to emphasize using measures that are not only reliable and valid, but also are standardized. The use of standardized measures allows for comparative research and also ensures that meta-analyses can be done on the data. As the use of secondary data sets for research and data mining becomes increasingly more feasible through electronic health records, the issue of how data are recorded may be less of an issue than how it is now.

The findings from this study demonstrate the importance of government policy that strongly encourages the use of standardized measures and processes for reusing electronic data for research purposes. Although some may claim that the freedom of investigators may be impacted, the policy focus has already shifted towards the use of standardized quality measures advocated by the Agency for Healthcare Research and Quality. Requiring new measures be collected along with older, “gold standard” measures in federally funded studies would begin the standardization process.

Another way to influence movement towards standardization is to change clinical reimbursement or research funding parameters to favor the measures or practices desired. Federal standards for meaningful use of electronic health records and change in reimbursement policies being implemented as required by the American Recovery and Reinvestment Act of 2009 are an example of this type of policy effort (HIMSS, 2009). Meaningful use of these records include 1) using certified electronic health records in a meaningful manner such as electronic prescribing, 2) certified electronic health records are connected in a manner that provides for electronic exchange of health information to improve quality of care, and 3) submission to the Secretary (of Health and Human Services) information on clinical quality measures (Federal Register, January 13, 2010, p. 1850). Improved reimbursement of entities using RXNorm for electronic prescribing with the embedded algorithms would be a practical application of this policy. In this way, the new measure can be used to triangulate the results and also test the measure against the gold standard, improving the quality of data measurement tools, as well as the validity of the new tool.

In the clinical realm, if the findings from this study are replicated in subsequent studies, the policy implications could have profound impact on how HHC is provided and perhaps even care in other settings. If medication regimens play an influential role as demonstrated in this study, it is possible that the import of this factor is greatly underestimated in the elderly home care population. This study found that regimen change is not the driving factor for the association of high risk medication regimens with readmission, but likely the complexity of the medication regimens. Even patients, who were for the most part cognitively intact, needed help with their medication regimens.

Patients who were readmitted to the hospital were not only sicker, but had more cognitive impairment, yet were expected to manage a much more difficult medication regimen than those who were not readmitted. Readmitted patients are in home health care a week less than those who are not readmitted. Although this provides savings for HHC, the use of hospital care and an admission to HHC for a second episode of care is far more costly than providing more intense care in the HHC setting at the beginning of the HHC episode or keeping the patient in the hospital slightly longer until stability in condition is assured.

In general, the focus on being homebound and having physical deficits opens the door to HHC. When physical deficits drive the admission, care is likely to be provided with greater intensity at the beginning of the episode of care. While front loading visits is a recommended practice (Briggs, 2006), there are no recommendations for retaining patients for longer periods of time in HHC. This practice prevents many patients who could benefit from supervision or assistance when they are at their most vulnerable, at the point of discharge, from being eligible for HHC. For those who do qualify for home health care, ideally, less supervision would be provided as patients become more functionally independent. Not only is this the point where they are likely to resume management of their medication regimen, this is also the point at which cumulative medication toxicity in the form of adverse drug reactions is likely to occur. Perhaps additional time should be spent verifying how medications are being used early in the HHC episode while the patient becomes used to the new regimen. Patients may also need encouragement to continue medications that are unfamiliar to them. This small amount of

help or review time may be extremely influential on keeping patients out of the hospital early in the HHC episode.

Later in the HHC episode of care, when patients may need to be monitored for adverse drug interactions and response to medical therapy, HHC is not available because patients are no longer considered medically unstable enough to need close monitoring and likely the physical dysfunction used as the basis for implementing HHC is improved. However, a change in policy that allows for HHC for medication monitoring, whether by phone, computer, or in person, might be especially cost effective at this point. Although a regulatory change of this magnitude may initially increase the cost of HHC, it may be an opportunity to reduce readmissions, and the potential for poor outcomes in the long run.

Implications for Nursing Practice

Findings from this study have important implications for clinical practice. It is clear that polypharmacy, PIM, and medication regimen complexity are at high levels, putting many patients at risk for re-hospitalization. These three factors account for a substantial portion of the concept of high risk medication regimens. High risk medication regimens in turn influence hospital readmissions. The high risk medication regimen needs to easily be identified and acted upon in order to prevent hospital readmissions. Computer programs that readily identify high risk medication regimens, assign a risk to the potential for drug interactions and adverse events, and more importantly, suggest safer alternatives for use should be made readily available for the provider at point of contact, rather than only having these types of programs in the pharmacy. These programs would help prevent poor medication choices from being made before dispensing of the drug and allow efficient medication reconciliation saving time and money.

The idea that not only can clinicians cause iatrogenic adverse drug reactions, but that they may also be causing iatrogenic readmissions by way of prescribing medications to prevent this outcome have profound implications for clinical practice. Clinicians must not only be aware of the potential risk of adverse drug reactions and interactions, they also must assess this potential in a very individual manner. The common practice of using drugs to prevent future events in elders may not be good practice and may actually harm more elders than are helped, especially when multiple preventive compounds are used. This is especially true for PIM, where zero tolerance is the accepted norm. However, very few tools, other than the Beers' criteria, exist for clinicians to assess the concept of high risk medication regimens. Clinical tools need to be developed and tested to measure these concepts, and further studies done in the clinical setting to monitor the effect of changing levels of these variables on outcomes and risk stratification. In the meantime, clinicians need to add another level of complexity to their practice, scrupulously monitoring the numbers of medications and the expectations for management of complex regimens.

Nurses and those caring for patients in home health care must learn to advocate for the patient in dealing with both the prescriber and the need for additional services. In addition, all levels of providers must know the side effect profile of commonly used drugs and the presentation of these effects in the elderly, especially given the aging of our population. This has profound effects on how geriatric curriculum is presented both in educational institutions and in continuing education venues. Families must also be taught this information as they are the prime caregivers for this group of patients. Finally, prescribers must take every opportunity to simplify the medication regimens of their

elderly patients. Armed with the knowledge about the link between these concepts and the risk of re-hospitalizations, clinicians can change practice and improve outcomes of our older adult patients.

Conclusion

Evaluation of the existing literature demonstrated a gap in knowledge about the role of medications in readmission to the hospital, particularly in the HHC population. Many authors mentioned high risk medication regimens without specifically defining the regimen, nor operationalizing the term. A number of factors are thought to compose high risk medication regimens including polypharmacy, potentially inappropriate medications, and medication regimen complexity. However, so far only polypharmacy has been associated with readmission, although both polypharmacy and potentially inappropriate medication use have been associated with adverse drug events. Medication regimen complexity has been studied in special populations like AIDS patients, but results in broader based studies have not found medication regimen complexity to be associated with adverse drug events at this point. Few studies are in agreement in defining or operationalizing these terms indicating that the study of high risk medication regimens is in its infancy. In addition, these concepts have not been well studied in either older adults or in the HHC population.

Therefore, an exploratory secondary analysis of OASIS data and medication records from 15 HHC agencies was undertaken to evaluate the effect of medication regimens on readmission in 911 older adults during their first episode of care after being admitted to HHC from the hospital in 2004. The endpoint of the study was readmission with the main predictors evaluated as comorbidity and high risk medication regimens,

which were hypothesized to be composed of polypharmacy, potentially inappropriate medication regimens, and medication regimen complexity. Evaluation of descriptive statistics revealed that this sample was similar to the HHC population in general, but there were significant differences in both medication use patterns and level of comorbidity compared to previous studies. Logistic regression was used to help determine possible other covariates for the structural equation modeling, which was then utilized to untangle the relationship between comorbidity, high risk medication regimens, and readmission.

The three research aims were posed and addressed in this study. Patients in HHC who were readmitted compared to those who were not readmitted used a larger number of medications, both appropriate and inappropriate, and have more complexity in their regimens. It was demonstrated that high risk medication regimens are indeed composed of polypharmacy, potentially inappropriate medication regimens, and medication regimen complexity, and that a model using this concept rather than individual medication variables proved to be the most parsimonious model. Finally, high risk medication regimens appear to have as much influence as comorbidity on readmission to the hospital.

The findings from this study have demonstrated the important role high risk medication regimens play in hospital readmissions in HHC patients. Important research, policy and clinical practice implications flow from this study. It is clear that future research should include high risk medication regimens as a predictor of readmission and that perhaps even previously completed studies may need to be reevaluated in light of these findings. In the policy arena, this study has important implications as to how HHC is delivered (follow up after discharge, front loading visits) and who should qualify for

HHC (illness versus functional capacity), while practice changes in the use of medications (prescribing practices, advocacy, knowledge about geriatric pharmacotherapy) may need to be implemented.

Most studies conclude the readmission is due to comorbidity or that discharge to home that is taking place too quickly. However, it is apparent that medication regimens themselves carry an inherent risk of readmission and should be evaluated as separate risk factors above that of comorbidity or length of stay. Increased attention to these medication related risk factors has the potential to save the health care system a great deal of money and our patient a great deal of pain and suffering.

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APPENDICES

Appendix A

Strategy for Literature Review

Keyword Search

Elderly

- *Aged
- Seniors
- *Geriatrics
- Elder
- Old Age
- Older Adults

Polypharmacy

- *Combination Drug Therapy
- *Drug Therapy
- Multiple Medications
- *Medication Errors
- Polypharmacy

Community Dwelling Patients

- *Home Care Services
- *Community Health Nursing
- *Home Care Agencies
- *Health Services for the Aged
- *Ambulatory Care
- Aging in Place
- Home Health Care

Potentially Inappropriate Meds

- High Risk Meds
- *Drug Interactions
- *Quality Assurance
- *Quality Control
- *Total Quality Management
- *Drug Utilization Review
- Inappropriate Meds
- Inappropriate Drugs
- Potentially Inappropriate Drugs
- PIM
- Inappropriate Prescribing
- *Adverse Drug Reaction Reporting System
- Adverse Drug Reaction
- Adverse Drug Event
- ADR
- ADE
- Beers Criteria
- Medication Appropriateness Index
- *Drug Utilization
- Medication Review

Difficult Medication Regimens

- Complex Medication Regimens
- *Self Administration
- *Self Medication
- Medication Self Administration
- Medication Complexity
- *Patient Compliance
- Patient Adherence
- *Treatment Refusal
- Medication Complexity Index
- Medication Regimen Complexity Index
- Non-compliance (under tx refusal)
- Non-adherence (under tx refusal)

Adverse Outcomes

- *Outcome Assessment
- Emergent Care
- *Emergency Services
- Emergency Room Visits
- *Hospitalization
- *Patient Re-admission
- *Institutionalization
- Nursing Home Placement
- *Nursing Homes
- *Death
- *Mortality
- *Falls
- Poisoning

Appendix B

Charlson Comorbidity Index

Final Charlson Comorbidity Index/Deyo Modification

7/4/2007

Retrieved from http://www.chaps.ucalgary.ca/ICD9_Enhanced_Charlson.txt

DC	Label	ICD9 Codes	Charlson Weight
1	Myocardial Infarction	'410','412'	1
2	Congestive Heart Failure	'39891','40201','40211','40291','40401','40403','40411','40413','40491','40493','4254','4255','4257','4258','4259','428'	1
3	Peripheral Vascular	'0930','4373','440','441','4431','4432','4438','4439','4471','5571','5579','V434'	1
4	Cerebrovascular	'36234','430','431','432','433','434','435','436','437','438'	1
5	Dementia	'290','2941','3312'	1
6	Chronic Pulmonary	'4168','4169','490','491','492','493','494','495','496','500','501','502','503','504','505','5064','5081','5088'	1
7	Connective Tissue Dx/ Rheumatic	'4465','7100','7101','7102','7103','7104','7140','7141','7142','7148','725'	1
8	Peptic Ulcer	'531','532','533','534'	1
9	Mild Liver Disease	'07022','07023','07032','07033','07044','07054','0706','0709','570','571','5733','5734','5738','5739','V427'	1
10	Diabetes w/o complications	'2500','2501','2502','2503','2508','2509'	1
11	Diabetes with complications	'2504','2505','2506','2507'	2
12	Paraplegia & Hemiplegia	'3341','342','343','3440','3441','3442','3443','3444','3445','3446','3449'	2
13	Renal Disease	'40301','40311','40391','40402','40403','40412','40413','40492','40493','582','5830','5831','5832','5834','5836','5837','585','586','5880','V420','V451','V56'	2
14	Cancer	'140','141','142','143','144','145','146','147','148','149','150','151','152','153','154','155','156','157','158','159','160','161','162','163','164','165','170','171','172','174','175','176','179','180','181','182','183','184','185','186','187','188','189','190','191','192','193','194','195','200','201','202','203','204','205','206','207','208','2386'	2
15	Mod or Severe Liver Disease	'4560','4561','4562','5722','5723','5724','5728'	3
16	Metastatic Carcinoma	'196','197','198','199'	6
17	AIDS/HIV	'042','043','044'	6
99		All others	0

Appendix C

PIM Tables

Table 1. Potentially Inappropriate Medications: Independent of Diagnoses or Conditions, from Fick et al. (2003, p. 2719), used with permission.

Drug/Drug Combinations with the Active Ingredient	Low Risk	High Risk
Propoxyphene (Darvon)	X	
Indomethacin (Indocin)		X
Pentazocine (Talwin)		X
Muscle relaxants and antispasmodics: methocarbamol (Robaxin), carisoprodol (Soma), chlorzoxazone (Paraflex), metaxalone (Skelaxin), cyclobenzaprine (Flexeril), and oxybutynin (Ditropan). Do not consider the extended-release Ditropan XL.		X
Flurazepam (Dalmane)		X
Amitriptyline (Elavil), chlordiazepoxide-amitriptyline (Limbitrol), and perphenazine-amitriptyline (Triavil)		X
Doxepin (Sinequan)		X
Meprobamate (Miltown and Equanil)		X
Doses of short-acting benzodiazepines: doses greater than lorazepam (Ativan), 3 mg; oxazepam (Serax), 60 mg; alprazolam (Xanax), 2 mg; temazepam (Restoril), 15 mg; and triazolam (Halcion), 0.25 mg		X
Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol), clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene)		X
Disopyramide (Norpace and Norpace CR)		X
Digoxin (Lanoxin) (should not exceed ≤ 0.125 mg/d except when treating atrial arrhythmias)	X	
Short-acting dipyridamole (Persantine). 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	X	
Methyldopa (Aldomet) and methyldopa-hydrochlorothiazide (Aldoril)		X
Reserpine at doses > 0.25 mg	X	
Chlorpropamide (Diabinese)		X
Gastrointestinal antispasmodic drugs: dicyclomine (Bentyl), hyoscyamine (Levsin and Levsinex), propantheline (Pro-Banthine), belladonna alkaloids (Donnatal and others), and clidinium-chlordiazepoxide (Librax)		X
Anticholinergics and antihistamines: chlorpheniramine (Chlor-Trimeton), diphenhydramine (Benadryl), hydroxyzine (Vistaril and Atarax), cyproheptadine (Periactin), promethazine (Phenergan), tripeleminamine, dexchlorpheniramine (Polaramine)		X
Diphenhydramine (Benadryl)		X
Ergot mesyloids (Hydergine) and cyclandelate (Cyclospasmol)	X	
Ferrous sulfate >325 mg/d	X	
All barbiturates (except phenobarbital) except when used to control seizures		X

Table 1 continued, from Fick et al. (2003, p. 2720).

Drug/Drug Combinations with the Active Ingredient	Low Risk	High Risk
Meperidine (Demerol)		X
Ticlopidine (Ticlid)		X
Ketorolac (Toradol)		X
Amphetamines and anorexic agents		X
Long-term use of full-dosage, longer half-life, non-COX-selective NSAIDs: naproxen (Naprosyn, Avapro, and Aleve), oxaprozin (Daypro), and piroxicam (Feldene)		X
Daily fluoxetine (Prozac)		X
Long-term use of stimulant laxatives: bisacodyl (Dulcolax), cascara sagrada, and Neoloid except in the presence of opiate analgesic use		X
Amiodarone (Cordarone)		X
Orphenadrine (Norflex)		X
Guanethidine (Ismelin)		X
Guanadrel (Hylorel)		X
Cyclandelate (Cyclospasmol)	X	
Isoxsuprine (Vasodilan)	X	
Nitrofurantoin (Macrochantin)		X
Doxazosin (Cardura)	X	
Methyltestosterone (Android, Virilon, and Testrad)		X
Thioridazine (Mellaril)		X
Mesoridazine (Serentil)		X
Short acting nifedipine (Procardia and Adalat)		X
Clonidine (Catapres)	X	
Mineral oil		X
Cimetidine (Tagamet)	X	
Ethacrynic acid (Edecrin)	X	
Desiccated thyroid		X
Amphetamines (excluding methylphenidate hydrochloride and anorexics)		X
Estrogens only (oral)	X	

Table 2 Potentially Inappropriate Medication Use: Considering Diagnoses or Conditions, from Fick et al. (2003, p. 2721), used with permission.

Disease	Drug	Low Risk	High Risk
Heart Failure	Disopyramide (Norpace), and high sodium content drugs (sodium and sodium salts [alginate bicarbonate, biphosphate, citrate, phosphate, salicylate, and sulfate])		X
Hypertension	Phenylpropanolamine hydrochloride (removed from the market in 2001), pseudoephedrine; diet pills, and amphetamines		X
Ulcers	NSAIDs and aspirin (<325 mg) (coxibs excluded)		X
Seizures or Epilepsy	Clozapine (Clozaril), chlorpromazine (Thorazine), thioridazine (Mellaril), and thiothixene (Navane)		X
Clotting Disorders, Anticoagulation	Aspirin, NSAIDs, dipyridamole (Persantin), ticlopidine (Ticlid), and clopidogrel (Plavix)		X
Bladder Outflow Obstruction	Anticholinergics and antihistamines, gastrointestinal antispasmodics, muscle relaxants, oxybutynin (Ditropan), flavoxate (Urispas), anticholinergics, antidepressants, decongestants, and tolterodine (Detrol)		X
Stress Incontinence	alpha-Blockers (Doxazosin, Prazosin, and Terazosin), anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride), and long-acting benzodiazepines		X
Arrhythmias	Tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)		X
Insomnia	Decongestants, theophylline (Theodur), methylphenidate (Ritalin), MAOIs, and amphetamines		X
Parkinson's Disease	Metoclopramide (Reglan), conventional antipsychotics, and tacrine (Cognex)		X
Cognitive Impairment	Barbiturates, anticholinergics, antispasmodics, and muscle relaxants. CNS stimulants: dextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), and pemolin		X
Depression	Long-term benzodiazepine use. Sympatholytic agents: methyldopa (Aldomet), reserpine, and guanethidine (Ismelin)		X
Anorexia and Malnutrition	CNS stimulants: DextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), pemolin, and fluoxetine (Prozac)		X
Syncope and Falls	Short- to intermediate-acting benzodiazepine and tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)		X
SIAHD; Hyponatremia	SSRIs: fluoxetine (Prozac), fluvoxamine (Luvox), citalopram (Celexa), paroxetine (Paxil), and sertraline (Zoloft)	X	

Table 2 Continued			
Disease	Drug	Low Risk	High Risk
Seizure Disorder	Bupropion (Wellbutrin)		X
Obesity	Olanzapine (Zyprexa)	X	
COPD	Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol), clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene); beta-blockers: propranolol		X
Chronic Constipation	Calcium channel blockers, anticholinergics, and tricyclic antidepressant (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)	X	

Appendix D

Medication Regimen Complexity Index

The Medication Regimen Complexity Index, Section A (George et al., 2004, p. 1374), used with permission.

Appendix II. Medication Regimen Complexity Index (MRCI)

MEDICATION REGIMEN COMPLEXITY INDEX

Patient ID: -----

Total no. of medications (including prn/sos medications): -----

Instructions

1. MRCI applies only to prescribed medications. All entries are to be made only based on information on the label or drug chart (at the time of dispensing or discharge). No assumptions are to be made based on clinical judgement.
2. There are three sections in the scale. Complete each section before proceeding to the next. At the end, add the scores for the three sections to give the MRCI.
3. If the same medication (same brand and same dosage form) is present more than once in different strengths in a regimen (e.g. Marevan 5mg, 3mg and 1 mg mdu), it is still considered as one medication.
4. In cases where the dosage is optional, choose the dosing instruction with the smallest dose/frequency. (e.g. Ventolin MDI 1-2 puffs, 2-3 times daily will get weightings for 'metered dose inhalers', 'variable dose' and 'twice daily'; but not for 'multiple units at one time')
5. In certain cases the dosing frequency needs to be calculated (e.g. Ranitidine 1mane and 1nocte is 1twice daily)
6. It is possible that with certain 'use as directed' instructions, the regimen will not get a score under dosing frequency (e.g. Prednisolone 5mg mdu)
7. If there is more than one dosing frequency direction, they should be scored for all the dosing frequency directions (e.g. Ventolin MDI 2 puffs bd and prn, will get scores for 'metered dose inhalers', 'multiple units at one time', 'twice daily' as well as 'prn')
8. Instances where two or more medications are mutually exclusive, they need to be scored twice or more as prn with the recommended dosing frequency (e.g. Ventolin MDI or Ventolin nebuliser twice daily will get scores for both 'metered dose inhalers' and 'nebuliser' under dosage forms, but needs to be scored two times for 'twice daily prn')
9. In cases where there is no matching option, choose the closest option (e.g. six times daily could be considered as 'q4h')

A) Circle the weighting corresponding to each dosage form (ONCE ONLY) present in the regimen.

	Dosage Forms	Weighting
ORAL	Capsules/Tablets	1
	Gargles/Mouthwashes	2
	Gums/Lozenges	2
	Liquids	2
	Powders/Granules	2
	Sublingual sprays/tabs	2
TOPICAL	Creams/Gels/Ointments	2
	Dressings	3
	Paints/Solutions	2
	Pastes	3
	Patches	2
	Sprays	1
EAR, EYE & NOSE	Ear drops/creams/ointments	3
	Eye drops	3
	Eye gels/ointments	3
	Nasal drops/cream/ointment	3
	Nasal spray	2
INHALATION	Accuhalers	3
	Aerolizers	3
	Metered dose inhalers	4
	Nebuliser	5
	Oxygen/Concentrator	3
	Turbuhalers	3
	Other DPIs	3
OTHERS	Dialysate	5
	Enemas	2
	Injections: Prefilled	3
	Ampoules/Vials	4
	Pessaries	3
	Patient controlled analgesia	2
	Suppositories	2
	Vaginal creams	2
Total for Section A		

DPI = dry-powder inhaler; MDI = metered-dose inhaler.

(continued on page 1375)

The Medication Regimen Complexity Index, Sections B and C (George et al., 2004, p. 1375), used with permission.

Appendix II. Medication Regimen Complexity Index (MRCI) (continued)

B) For each medication in the regimen tick a box [✓] corresponding to the dosing frequency. Then, add the no. of [✓] in each category and multiply by the assigned weighting. In cases where there is no exact option, choose the best option.

Dosing Frequency	Medications	Total	Weighting	Weighting × No. of medications
Once daily			1	
Once daily prn			0.5	
Twice daily			2	
Twice daily prn			1	
Three times daily			3	
Three times daily prn			1.5	
Four times daily			4	
Four times daily prn			2	
q 12h			2.5	
q 12h prn			1.5	
q 8h			3.5	
q 8h prn			2	
q 6h			4.5	
q 6h prn			2.5	
q 4h			6.5	
q 4h prn			3.5	
q 2h			12.5	
q 2h prn			6.5	
prn/sos			0.5	
On alternate days or less frequently			2	
Oxygen prn			1	
Oxygen <15hrs			2	
Oxygen >15hrs			3	
Total for Section B				

C) Tick a box [✓] corresponding to the additional directions, if present in the regimen. Then, add the no. of [✓] in each category and multiply by the assigned weighting.

Additional Directions	Medications	Total	Weighting	Weighting × No. of medications
Break or crush tablet			1	
Dissolve tablet/powder			1	
Multiple units at one time (e.g. 2 tabs, 2 puffs)			1	
Variable dose (e.g. 1-2 caps, 2-3 puffs)			1	
Take/use at specified time/s (e.g. mane, nocte, 8 AM)			1	
Relation to food (e.g. pc, ac, with food)			1	
Take with specific fluid			1	
Take/use as directed			2	
Tapering/increasing dose			2	
Alternating dose (e.g. one mane & two nocte, one/ two on alternate days)			2	
Total for Section C				

Medication Regimen Complexity = Total (A) + Total (B) + Total (C)=

DPI = dry-powder inhaler; MDI = metered-dose inhaler.