INVESTIGATING THE EFFECTS OF POLYPHARMACY AMONG ELDERLY PATIENTS WITH DIABETES ON GLYCEMIC CONTROL AND CLINICAL OUTCOMES IN HOME HEALTH CARE

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The focus of this research study is glycemic control in the presence of multiple morbidities and polypharmacy in homebound individuals with Type 2 diabetes aged 65 years and older. The research method is a quantitative retrospective cohort study of discharged patients of a nonprofit community-based home health agency from January 1, 2010, to December 31, 2011, using OASIS data. Glycemic control is assessed using the hA1C laboratory test following the recommendation of the American Diabetes Association. The study documents a moderate significant association between glycemic control, polypharmacy and comorbid conditions, indicating that homebound individuals with Type 2 diabetes aged 65 years and older are less likely to have optimal glycemic control in the presence of multiple morbidities and polypharmacy. There continues to be a need for scientific research in this population cohort; and the dose-response association between antidiabetic therapy interventions designed to lower blood glucose levels in the presence of chronic disease and polypharmacy.

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CHAPTER 1

INTRODUCTION

The focus of this research study is glycemic control in the presence of multiple morbidities and polypharmacy in homebound individuals with Type 2 diabetes aged 65 years and older. The study explores the relationships between glycemic control and diabetes disease severity (diabetic manifestations), polypharmacy (medications, therapeutic subclasses and categories), comorbid conditions, and adverse clinical outcomes. In this chapter, I discuss diabetes mellitus and its association with chronic conditions and polypharmacy, and the impact on home health care. Additionally, this chapter addresses the statement of the research problem, rationale for the study, research purpose and questions, and the significance of the study for practice and policy.

Diabetes Mellitus

Diabetes mellitus (diabetes) encompasses a group of endocrine disorders with no known distinct etiology or pathogenesis characterized by chronic hyperglycemia (elevated blood glucose) with disturbances of carbohydrate, fat and protein metabolism resulting from defects of insulin secretion, insulin action or both (Crandall,2007; American Diabetes Association, 2004; Srinivasan, Taub, Khunti, & Owens, 2008). It has been estimated that 90-95% of the elderly have Type 2 diabetes, which results from "a combination of resistance to insulin action and an inadequate compensatory insulin secretory response" (ADA, 2004). Age-related biological changes in the human body contribute to the high prevalence of diabetes in the elderly, i.e. reduction in lean body mass with alteration of body fat distribution; a decline in the ability of the blood to maintain normal glucose and blood glucose levels; tissue cells

become less sensitive to insulin; defects in carbohydrate metabolism; reduced response to glucagon; and a reduction in renal function (Hornick & Aron, 2008; Odegard, Setter, & Neumiller, 2007; Mangoni & Jackson, 2003; Meneilly & Tessier, 2001).

Elderly patients with diabetes are also disproportionately affected by other chronic health conditions (Ober, Watts, & Lawrence, 2006; Good, 2002; Ibrahim, Kang, & Dansky, 2005; Austin, 2006; Meneilly & Tessier, 2001). Among the elderly with diabetes, approximately 75% have 2 or more comorbid conditions (Caughey, Roughead, Vitry, McDermott, Shakib, & Gilbert, 2010). The presence of diabetes in the elderly is a significant risk factor of macrovascular events (cardiovascular, cerebrovascular, and peripheral vascular disease); associated with an increased risk of microvascular (retinopathy, neuropathy, and nephropathy) complications; a strong predictor of functional decline; and impaired cognitive function (Hachinski, 2008; Reusch, 2003; Meneilly & Tessier, 2001). Research has found strong correlations between the risk of microvascular and macrovascular changes and hemoglobin A1C values, duration of diabetes, hypertension, and hyperlipidemia (Meneilly & Tessier, 2001; Reusch, 2003). As a complex chronic condition involving multiple morbidities, elderly people with diabetes experience an increase in utilization of health care resources; and an increase need for formal and informal community resources (Sharkey, 2005; Gregg & Brown, 2003).

Polypharmacy, defined as the total number of different medications that a patient uses concomitantly (Austin, 2006; Good, 2002), in the elderly has been associated with adverse drug events, drug-drug interaction, potential duplication of therapy, increased costs, decreased adherence to the drug regimen, medication errors, an increased risk of hospitalization, emergency department visits, and decreased quality of life (Austin, 2006; Bjerrum, Sogaard,

Hallas, & Kragstrup, 1998). Diabetic patients are at high risk for polypharmacy. The clinical management of diabetes (Figure 1.1) presents a pharmacological triad, first the management of blood glucose levels, second the management of the microvascular and macrovascular associated diseases, and third the management of other chronic conditions not associated with diabetes, resulting in complex medication regimens. However, clinical practice guidelines rarely address the treatment of patients with 3 or more chronic diseases, thus increasing the potential for drug-drug interactions and adverse events (Boyd, Darer, Boult, Fried, Boult, & Wu, 2005).

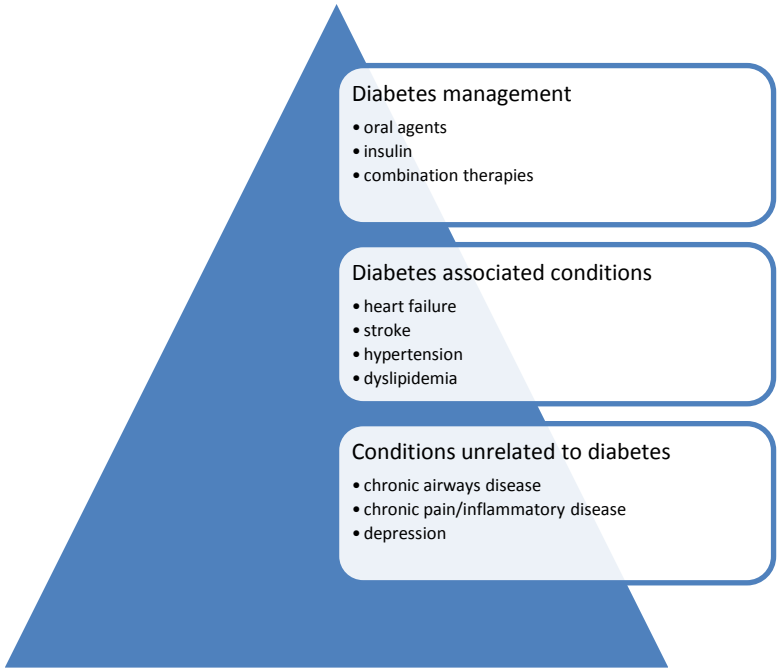

Figure 1.1. Clinical management of diabetes.

For the elderly patient with diabetes, the management of multiple comorbid conditions and complex medication regimens, along with the issues of functional impairments and support systems requires constant assessment and reassessment. This patient population will have an

increased need for formal and informal community-based systems of care as the disease progresses. Medicare reimbursed home health is formal community-based care established to assist with the transitions of short term post-acute or exacerbations of chronic conditions, disabilities, or terminal illnesses for the homebound patient (Caffrey, Sengupta, Moss, Harris-Kojetin, & Valverde, 2011). For this patient population, referral for home health care begins with the inability of the patient to access care in the community secondary to severity of illness or functional impairment. For the elderly diabetic population, poor blood glucose control, history of frequent hospitalizations or unstable conditions following hospitalization or outpatient health services, inadequate medication knowledge and/or appropriate medication use, multiple medication changes, older age, multiple chronic conditions, inadequate social support, or new diagnoses, are common reasons for referral to home health services (Corbett, Cook, & Setter, 2003). In 2007 the National Home and Hospice Care Survey estimated 1,459,900 Medicare beneficiaries received home health care per day, of which 68.7% were aged 65 years and over; the primary diagnosis for admission to home health services was diabetes mellitus (10.1%), and among all listed diagnosis an additional 30.6% of beneficiaries had diabetes (Caffrey et al., 2011). The total incurred home health care costs for adult diabetics in 2007, were estimated at $9.3 billion; an additional $13.9 billion was spent on antidiabetic agents, insulin and diabetic supplies; and another $26 billion spent on retail prescriptions (Dall, Mann, Zhang, Martin, Chen, & Hogan, 2008).

Statement of the Research Problem

Diabetes disproportionately affects the elderly. Prevalence rates for diabetes are projected to increase globally, with the largest group being people aged 65 years and older;

based on estimates from 2000 to 2030, the top three countries identified are India (31.7 million to 79.4 million), China (20.8 million to 42.3 million), and the United States (17.7 million to 30.3 million) (Wild, Roglic, Green, Sicree, and King, 2004; Boyle, Honeycutt, Venkat Narayan, Hoerger, Geiss, Chen, and Thompson, 2001). In 2010 among U.S. residents aged 65 years and older, it has been estimated that 26.9% (10.9 million) had diagnosed diabetes (Centers for Disease Prevention and Control, 2011).

The Agency for Healthcare Research and Quality (2010) report that only 58.0% of adults aged 60 years and over with diagnosed diabetes between the years 2005-2008 had their hA1C under optimal control; the rate was significantly lower for minorities, Blacks and Mexican Americans (47.6% and 43.9%, respectively) compared to Whites (56.3%). In a study conducted by Dalton, Garvey, and Samia (2006), of home care patients (*N* = 166) aged 18 years and older with Type 1 or Type 2 diabetes, approximately 50% of diabetic patients among three study groups were discharged with blood glucose levels that did not meet American Diabetes Association guideline, hA1C < 7%. Additional findings by Bowles, Pham, O'Connor, and Horwitz (2009), of home care patients from four different agencies (*N* = 303) aged 55 years and older with diabetes, indicate that compared with guideline recommendations only 32% of reported patients has a hA1C within normal range.

In a cross-sectional study of diabetics aged 65 years or older conducted by Caughey, Roughead, Vitry, McDermott, Shakib and Gilbert (2010) using prescription dispensing data from the Australian Department of Veterans' Affairs, the prevalence of comorbid conditions in the elderly with diabetes and the prescribing of potentially inappropriate medications or treatment conflicts were examined. Study results identify of the 18,968 diabetics age $\geq$ 65 years, median

age 82 years (*IQR* 79-85), the median number of comorbidities was 5 (*IQR* 5-8), with the median number of unique medications dispensed was 10 (*IQR* 7-14), with over 70% dispensed 5 or more unique medications (Caughey, Roughead, Vitry, McDermott, Shakib & Gilbert, 2010). Additional findings from this study indicate 40% of the comorbidity could be attributed to diabetes associated cardiovascular conditions and that 40% of all medicines used was attributed to the dispensing of diabetes guideline treatment which includes the management of both diabetes and associated cardiovascular comorbidities (Caughey, Roughead, Vitry, McDermott, Shakib & Gilbert, 2010).

Rationale for the Study

In this retrospective cohort study, I used the conceptual model presented in Figure 1.2, to categorize factors that may influence glycemic control in homebound individuals with Type 2 diabetes aged 65 years and older. This model suggests that population characteristics, economic factors, health-related factors, functional impairments, life system profile, and intensity of medical services may have an influence on glycemic control in this population. In the elderly diabetic, the ability to afford medications, symptom management of chronic conditions, the presence of limitations in cognition and vision, inability to manage medications, and the lack of supportive assistance has been associated with poor diabetes control (O'Reilly, 2005). I believe that the health-related factors of multiple chronic conditions and complex medication regimens to manage those conditions have a significant impact on glycemic control. My intent is to use this framework of diabetes disease severity (presence of diabetic manifestations) and comorbid conditions (diabetes related conditions, and non-related conditions), to examine the role of multiple drug regimens (polypharmacy) on glycemic control

and adverse clinical outcomes. Research has identified polypharmacy as an independent risk factor for serious hypoglycemia in the elderly patient with diabetes (Shorr, Ray, Daughtery, & Griffin, 1997; Chelliah & Burge, 2004; Salem, Fathallah, Hmouda, & Bouraoui, 2011); and the use of multiple therapeutic drug categories as an independent risk factor for adverse drug-drug interactions (Sharkey, Browne, Ory, & Wang, 2005; Caughey, Roughead, Vitry, McDermott, Shakib & Gilbert, 2010).

Empirical research has found independent of other factors, increased use of multiple therapeutic categories were associated with sociodemographic characteristics (gender, age, living arrangement, marital status, and medication coverage), medical conditions (diabetes, heart problems, and lung disease) and inability to self-manage medications (Sharkey, Browne, Ory, & Wang, 2005). Previous research has identified intensity of home health services, polypharmacy, lack of knowledge or understanding, cognitive status, older age, living alone, and costs of medications as risk factors for medication mismanagement in older people receiving home health care services (Flaherty, Perry, Lynchard, & Morley, 2000; Meredith, Feldman, Frey, Hall, Brown, & Ray, 2001).

Statement of the Purpose

The purpose of this study is to explore the relationship between glycemic control and diabetes disease severity, polypharmacy, comorbid conditions, and adverse clinical outcomes among homebound individuals with Type 2 diabetes aged 65 years and older. The study hypothesis is on average, the probability of optimal glycemic control (hA1C < 7%) declines in homebound individuals with Type 2 diabetes aged 65 years and older in the presence of multiple morbidities and polypharmacy.

Research Questions

The study is designed to answer eight quantitative questions, 5 descriptive and 3 relational.

Descriptive Questions

1. What is the level of glycemic control in homebound individuals with Type 2 diabetes aged 65 years and older when discharged from home health services?
2. What is the level of polypharmacy in homebound individuals with Type 2 diabetes aged 65 years and older?
3. What is the level of diabetes disease severity in homebound individuals with Type 2 diabetes aged 65 years and older?
4. What is the level of comorbid conditions in homebound individuals with Type 2 diabetes aged 65 years and older?
5. What is the level of diabetes related adverse outcomes in homebound individuals with Type 2 diabetes aged 65 years and older?

Relational Questions

6. What is the relationship between diabetes disease severity and glycemic control in homebound individuals with Type 2 diabetes aged 65 years and older?
7. What is the relationship between comorbid conditions and glycemic control in homebound individuals with Type 2 diabetes aged 65 years and older?
8. What is the relationship between polypharmacy and glycemic control in homebound individuals with Type 2 diabetes aged 65 years and older?

Practice and Policy Significance

This study generated information about glycemic control levels in homebound individuals with Type 2 diabetes aged 65 years and older and the relationships with multiple comorbid conditions and polypharmacy. More research has been needed in this patient population to describe the levels of glycemic control in the presence of multiple morbidities and polypharmacy; and how medication patterns affect the burden of disease and clinical outcomes. The complexity of medication regimens, the potential for poor blood glucose control during periods of exacerbation of related and non-related diabetic disorders, as well as, the age-associated changes in drug pharmacokinetics and pharmacodynamics suggest that this population cohort will need aggressive management to maintain homeostasis employing formal and informal care models. Current medical policy employs a continuum of care that transitions the complex patient through alternative levels of care that oftentimes result in a loss of continuity and integration. Home health professionals, as ancillary members of the medical care home, share the responsibility of medication management and symptom control in this population during periods of destabilization; implementing, educating and monitoring the effects of treatment regimens. Results of this study provide support for a more thorough analysis of medication regimens and the potential outcomes associated with the use of multiple therapeutic drug subclasses which should lead to a reevaluation of service delivery, service needs, and coordination between formal care, the medical care home and home health agency, and informal care, community-based care.

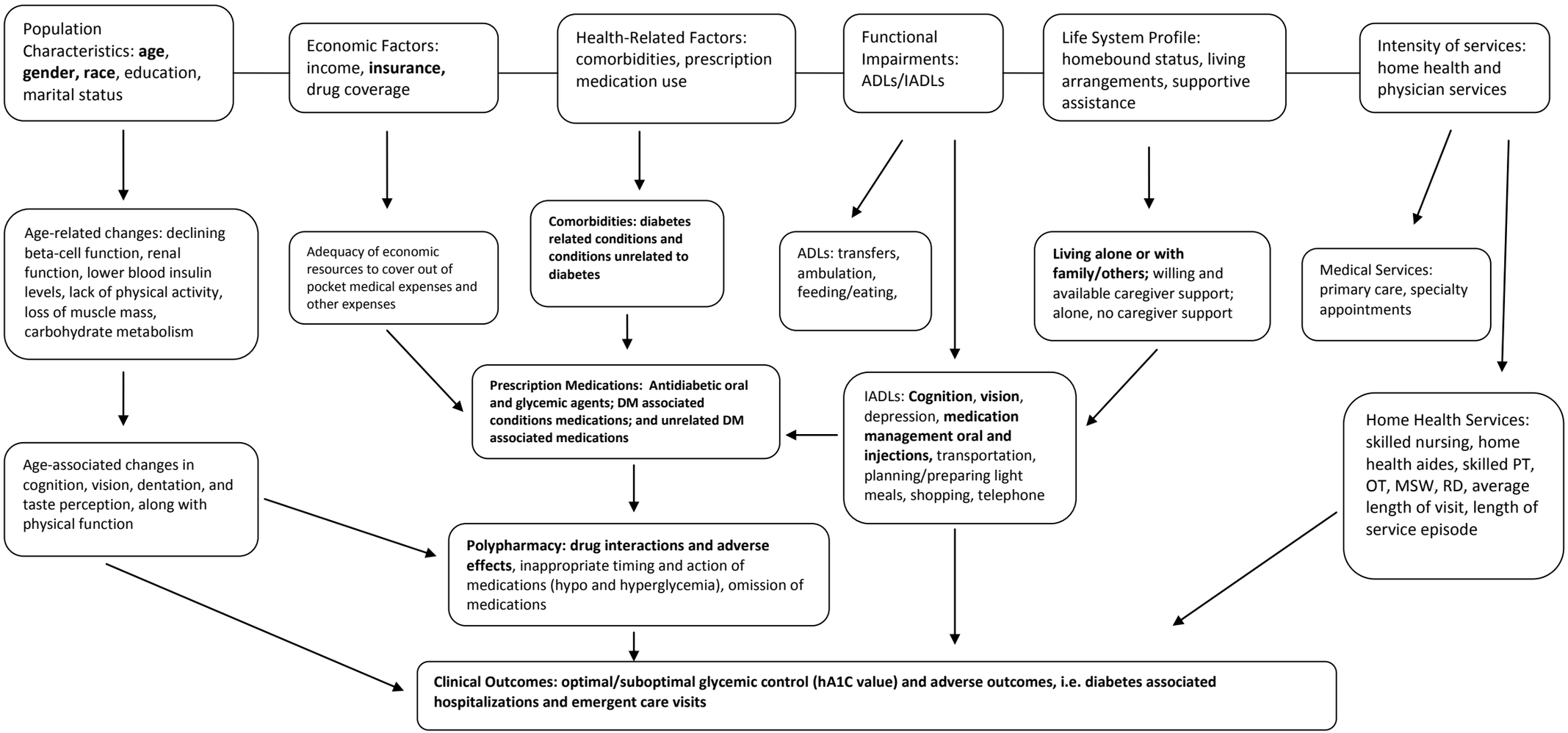

Figure 1.2. Factors that may influence glycemic control in homebound individuals with Type 2 diabetes aged 65 years and older.

CHAPTER 2

LITERATURE REVIEW

The focus of this chapter is a presentation of the research literature regarding elderly individuals with diabetes and its association with polypharmacy (drug-drug interactions, adverse clinical outcomes), the impact of age-associated changes in pharmacokinetics and pharmacodynamics, and comorbid conditions as they relate to glycemic control. The primary objective of diabetes disease management is glycemic control, as such; pharmacotherapy is the cornerstone of diabetes clinical management. Studies suggest that tighter glycemic control reduces the chance and severity of microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular (ischemic heart disease, cerebrovascular disease, and peripheral vascular disease) complications associated with prolonged hyperglycemia (Eldor & Raz, 2009). Thus, as the duration of diabetes progresses the need for multiple drug therapies to lower blood glucose levels increases. Huang (2007), reports that the average number of prescribed medications related to diabetes has now risen to four.

Other factors to consider for elderly patients with diabetes are the age-associated changes in pharmacokinetics, the movement of drugs into, through and out of the body (Kopacek, 2007) and pharmacodynamics, the target organ sensitivity to the drug (Chutka, Evans, Fleming, & Mikkelson, 1995). Age-associated pharmacokinetic changes include a reduction in renal and hepatic clearance and an increase in volume of distribution of lipid soluble drugs leading to a prolongation of plasma elimination half-life (Mangoni & Jackson, 2003; Kopacek, 2007). Turnheim (2003) posits that the most important pharmacokinetic change in the elderly is the reduction of renal drug elimination indicating age-dependent

decline of total clearance is to be expected for all drugs that are predominantly eliminated by the kidneys resulting in increased drug serum levels. The decline in renal function is closely related to the incidence of adverse drug reaction, toxicity may develop slowly and may not appear until days or weeks after medication is started (Ruscin, 2009; Muhlberg & Platt, 1999; Lindeman, Tobin, & Shock, 1985). Some examples of drugs effects augmented in this manner are postural hypotension with agents that lower blood pressure, dehydration, hypovolemia, and electrolyte disturbances in response to diuretics, bleeding complications with anticoagulants, hypoglycemia with antidiabetic agents, gastrointestinal irritation with non-steroidal anti-inflammatory drugs, and cognitive functions and motor coordination with anticonvulsants and centrally acting antihypertensive (Turnheim, 2003).

The ability of the drug to bind to its target organ and the concentration at the receptor site influence the drug's effect (Mooney, 2007). Age-associated changes in pharmacodynamics result in alterations in receptor binding or in post receptor response resulting in drug-drug interactions with an increased or decreased drug effect (Moroney, 2007; Chutka, Evans, Fleming, & Mikkelson, 1995). Mangoni and Jackson (2003) concluded that the general overall effect of age-associated changes in pharmacodynamics led to increased sensitivity to drugs. Chutka and colleagues (1995) concluded that these changes in pharmacokinetics and pharmacodynamics may result in a prolonged drug half-life, an increased potential for drug toxicity, and a greater likelihood for adverse drug reactions. For the aging individual, the ability to effectively metabolize and excrete multiple medications is impaired (Larsen & Hoot Martin, 1999). Nearly and White (2001) report that approximately 70 to 80% of elderly patients

experience side effects of medications, and they experience them two to three times more frequently than younger adults (as cited in Frazier, 2005).

Research conducted by Willey, Andrade, Cohen, Fuller, and Gurwitz (2006) identified treatment with multiple oral agents as a strong predictor of poor glycemic control. Willey and colleagues evaluated antidiabetic treatment patterns and glycemic control in a retrospective study design among patients age 18 years and older with Type 2 diabetes mellitus from January 1, 2002 to December 31, 2002 enrolled in mixed-model HMO in New England. Optimal glycemic control was measured as glycosylated hemoglobin < 7%. The sample size was 4,282; the mean age of the participants was 64 years (range 20 to 96 years). Antidiabetic treatment patterns revealed 25% (1050) received 1 oral agent, 11% (486) received 2 oral agents, 1% (56) received 3 or more oral agents; 2% (84) received combination regimen of insulin and oral agent, 2.5% (107) received insulin only, 58% (2499) were not receiving antidiabetic medications. Of the study population, only 1873 participants had recorded hemoglobin A1C values, of this group 1075 were receiving antidiabetic medications, 39% (414) achieved optimal glycemic control (A1C < 7%). The proportion of patients with optimal control was highest among those receiving a single oral agent (47%) and lowest among those receiving 3 or more oral agents (13%).

Ibrahim, Kang, and Dansky (2005) examined the drug regimens of diabetic patients receiving home health care services to measure the prevalence of polypharmacy and to assess the likelihood of drug-drug interactions, a consequence of polypharmacy. The sample size was 139 diabetic patients, mean age 74 and the mean number of comorbidities was 3. Study findings reveal 88% of the participants were subject for polypharmacy ($\geq$ 5 medications) and

the average number of prescribed medications taken daily was 8.9 (*SD* 3.4), range 2 to 19; a severe drug-drug interaction existed for 38% of the patients; 92.8% were at risk for moderated drug-drug interactions and 70.5% could potentially have mild drug-drug interactions.

Data from the National Health and Nutrition Examination Surveys for time periods 1988 to 1994 (NHANES III) and 1999 to 2004 (NHANES) was analyzed by Suh, Kim, Choi, and Plauschinat (2007) comparing the prevalence of Type 2 diabetes mellitus in the U.S. elderly population age 65 years and older; measuring changes in the rates of glycemic control; and determining the effect of comorbid conditions on treatment rates and rates of glycemic control. In this analysis, glycemic control was measured as hemoglobin A1C < 7%. The sample size for NHANES III was 612 elderly patients aged 65 years and older with diabetes mellitus; and NHANES sample size was 608. The results indicated the prevalence of Type 2 diabetes mellitus increased from 12% to 14%; many patients had comorbid conditions, NHANES 36.7% had nephropathy, 31.5% renal insufficiency, 20.2% history of myocardial infarction, and 17.8% congestive heart failure; the proportion of patients treated with antihyperglycemic medications increased from 75.1% to 85.6% and glycemic control rates improved from 44.7% to 54.8%. In the presence of comorbid conditions, nephropathy or renal insufficiency, 40% of those patients were less likely to achieve glycemic control (hemoglobin A1C <7%). The researchers concluded that despite improvements in rates of treatment and glycemic control, approximately half of elderly patients with Type 2 diabetes mellitus have hemoglobin A1C levels of 7% or higher and that the presence of comorbid conditions may impact the clinical management of diabetes mellitus.

For the elderly diabetic, tight glycemic control reduces the risk of diabetes related complications but is a significant risk factor for drug-induced hypoglycemia (Hornick & Aron, 2008). Advanced age is a risk factor for hypoglycemia secondary to age-related changes of decreased renal function, slowed hormonal regulation and counter-regulation (insulin-glucagon response), suboptimal hydration, and slowed intestinal functioning (absorption) (Ober, Watts, & Lawrence, 2006; Odegard, Setter, & Neumiller, 2007; Hornick & Aron, 2008). Elderly patients with diabetes often have compromised renal function, which interferes with drug elimination and thus, predisposes them to the potential for hypoglycemia. Chelliah and Burge (2004) assert that hypoglycemia is the major complication and barrier to achieving normal glycemic goals in elderly patients with diabetes secondary to aggressive management of hyperglycemia. Research findings of Shorr, Ray, Daughtery and Griffin (1997) indicate the risk of hypoglycemia is highest among patients who are over the age of 80 and use five or more concomitant medications. Concurrent with the presence of polypharmacy, is the fact that hypoglycemia is a significant adverse effect of at least half of the pharmacologic agents currently available for the treatment of Type 2 diabetes (Chelliah & Burge, 2004).

In a literature review conducted by Salem, Fathallah, Hmouda, and Bouraoui (2011) on the incidence of drug-induced hypoglycemia in adults, they report antidiabetic agents, as well as non-steroidal anti-inflammatory drug (NSAIDS), analgesics, antibiotics, antimalarials, antiarrhythmics, antidepressants, and other miscellaneous agents induce hypoglycemia by stimulating insulin release, reducing insulin clearance or interfering with glucose metabolism. Citing research conducted by Lease and colleagues, 25% to 30% of insulin treated diabetic patients experience one or more severe hypoglycemic episode every year (Salem, Fathallah,

Hmouda, & Bouraoui, 2011). For the elderly patient with diabetes, medication regimens containing these drugs must be managed effectively to reduce the drug-induced adverse effect on blood glucose levels.

Bertoni, Krop, Anderson, and Brancati (2002), examined the incidence of serious diabetes complications in a nationally representative cohort of U.S. elders with diabetes, 148,562 Medicare beneficiaries aged 65 years and older in 1994. Study reports that diabetes is associated with excess mortality in U.S. elders, even in those aged 85 years and older; the leading causes of diabetes-related morbidity in elderly individuals are ischemic heart disease and stroke; and of the metabolic complications, hypoglycemia (28.3%) occurred most frequently (Bertoni, Krop, Anderson, & Brancati, 2002).

In a cross-sectional study of diabetics aged 65 years or older conducted by Caughey, Roughead, Vitry, McDermott, Shakib and Gilbert (2010), the most prevalent non-diabetes related comorbid conditions reported were gastroesophageal reflux, depression, chronic airways disease, and chronic pain/inflammatory disease. The prescribed medications for these conditions, arthritis, heart failure, chronic airways disease, and diseases treated with systemic corticosteroids, increase the potential for treatment conflicts and inappropriate prescribing (Caughey, Roughead, Vitry, McDermott, Shakib & Gilbert, 2010). Systemic corticosteroids can increase blood glucose and the risk of hyperglycemia and NSAIDS can increase fluid retention, resulting in increased blood pressure and exacerbation of hypertension secondary to impaired renal function (Caughey, Roughead, Vitry, McDermott, Shakib & Gilbert, 2010). The potential inappropriate prescribing issues were directly related to the potential for impaired renal

function in the elderly, increasing the risk of hypoglycemia (Caughey, Roughead, Vitry, McDermott, Shakib & Gilbert, 2010).

Sharkey, Browne, Ory, and Wang (2005) investigated prescription medication use among homebound older adults, identifying the therapeutic prescription medication categories used by these individuals and the factors associated with use of multiple therapeutic categories. Data for analysis was collected from baseline Nutrition and Function Study in-home assessment between October 2000 and May 2001, sample size 326, aged 60 years and older. Results of the study reveal the mean number of different prescription medications taken on a daily basis was 6.4 (*SD* 4.2); and the mean number of different therapeutic categories was 3.7 (*SD* 1.9). More than 72% of the participants took medications from three to four different therapeutic categories and 31.6% used $\geq$ 5 different therapeutic categories. The most prevalent comorbid conditions were arthritis (78.8%) and hypertension (73%); followed by heart problems, inclusive of congestive heart failure (63.5%), diabetes (37.4%), and lung disease (28.2%). Study findings are consistent with the literature regarding the increased potential for adverse drug-drug interactions which may alter drug pharmacokinetics/pharmacodynamic profiles and utilization of drugs in the older adult.

A cross-sectional analysis of a population based cohort in 1998 was conducted by Jyrkka, Enlund, Kurhonen, Sulkava, and Hartikainen (2009), investigating the number and type of medical diagnoses and symptoms and to evaluate the role of different factors associated with polypharmacy (defined as the use of six to nine drugs) and excessive polypharmacy (defined as the use of $\geq$ 10 drugs). The data for analysis was obtained from the Kuopio 75+ Study, which drew a random sample of 700 elderly residents' aged 75 years and older living in the city of

Kuopio, Finland from the population register. The sample for the study was 523 homebound elderly. Results of the study mean number of drugs taken per participant was 7.4 in the polypharmacy group (2.6 drugs per disease) and 12.1 in the excessive polypharmacy group (3.6 drugs per disease). The most commonly used drugs were cardiovascular drugs, 94% polypharmacy group (2.9 drugs per person) and 97% excessive polypharmacy group (3.8 drugs per person); followed by analgesics, 76% polypharmacy group (1.2 drugs per person) and 89% excessive polypharmacy group (1.7 drugs per person). Poor self-reported health, diabetes mellitus, depression, pain, heart disease, and obstructive pulmonary disease were significantly associated with polypharmacy and excessive polypharmacy, with obstructive pulmonary disease most strongly associated with both categories. The study results are consistent with studies involving elderly subjects reporting congestive heart failure, coronary heart disease, and diabetes as risk factors for polypharmacy.

This chapter summarizes the research literature, identifying results and conclusions, which affirm that high numbers of prescription medications taken daily in the elderly population with multiple morbidities and the increased potential for adverse clinical outcomes calls for a thorough assessment of medication regimens with each medical encounter. The prevalence of diabetes combined with multiple morbidities promotes polypharmacy; in addition, age-related physiological changes and age-associated changes in pharmacokinetics and pharmacodynamics place the elderly patient with diabetes at significant risk for poor diabetes control with concomitant increased utilization of health care resources and increased costs.

CHAPTER 3

METHOD

This chapter describes the design and research methods that were implemented to describe glycemic control and the relationships between diabetes disease severity, comorbid conditions, and polypharmacy in homebound individuals aged 65 years and older with Type 2 diabetes. A description of the sample size and characteristics, procedures for sample recruitment, data collection, and human rights protections are included as well. Additionally study variables and data analysis procedures are documented.

Research Methodology and Design

This is a quantitative retrospective cohort study that determined the probability of optimal glycemic control in the presence of multiple morbidities and polypharmacy. The main purpose is to describe several variables that have been identified in the literature and observed in practice (glycemic control, diabetes severity, multiple morbidities and polypharmacy) while exploring the relationship between them in homebound individuals aged 65 years and older with Type 2 diabetes. Data is collected through the use an electronic database and medical record reviews. The data is then converted to numerical form to enable statistical analyses.

Sample

This study used consecutive sampling of all discharged patients of a nonprofit community-based home health agency from January 1, 2010 to December 31, 2011. The inclusion criteria for study participation are: diagnosis code of Type 2 diabetes from the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD- 9)* ranging from 250.00 to 250.82, admission for diabetes disease management, minimum age 65 years, on

service a minimum of 60 days, discharge dates between January 1, 2010 and December 31, 2011. The rationale for the admission for diabetes disease management and minimum length of service of 60 days is due to the study outcome measure, glycemic control. The reason for the age criterion aged 65 years and older, is the high prevalence of Type 2 diabetes in the elderly. Patients are included only once in the study, readmitted patients are excluded. Records of deceased patients, those not admitted for diabetes disease management and those patients transferred to alternative levels of care without further home health services are excluded as well. The study population consisted of 232 cases of homebound individuals with Type 2 diabetes, median age 76.5 (*IQR* 69 - 83). Refer to Table 4.1 for a full description of population characteristics.

Sample Size

The research questions required correlation and regression analyses to explore the effects of the predictors (sociodemographic, functional status, diabetes disease severity, multiple morbidities and polypharmacy) on glycemic control. To determine sample size for statistics used to examine relations, according to Wilson & Morgan (2007) the general rule is no less than 50 participants for a correlation or regression with the number increasing with larger numbers of independent variables. Wilson and Morgan (2007) discuss Green's rules which suggests $N > 50 + 8$ (m) (where m is the number of independent variables) for testing the multiple correlation and $N > 104 + m$ for testing individual predictors (assuming a medium size relationship); the recommendation if testing both use the larger sample size. Applying Green's rules, the sample size for this study, set of eight predictors, should be 112 (104 + 8). The study sample ($N = 120$) for analysis are those with recorded hA1C laboratory values.

Human Rights Protection

The study was approved for expedited review by the University of North Texas Institutional Review Board and by the home health agency. The Centers for Medicare and Medicaid Services (CMS) mandate that each patient be provided with a privacy statement on admission to a home health care agency (Anderson & Mignor, 2000). Confidentiality is addressed by CMS, which allows the use of aggregate Outcome and Assessment Information Set (OASIS) data for publications and research (CMS, 2003).

Subjects' respect, privacy and information confidentiality is protected using a numbered code on the data collection tool. I assigned a study identification number to each record. No names or identifying information was gathered on the data collection tool; and all documents were stored in a locked and secure file cabinet. I then entered all data into Statistical Package for the Social Sciences statistical software, version 20, using only the numeric identification code to identify participants.

Data Collection Procedure

Security based access to the agency information system was provided to me for data collection. A list of all the discharged patients who met the inclusion criteria is obtained. Each individual record is reviewed for inclusion in the study, the initial 485 (plan of care), OASIS and discharge OASIS, with results documented on the data collection tool. I then transferred the data to a master Excel file. I completed direct medical record review for the hA1C laboratory test results, of each included record on-site at field offices located in Denton, Garland, Fort Worth and Allen, Texas. This information was then entered into the master Excel file. All data is transferred from the master Excel file to a SPSS file for analysis.

Instruments

The OASIS is a tool for the collection of health status and functional limitations data at points along a continuum of care from admission through discharge for those individuals receiving home health care services. The OASIS is the intellectual property of the Center for Health Services and Policy Research and is used with permission. Data for this study is gathered for the sociodemographic and functional status variables, at admission and discharge. Validity and reliability estimates for the OASIS have been well documented (Shaughnessy & Crisler, 1995).

Dependent Variable

Assessment of Glycemic Control

The current consensus guidelines from the American Diabetes Association recommend that the goals of antidiabetic therapy should be to lower hemoglobin A1C to < 7% in non-pregnant adults (ADA, 2010). This study used the ADA recommended level (hA1C < 7%) as the outcome measure for optimal glycemic control. The laboratory test results of the hA1C obtained within 30 days prior to discharge date from home health services was used for analysis. The hA1C is measured as a continuous variable for correlation analysis, and categorical for bivariate and binary for regression analyses.

Independent Variables

Identification of and Categorization of Polypharmacy

Polypharmacy is defined as the concomitant use of 5 or more prescribed medications in the same patient. Medications are compiled from the medication profile recorded on date of discharge from home health services. To calculate the total number of medications for each

patient, the following guidelines are employed: 1) total number of medications include prescription and over-the-counter non-steroidal anti-inflammatory drugs; 2) routine and as needed medications are not differentiated; 3) each medication is counted as one; 4) multiple types of insulin are combined into a single category of glycemics and counted as one; 5) excluded medications included all other over the counter medications, nutritional supplements, vitamins, inhalants, topical agents, and ophthalmic agents. Medications are excluded based on their targeted area of effect. The number of medications is measured as a continuous variable for correlation analysis, and categorical for bivariate and binary for regression analyses.

To investigate the influence of multiple drug regimens on glycemic control and the potential of drug-associated hypo/hyperglycemia, the medications for each subject is further categorized by therapeutic category and subclass, adapted from *2011 American Hospital Formulary Service (AHFS) Drug Information*. The number of therapeutic categories and subclasses is measured as a continuous variable for correlation analysis, and categorical for bivariate and binary for regression analyses. The agency administrative database contained a program that identified drug-drug interactions, classifying each drug-drug interaction into one of three severity categories, severe, moderate and mild. Identification of drug-drug interactions that may be related to glycemic control or adverse outcomes is included in the analysis.

Identification and Categorization of Comorbid Conditions

Diabetes disease severity is defined by the presence of diabetic manifestations (ICD-9-CM 250.4x, 250.5x, 250.6x, 250.7x, 250.8x), measured as a continuous variable for correlation analysis and categorical for bivariate and binary for regression analyses. Comorbid conditions

documented at admission are recorded, identifying diabetes associated conditions of hypertensive disease (ICD-9-CM 401.x-405.x), hyperlipidemia(ICD-9-CM 272.x); vascular associated conditions of retinopathy (ICD-9-CM 362.x), chronic kidney disease (ICD-9-CM 585.x), ischemic heart disease (ICD-9-CM 410.x-414.x), dysrhythmias (ICD-9-CM 427.x), congestive heart failure (ICD-9-CM 428.x), cerebrovascular disease (ICD-9-CM 430.x- 438.x), neuropathy (ICD-9-CM 357.2, 337.1), peripheral circulation disorders (ICD-9-CM 443.8x); and conditions not related to diabetes, gastroesophageal reflux (ICD-9-CM 530.81), depression (ICD-9-CM 311.x), chronic airways diseases (ICD-9-CM 490.x -496.x), chronic pain/inflammatory disease (ICD-9-CM 714.x- 715.x), and osteoporosis (ICD-9-CM 733)in the study population. The number of comorbidities is measured as a continuous variable for correlation analysis, and categorical for bivariate and binary for regression analyses.

Assessment of Adverse Outcomes

Adverse outcomes are defined as diabetes associated hospitalizations or emergent care visits. Dichotomous variables are constructed using 4 questions from the discharge OASIS. The first question concerns emergent care: "Since the last time OASIS data were collected, has the patient utilized a hospital emergency department (includes holding/observation)?" Selection responses were no; yes, used hospital emergency department WITHOUT hospital admission; yes, used hospital emergency department WITH hospital admission; and unknown. A dichotomous variable is constructed (EMERCARE). The second question concerns reason for emergent care: "For what reason(s) did the patient receive emergent care (with or without hospitalization)?" The third question concerns hospital admission: "To which Inpatient Facility has the patient been admitted?" Selection responses were hospital; rehabilitation facility;

nursing home; hospice; and no inpatient facility admission. A dichotomous variable is constructed (HOSPADM). The fourth question concerns reasons for hospitalization: "For what reason(s) did the patient require hospitalization?" There are twenty selection response items; the responses "Hypo/Hyperglycemia, diabetes out of control" and "Improper medication administration, medication side effects, toxicity, anaphylaxis" were selected. The dichotomous variable OUTCOME is constructed using the selection responses included in reason(s) for hospitalization and emergent care. All responses are coded as yes, no, and not applicable.

Identification and Definition of Other Patient Characteristics

Sociodemographic

The following data on study population characteristics is collected from the discharge OASIS: age at time of discharge, gender, race, living arrangement, and insurance. Age is measured as a continuous variable with 65 years as the minimum. Race is categorized as White; Black or African American; Hispanic or Latino; and all others (American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander), measured as White and non-White. Insurance status is defined as the payment source for home care, Medicare; Medicare managed care; private (inclusive of commercial insurance and private pay); and VA (Veterans Administration). Living arrangement is defined by the answer to the following question on the OASIS: "Which of the following best describes the patient's residential circumstance and availability of assistance?" Instructions are to check one box only, patient lives alone; patient lives with other person (s) in the home; and patient lives in congregate situation (e.g., assisted living). A categorical variable is constructed for HOUSEHOLD, with alone, no assistance

available; and with others, around the clock assistance. Those patients residing in congregate housing are combined with the category, with others, around the clock assistance.

Functional Status

OASIS questions are utilized to define the selected functional levels of vision, cognition, and medication management. The question addressing vision; assesses vision "with Corrective lenses if patient usually wears them." The selection response items are " normal, sees adequately in most situations; can see medication labels, newsprint; partially impaired: cannot see medication labels or newsprint, but can see obstacles in path, and the surrounding layout; can count fingers at arm's length; and severely impaired: cannot locate objects without hearing or touching them or patient nonresponsive." A categorical variable is constructed (VISION) with responses intact for normal and impaired for both partially impaired and severely impaired responses.

The question addressing cognition; assesses cognitive functioning: "Patient's current (day of assessment) level of alertness, orientation, comprehension, concentration, and immediate memory for simple commands." There are 5 selection response items available, the first is "alert/oriented, able to focus and shift attention, comprehends and recalls task directions independently;" the remaining four responses require some level of assistance, therefore the categorical variable COGNITION has responses intact for alert/oriented and impaired.

There are two questions addressing medication management, the first assesses management of oral medications: "Patient's current ability to prepare and take all oral medications reliably and safely, including administration of the correct dosage at the

appropriate times/intervals. (NOTE: This refers to ability, not compliance or willingness.)" There are 4 selection responses, the first "able to independently take the correct oral medication(s) and proper dosage(s) at the correct times;" the remaining three require some level of assistance. The second question assessing medication management; assesses management of injectable medications: "Patient's current ability to prepare and take all prescribed injectable medications reliably and safely, including administration of correct dosage at the appropriate times/intervals. Excludes IV medications." There are 4 selection responses, the first "able to independently take the correct medication(s) and proper dosage(s) at the correct times;" the remaining three require some assistance. A level of assistance would be required if patient is unable to independently manage oral or injectable medications, therefore a single categorical variable is constructed for MEDMGMT with responses independent and dependent.

Statistical Analysis

Statistical analyses are conducted using IBM SPSS® software, Version 20.0 (IBM Corp., Armonk, NY) with the level of significance set at $\alpha < 0.05$. The Kolmogorov-Smirnov and the Shapiro-Wilk statistic are employed to assess normality of the distribution of scores on the dependent variable and all predictors. Both tests are statistically significant, indicating violation of the assumption of normality ($p = 0.001$), scores are not normally distributed. As a result, nonparametric tests are employed for analyses. Descriptive statistics are used to answer descriptive questions. To answer relational questions, bivariate analysis, with the chi-square test for independence and post hoc tests (comparing the standardized residual to the critical value +/- 1.96) are utilized to determine which cells produced the statistically significant

difference; and Spearman's rank order correlation coefficient is employed to determine the direction and magnitude of the relationships.

Exploratory data analysis is conducted to describe differences between groups. The median values of the predictor variables (diabetes disease severity, total medications, total therapeutic subclass and categories, and comorbid conditions), and glycemic control are compared for sociodemographic subgroups. The Mann-Whitney U test is employed to test the differences between gender and medication management; the Kruskal-Wallis is used to test the difference between age and race. Logistic regression analysis of glycemic control is performed, using a forced entry method where all the predictor variables are tested in one block to assess the effects of diabetes disease severity, polypharmacy and comorbid conditions while controlling for the sociodemographic variables, age, gender, and race; and the functional status variable, medication management.

Additional data analysis involved the analysis of missing data for each of the predictor variables (Model 1 and Model 2) to investigate the degree to which they can predict optimal glycemic control. Mahalanobis distance within regression procedure is employed on the dependent variable hemoglobin A1C (largest number of cases 120). For Model 1, the critical value of chi-square at $p < .001$ and $df = 8$ is 26.13 (Mertler & Vannatta, 2010). Cases with a Mahalanobis distance greater than 26.13 are considered multivariate outliers for the variables age1, gender, race1, medman, ENDO1, tcom, tomeds, categ1 (Mertler & Vannata, 2010). For Model 2, the critical value of chi-square at $p < .001$ and $df = 7$ is 24.32 (Mertler & Vannatta, 2010). Cases with a Mahalanobis distance greater than 24.32 are considered multivariate outliers for the variables age1, gender, race1, medman, ENDO1, oralgly2 and toclass (Mertler &

Vannata, 2010). The Mahalanobis maximum distances are 14.09 and 11.32, respectively; both less than the critical values, no outliers identified; concluded no violation of the multicollinearity assumption. Collinearity diagnostics within regression are also employed, tolerance levels are > .2 and variance levels are < 5 for both models, thus no problem with multicollinearity is detected.

CHAPTER 4

RESULTS

Sample Characteristics

Descriptive characteristics of the sample are presented in Table 4.1. The sample population consisted of 120 cases of homebound individuals with Type 2 diabetes aged 65 years and older, median age 75 (*IQR* 69 - 82). The majority of the population lived with others (75.8%), is cognitively intact (82.5%), with normal vision (57.5%), and independent in medication management (55.8%). There is a disproportionate representation of Whites (71.7%) to non-Whites (28.3%), with 57.5% being female. Medicare is the primary payer for home health care services at 91.7%; the majority, 76.7% utilizing traditional Medicare benefits.

The median hemoglobin A1C value is 6.6% (*IQR* 6.0 – 7.2), with the range of values being 5.5% to 8.3%. The majority (61.7%) of cases have optimal glycemic control (< 7%). As shown in Table 4.2, the most frequent form of antidiabetic therapy is insulin, 33.3%, followed by a single oral medication, 25.8%; the most frequent combination therapy is a single oral medication plus insulin 14.2%. There are 7.2% that do not take any antidiabetic medications.

Within the sample, 97.5% of the cases are subject to polypharmacy (5 or more different medications). The most frequent (17.5%) and median number of different medications taken daily is 9 (*IQR* 7 – 11). There are three cases (2.5%) taking 4 or fewer medications and four cases (3.3%) taking 15 or more medications. Similarly, the most frequent (15.8%) and median number of different therapeutic subclasses of medications taken daily is 9 (*IQR* 7 – 10). There are four cases (3.3%) taking 4 or fewer therapeutic subclasses and four cases (3.3%) taking 14 or more. The total number of different therapeutic categories of medications taken range from

1 to 8 with 5 (*IQR* 4 – 6) as the median and most frequent (30.8%). There are four cases (3.3%) taking 2 or fewer and ten cases (8.3%) taking 7 or more.

Table 4.1

Median, Interquartile Range, Frequencies and Percentages of the Population and Study Sample Characteristics

	Excluded Population			Sample Population		
	Range	n	%	Range	n	%
Age	65 - 95	112	100	65 - 95	120	100
Median 77.5 years				75 years		
IQR 69 - 83 years				69 - 82		
Gender						
Male		46	41.1		51	42.5
Female		66	58.9		69	57.5
Race						
White		82	73.2		86	71.7
Black		14	12.5		16	13.3
Hispanic		11	9.8		14	11.7
Other		5	4.5		4	3.3
Insurance						
Medicare		90	80.4		92	76.7
Medicare HMO		22	19.6		18	15.0
Private		0	0		4	3.3
VA		0	0		6	5.0
Living Arrangement						
Alone		18	16.1		29	24.2
w Others		94	83.9		91	75.8
Medication Management						
Independent		66	58.9		67	55.8
Dependent		46	41.1		53	44.2
Cognition						
Intact		93	83		99	82.5
Impaired		19	17		21	17.5

(*table continues*)

Table 4.1 (*continued*).

	Excluded Population			Sample Population		
	Range	n	%	Range	n	%
Vision						
Normal		70	62.5		69	57.5
Impaired		42	37.5		51	42.5
Diabetes Disease Severity	1 to 7	112	100	1 to 7	120	100
Median = 1		68	60.7		77	64.2
IQR 1 - 2						
Total Comorbid Conditions	1 to 12	112	100	1 to 12	120	100
Median = 4		22	19.6	4	30	25
IQR 2 - 5				*IQR 3 - 5*		
Total Medications	1 to 22	112	100	1 to 22	120	100
Median = 8		16	14.3	9	21	17.5
IQR 7 - 10				*IQR* 7 - 9		
Total Therapeutic Subclass	1 to 21	112	100	1 to 21	120	100
Median = 8		40	17.2	9	19	15.8
IQR 6 - 9				*IQR* 7 - 10		
Total Therapeutic Categories	1 to 8	112	100	1 to 8	120	100
Median = 5		40	35.7	5	37	30.8
IQR 4 - 5.75				*IQR 4* - 6		

Note. Excluded population refers to cases without recorded hA1C values.

Diabetes disease severity measured as the prevalence of diabetic manifestations with associated conditions in the sample population is low. The majority (64.2%) of the sample present without manifestations; 14.2% had 2 diabetic manifestations with associated conditions; and 3.3% had 4 or more. The most frequent (25%) and the median number of comorbid conditions is 4 (*IQR* 3 – 5); 2.5% of cases with 10 or more. Refer to Table 4.3, for a full list of diabetic manifestations and comorbid conditions. Diabetes associated hospitalizations or emergent care visits is very low. There are 6 (5%) cases with reported emergency room visits

with 5 of those cases resulting in hospital admission. The principle reason was hypo/hyperglycemia, diabetes out of control in all instances.

Table 4.2

Antidiabetic Therapy Frequencies (%)

			hA1C < 7%	
	n	%	n	%
Single Oral Medication	31	25.8	26	83.9
Sulfonylurea				
Metformin				
TZD				
2 Oral Medications	13	10.8	10	76.9
Sulfonylurea				
Sulfonylurea + Metformin				
3 Oral Medications	5	4.2	2	40.0
Sulfonylurea + Metformin + TZD				
1 Oral + Insulin	17	14.2	10	58.8
Sulfonylurea + Insulin				
Metformin + Insulin				
2 Oral + Insulin	5	4.2	2	40.0
Sulfonylurea + Metformin + Insulin				
Insulin only	40	33.3	16	40.0
No Antidiabetic Medications	9	7.5	8	88.9

Note. Sample N = 120; hA1C N = 74. Thiazolidinediones (TZD). Sulfonylurea (glipizide, glyburide, glimepiride)

Table 4.3

Sample Frequencies (%) Diabetic Manifestations and Comorbid Conditions

	n	%
Diabetic Manifestations		
Renal	12	10.0
Ophthalmic	13	10.8
Neurological	9	7.5
Peripheral Circulatory Disorder	6	5.0
Diabetic Hypoglycemia	2	1.7

(*table continues*)

Table 4.3 (*table continued*).

	n	%
Diabetes Associated Conditions		
Hyperlipidemia	32	26.7
Hypertensive Disease	102	85.0
Hypertension	88	73.3
Chronic Kidney Disease	19	15.8
End Stage Renal Disease	10	8.3
Ischemic Heart Disease	29	24.2
Coronary Atherosclerosis	16	13.3
Dysrhythmias	20	16.7
Atrial Fibrillation	18	15.0
Congestive Heart Failure	25	20.8
Cerebrovascular Disease	12	10.0
Neuropathy	9	7.5
Peripheral Neuropathy	7	5.8
Peripheral Circulatory Disorder	3	2.5
Non-Associated Disorders		
Gastroesphageal Reflux	20	16.7
Depression	17	14.2
Chronic Obstructive Pulmonary Disease	25	20.8
Chronic Pain/Inflammatory Disease	16	13.3
Osteoporosis	8	6.7

Note. Sample N = 120

Bivariate and Correlation Analyses

The study hypothesis is on average, the probability of optimal glycemic control declines in homebound individuals with Type 2 diabetes aged 65 years and older in the presence of multiple morbidities and polypharmacy. Bivariate analyses, employing the chi-square test for independence are used to identify and test the relationships between glycemic control and diabetes disease severity (diabetic manifestations), polypharmacy (total medications, therapeutic subclasses and categories), and comorbid conditions. Spearman's rank order

correlation (Table 4.8) is performed to determine the direction and magnitude of the relationships.

There is a statistically significant relationship between glycemic control and diabetes disease severity, χ^2 (2, n = 120) = 8.663, p = .003. Post hoc testing revealed a specific finding that among those homebound individuals with diabetic disease manifestations, there are more (56%) with suboptimal glycemic control than would be expected (Table 4.4). There is a weak, positive association between glycemic control and diabetes disease severity, r_s = .26, n = 120, p = .004, with 6.8 % shared variance.

Table 4.4

Bivariate Association Between Glycemic Control and Diabetes Disease Severity

		ENDO1		Total
		0	1	
hA1C				
	Count	19	55	74
< 7%	Expected Count	26.5	47.5	74
	% within ENDO1	44.2%	71.4%	61.7%
	Std. Residual	-1.5	1.1	
	Count	24	22	46
>= 7%	Expected Count	16.5	29.5	46
	% within ENDO1	55.8%	28.6%	38.3%
	Std. Residual	1.9	-1.4	
Total	Count	43	77	120
	Expected Count	43	77	120
	% within ENDO1	100.0%	100.0%	100.0%

Note. hA1C= glycemic control. ENDO1 = diabetes disease severity, ENDO1-1 = no manifestations, ENDO1- 0 = diabetic manifestations.

The relationship between glycemic control and total number different medications taken daily is significant, χ^2 (2, n = 117) = 8.004, p = .018. Post hoc tests support a specific finding that among those homebound individuals with Type 2 diabetes aged 65 years and older taking 11 or more different medications daily, there are more (55%) with suboptimal glycemic control than would be expected (Table 4.5). There is a weak, positive association between glycemic control and the total number of different medications taken daily, r_s = .23, n = 120, p = .01, with 5.3% shared variance.

Table 4.5

Bivariate Association Between Glycemic Control and Total Number of Different Medications

		Meds3			Total
		1 5-8	2 9 -10	3 11+	
hA1C					
	Count	33	22	18	73
< 7%	Expected Count	28.1	20	25	73
	% within Meds3	73.3%	68.8%	45.0%	62.4%
	Std. Residual	0.9	0.5	-1.4	
	Count	12	10	22	44
>= 7%	Expected Count	16.9	12	15	44
	% within Meds3	26.7%	31.2%	55.0%	37.6%
	Std. Residual	-1.2	.-6	1.8	
Total	Count	45	32	40	117
	Expected Count	45	32	40	117
	% within ENDO1	100.0%	100.0%	100.0%	100.0%

Note. hA1C= glycemic control. Meds3 = total number of different medications.

There is a significant relationship between glycemic control and total number of therapeutic drug subclasses taken daily, χ^2 (2, n = 120) = 9.827, p = .007. Post hoc testing

supports a specific finding that among those homebound individuals with Type 2 diabetes aged 65 years and older taking 7 or fewer therapeutic subclasses daily, there are more (74%) with optimal glycemic control than would be expected (Table 4.6). Likewise, there is a weak, positive association between glycemic control and total number of therapeutic subclasses taken daily, r_s = .22, n = 120, p = .016, with 4.8% shared variance.

Table 4.6

Bivariate Association Between Glycemic Control and Total Number of Therapeutic Drug Subclasses

		Therapeutic Subclass			Total
		1 <= 7	2 8 - 9	3 10+	
hA1C					
	Count	31	25	18	74
< 7%	Expected Count	25.9	22.2	25.9	74
	% within Tclass	73.8%	69.4%	42.9%	61.7%
	Std. Residual	1.0	0.6	-1.6	
	Count	11	11	24	46
>= 7%	Expected Count	16.1	13.8	16.1	46
	% within Tclass	26.2%	30.6%	57.1%	38.3%
	Std. Residual	-1.3	-0.8	2	
Total	Count	42	36	42	120
	Expected Count	42	36	42	120
	% within ENDO1	100.0%	100.0%	100.0%	100.0%

Note. hA1C= glycemic control. Tclass = therapeutic class.

The relationship between glycemic control and comorbid conditions is significant, χ^2 (1, n = 120) = 4.169, p = .041. Post hoc testing supports a specific finding that among those homebound individuals with Type 2 diabetes aged 65 years and older that have 6 or more comorbid conditions, there are more (56%) with suboptimal glycemic control than would be

expected (Table 4.7.). However, the Spearman's rho coefficients indicated no association between glycemic control and comorbid conditions, $r_s = .13$, $n = 120$, $p = .164$. There was not a significant relationship between glycemic control and total number of therapeutic categories, χ^2 (2, $n = 120$) = 2.259, $p = .323$; and $r_s = .078$, $n = 120$, $p = .400$.

To determine if age influences the association between glycemic control, diabetes disease severity, polypharmacy and comorbid conditions, the sample is split into two groups, those aged 65 to 76 years (young old) and those aged 77 to 95 years (oldest old). As shown in Table 4.9, among the young old, glycemic control has a statistically significant association with diabetes disease severity, total number of comorbid conditions, total number of different medications and total number of therapeutic subclasses took daily. The Spearman's rank coefficients are all positive indicating a positive correlation between glycemic control and the four variables. There is a moderate association between glycemic control and diabetes disease severity, $r_s = .41$, $n = 64$, $p = .001$, with 16.8% shared variance. The chi-square test for independence indicates a statistically significant relationship between glycemic control and diabetes disease severity controlling for age, χ^2 (1, $n = 64$) = 8.862, $p = .003$. Post hoc test supports a specific finding that among those aged 65 to 76 years with diabetic disease manifestations, there are more (60%) with suboptimal glycemic control than expected.

Table 4.7

Bivariate Association Between Glycemic Control and Comorbid Conditions

		Tcom		Total
		0	1	
hA1C				
	Count	11	63	74
	Expected Count	15.4	58.6	74
< 7%	% within tcom	44.0%	66.3%	61.7%
	Std. Residual	-1.1	0.6	
	Count	14	32	46
	Expected Count	9.6	36.4	46
>= 7%	% within tcom	56.0%	33.7%	38.3%
	Std. Residual	1.4	-0.7	
Total	Count	25	95	120
	Expected Count	25	95	120
	% within ENDO1	100.0%	100.0%	100.0%

Note. hA1C= glycemic control. Tcom = total comorbid conditions, Tcom-1 = 1-5 conditions, Tcom-0 = 6+ conditions.

Table 4.8

Spearman's Rank Order Intercorrelations of Study Variables

	1	2	3	4	5	6
1. Glycemic Control		.264**		.226*	.219*	
2. Diabetes Disease Severity	.264**		.577**			.143*
3. Total Comorbid Conditions		.577**		.166*	.212**	.131*
4. Total Medications	.226*		.166*		.943**	.668**
5. Total Therapeutic Subclass	.219*		.212**	.943**		.722**
6. Total Therapeutic Category		.143*	.131*	.668**	.722**	

* $p < .05$, **p < .01

Table 4.9

Intercorrelations of Study Variables for Diabetic Adults Age 65 to 76 years

	1	2	3	4	5	6
1. Glycemic Control		.406**	.280*	.317*	.293*	
2. Diabetes Disease Severity	.406**		.559**			
3. Total Comorbid Conditions	.280*	.559**			.187*	
4. Total Medications	.317*				.929**	.728**
5. Total Therapeutic Subclass	.293*		.187*	.929**		.780**
6. Total Therapeutic Category				.728**	.788**	

* $p < .05$, **p < .01.

There is a weak association between glycemic control and total number of comorbid conditions, $r_s = .28$, $n = 64$, $p = .025$, with 7.8% shared variance. The chi-square test for independence indicates a statistically significant relationship between glycemic control and total number of comorbid conditions controlling for age, χ^2 (2, $n = 64$) = 8.950, $p = .011$. Post hoc testing supports a specific finding that among those aged 65 to 76 years that have 6 or more comorbid conditions, there are more (67%) with suboptimal glycemic control than would be expected.

There is a moderate association between glycemic control and total number of different medications took daily, $r_s = .32$, $n = 64$, $p = .011$, with 10.2% shared variance. The chi-square test for independence indicates a statistically significant relationship between glycemic control and total number of different medications took daily, controlling for age, χ^2 (1, $n = 63$) = 3.879, $p = .049$. Post hoc testing supports a specific finding that among those aged 65 to 76 years that take 11 or more different medications daily, there are more (54.5%) with suboptimal glycemic control than would be expected.

There is a moderate to low, association between glycemic control and total number of different therapeutic subclasses took daily, r_s = .29, n = 64, p = .019, with 8.4% shared variance. The chi-square test for independence indicates a statistically significant relationship between glycemic control and total number of therapeutic subclasses took daily, controlling for age, χ^2 (1, n = 64) = 3.887, p = .049. Post hoc testing supports a specific finding that among those aged 65 to 76 years that take 8 or more therapeutic subclasses daily, there are more (47.4%) with suboptimal glycemic control than would be expected. Spearman's rank coefficient is not statistically significant between glycemic control and total number of therapeutic categories taken daily, among those homebound individuals aged 65 to 76 years with Type 2 diabetes, (r_s = .09, n = 64, p = .490).

In contrast, among the oldest old, Spearman's rank coefficients are not statistically significant between glycemic control and diabetes disease severity, polypharmacy (total medications, therapeutic subclasses and categories), and comorbid conditions. However, the chi-square test for independence indicates a statistically significant relationship between glycemic control and total number of different medications took daily, for those aged 77 years and older, χ^2 (1, n = 54) = 3.971, p = .046. Post hoc testing supports a specific finding that among those aged 77 years and older, that took 11 or more different medications daily, and there are more (55.6%) with suboptimal glycemic control than would be expected.

Similar findings were found when examining the influence of gender on the relationships between glycemic control, diabetes disease severity, polypharmacy, and comorbid conditions. As shown in Table 4.10, among females, glycemic control has a statistically significant association with diabetes disease severity, total number of different

medications taken daily and total number of therapeutic subclasses taken daily. There continues to be a positive association between the variables. There is a moderate association between glycemic control and diabetes disease severity, $r_s = .34$, $n = 69$, $p = .005$, with 11.6% shared variance. The chi-square test for independence indicates a statistically significant relationship between glycemic control and diabetes disease severity controlling for gender, χ^2 (1, $n = 69$) = 7.545, $p = .006$. Post hoc testing supports a specific finding that among females with diabetic disease manifestations, there are more (59.3%) with suboptimal glycemic control than would be expected.

Table 4.10

Intercorrelations of Study Variables for Female type 2 Diabetic Adults

	1	2	3	4	5	6
1. Glycemic Control		.335**		.274*	.249*	
2. Diabetes Disease Severity	.335**		.531**	.184*	.204*	.225**
3. Total Comorbid Conditions		.531**		.208*	.239**	.201*
4. Total Medications	.274*	.184*	.208*		.935**	.653**
5. Total Therapeutic Subclass	.249*	.204*	.239**	.935**		.694**
6. Total Therapeutic Category		.225**	.201*	.653**	.694**	

* $p < .05$, **p < .01.

The association between glycemic control and total number of different medications taken daily is weak, $r_s = .27$, $n = 69$, $p = .023$, with 7.3% shared variance. The chi-square test for independence indicates a statistically significant relationship between glycemic control and total number of different medications taken daily controlling for gender, χ^2 (2, $n = 69$) = 9.272,

p = .010. Post hoc testing supports a specific finding that among females taking 11 or more different medications daily, there are more (63.6%) with suboptimal glycemic control than would be expected. Likewise, the association between glycemic control and total number of therapeutic subclasses took daily is weak, r_s = .25, n = 69, p = .039, with 6.3% shared variance. The chi-square test for independence indicates a statistically significant relationship between glycemic control and total number of therapeutic subclasses taken daily controlling for gender, χ^2 (2, n = 69) = 8.444, p = .015. Post hoc testing supports a specific finding that among females taking 10 or more therapeutic subclasses daily, there are more (63.6%) with suboptimal glycemic control than would be expected. When controlling for female gender, the variables, total comorbid conditions and total therapeutic categories were not significantly associated with glycemic control. In contrast, and similar to the findings among the oldest old, for males glycemic control is not significantly associated with diabetes disease severity, polypharmacy and comorbid conditions.

Exploratory Data Analyses

To explore the median differences between glycemic control and diabetes disease severity, polypharmacy, and comorbid conditions of males and females, and medication management the Mann-Whitney U test is employed. There is no statistically significant difference in glycemic control, diabetes disease severity, polypharmacy (total medications, total therapeutic subclass and categories), and comorbid conditions of males and females. A Mann-Whitney test indicated a statistically significant difference in glycemic control of those that are independent in medication management (Md = 6.2, n = 67) and those dependent (Md = 7.0, n = 53), U = 1277, Z = -2.64, p = .008, r = .24.

The Kruskal-Wallis test is employed to explore the median differences across age and race. There is no statistically significant difference in glycemic control, diabetes disease severity, polypharmacy, and total number of comorbid conditions across three different age groups. There is no statistically significant difference in glycemic control, polypharmacy, and comorbid conditions across four difference racial groups. However, there is a statistically significant difference in diabetes disease severity across four different racial groups (Whites, n = 86, Blacks, n = 16, Hispanic, n = 14, Other, n = 4), χ^2 (3, n = 120) = 11.941, p = .008. Post hoc tests are performed using Mann-Whitney U to determine which groups are statistically significant from one another, with a Bonferroni adjusted $\alpha < .025$. The presence of diabetic manifestations is higher in Hispanics (Md = 2.5, n = 14) than Whites (Md = 1, n = 86), U = 385, Z = -2.463, p = .014, r = .25; and Blacks (Md =1, n = 16), U = 39, Z = -3.453, p = .001, r = .32; both groups have a small effect size, with a slightly larger difference between Blacks and Hispanics (r = .32).

Exploratory Logistic Regression

Direct logistic regression is employed to estimate the association between predictors, age, gender, race, medication management, diabetes disease severity, total number of comorbid conditions, total number of different medications took daily, and total number of therapeutic drug categories took daily on the likelihood that homebound diabetic adults achieve optimal glycemic control. The full model containing all eight predictors is statistically significant, χ^2 (8, N = 117) = 25.377, p = .001, indicating a good model fit to the data. The results of the Hosmer and Lemeshow test indicate further support for the model ($p > .05$). The model as a whole explains between 19.5% (Cox and Snell R square) and 26.6% (Nagelkerke R squared)

of the variability in optimal glycemic control. The sensitivity of the model is 84.9%, and the specificity of the model is 47.7%, correctly classifying 70.9% of the cases overall.

Age, gender, total number of therapeutic drug categories took daily, and total number of different medications took daily have a negative influence on optimal glycemic control; however, only total number of different medications took daily (polypharmacy) is significant. In addition to polypharmacy, medication management and diabetes disease severity contribute significantly to the predictive ability of the model. As shown in Table 4.11, the strongest predictor of optimal glycemic control is diabetes disease severity, with an odds ratio of 3.655, meaning that those homebound Type 2 diabetic adults without diabetic manifestations were over 3 times more likely to achieve optimal glycemic control than those with diabetic manifestations, controlling for all other factors in the model. Likewise, the predicted odds ratio of optimal glycemic control for homebound Type 2 diabetic adults independent in medication management are over 3 times more likely to achieve optimal glycemic control than those dependent in medication management, all else equal. The odds ratio for total number of different medications took daily .279 is less than 1, indicating that for every additional medication beyond 11 taken daily, homebound Type 2 diabetic adults are .279 times less likely to have optimal glycemic control, controlling for other factors in the model. The variables for race and total number of comorbid conditions are not significant in the model.

Logistic regression Model 2 estimates the association of multiple therapeutic drug subclasses and antidiabetic therapy, on the likelihood of achieving optimal glycemic control. The full model containing seven predictors is statistically significant, χ^2 (7, N = 111) = 24.907,

p = .001, indicating a good model fit to the data. The results of the Hosmer and Lemeshow test indicate further support for the model (p > .05). The model as a whole explains between 20.1% (Cox and Snell R square) and 27.1% (Nagelkerke R squared) of the variability in optimal glycemic control. The sensitivity of the model is 80.3%, and the specificity of the model is 60.0%, correctly classifying 72.1% of the cases overall.

As shown in Table 4.11, neither of the demographic control variables selected for this study is significant in predicting optimal glycemic control. Although not significant, gender continues to have a negative influence on optimal glycemic control. Medication management and diabetes disease severity continue to be significant predictors of optimal glycemic control, (p < .05). Homebound Type 2 diabetic adults without diabetic manifestations and independent in medication management are over 2 times more likely to achieve optimal glycemic control than those with diabetic manifestations and dependent in medication management. The strongest predictor of optimal glycemic control was antidiabetic therapy, with an odds ratio of 3.330, meaning that those homebound Type 2 diabetic adults using a combination of oral medications were over 3 times more likely to achieve optimal glycemic control than those using insulin combination therapies, controlling for all other factors in the model. The total number of therapeutic drug subclasses did not help to explain the variability in optimal glycemic control.

Contrary to expectations, the regression analyses indicate that total numbers of comorbid conditions, therapeutic drug subclasses and drug categories are not significant predictors of optimal glycemic control in the sample population. To further explore the influence of comorbid conditions and multiple drug regimens, a correlation analysis between glycemic control and vascular conditions (largest group identified in the sample population),

and cardiovascular agents is conducted. Glycemic control is not significantly associated with vascular conditions (r_s = -.077, n = 104, p = .440). There is a weak, positive association between glycemic control and cardiovascular drugs, r_s = .25, n = 115, p = .008, with 6.3% shared variance. When regressed on optimal glycemic control, cardiovascular drugs are not significant in the model controlling for the effects of age, diabetic manifestations, and antidiabetic therapy.

Table 4.11

Odds Ratios for Exploratory Logistic Regression Models Predicting Glycemic Control

	Model 1			Model 2		
		95% C.I. for Odds Ratio			95% C.I. for Odds Ratio	
	Odds Ratio	Lower	Upper	Odds Ratio	Lower	Upper
Age (age1 - 65 to 76 years)	0.942	0.392	2.264	1.024	0.417	2.511
Gender (female)	0.963	0.400	2.321	-0.736	0.292	1.854
Race (race1 - White)	1.039	0.393	2.746	1.140	0.423	3.076
Medication Management (medman)	3.134*	1.300	7.558	2.425*	1.014	5.798
Diabetes Disease Severity (ENDO1)	3.655**	1.436	9.303	2.963*	1.210	7.257
Therapeutic Categories (categ1)	0.947	0.347	2.583	—	—	—

(*table continues*)

Table 4.11 (*continued*).

	Model 1			Model 2		
		95% C.I. for Odds Ratio			95% C.I. for Odds Ratio	
	Odds Ratio	Lower	Upper	Odds Ratio	Lower	Upper
Total Medications (tomeds)	0.279*	0.098	0.795	—	—	—
Comorbid Conditions (tcom)	1.184	0.405	3.457	—	—	—
Therapeutic Subclass (toclass)	—	—	—	1.659	0.647	4.256
Antidiabetic Therapy (oralgly2)	—	—	—	3.330*	1.256	8.829
Constant	0.599			-0.265		

Note. Model 1. N = 117; *p < .05, **p = .01. Model 2. N = 111; *p < .05.

Summary of Results

The results of the data analyses of the sample population of homebound individuals with Type 2 diabetes aged 65 years and older are presented in this chapter. Addressing the descriptive questions, 61.7% of the sample met the recommended level of glycemic control, hA1C < 7%; 97.5% of the cases are subject for polypharmacy; with the majority (64.2%) presenting without diabetic manifestations. The highest proportion (25%) of cases presents with 4 comorbid conditions; with only 5% of the sample experiencing diabetes associated emergency room visits and/or hospital admission.

Addressing the relational questions, there is a weak positive association between glycemic control and diabetes disease severity, total number of different medications and

therapeutic drug subclasses took daily. The presence of diabetic manifestations explains nearly 7% of the variance in glycemic control with polypharmacy (the total numbers of different medications and therapeutic drug subclasses took daily) explaining 5% of the variance. When examining the influences of age and gender, it is revealed that those aged 65 to 76 years and female gender specify the strength of the association, with the presence of diabetic manifestations explaining nearly 17% of the variance in glycemic control among those aged 65 to 76 years and nearly 12% among females. The presence of polypharmacy explains between 8% (therapeutic drug subclasses) and 10% (total medications) of the variance in glycemic control among those aged 65 to 76 years and 6% (therapeutic drug subclasses) to 7% (total medications) among females. In addition, when age is not taken into account in the analysis, it suppresses the association between glycemic control and the total number of comorbid conditions among those aged 65 to 76 years. The number of comorbid conditions helps to explain nearly 8% of the variance in glycemic control among those aged 65 to 76 years.

The exploratory data analyses demonstrated a significant difference in the hA1C levels among those independent in medication management and those dependent in medication management; achieving optimal glycemic control was greater among those independent in medication management. There is a significant difference in the presence of diabetic manifestations across four racial groups; Hispanics with two manifestations, while Whites and Blacks had none, with a slightly larger difference between Blacks and Hispanics. Results of the exploratory regression analyses identify medication management, presence of diabetic manifestations, polypharmacy (total number of different medications took daily) and antidiabetic therapy as significant predictors of optimal glycemic control. Contrary to

expectations, optimal glycemic control was not explained by the total numbers of comorbid conditions, therapeutic drug subclasses and drug categories across the regression models.

CHAPTER 5

DISCUSSION

The focus of this research is glycemic control in homebound individuals with Type 2 diabetes aged 65 years and older in the presence of multiple morbidities and polypharmacy. The objective is to find out if the health-related factors of multiple chronic conditions and complex medication regimens to manage those conditions have a significant impact on glycemic control. The study documents a moderate association between glycemic control, polypharmacy and comorbid conditions.

Within the sample, 97.5% of the cases are subject to polypharmacy, the median number of different medications taken daily is 9 (*IQR 7- 11),* the median number of comorbid conditions is 4 (*IQR* 3-5), which are higher than previous studies in this population cohort. The association between glycemic control and diabetes disease severity with associated conditions has not been previously isolated in a research study. The recommended level of glycosylated hemoglobin is achieved by 61.7% of the sample population which appears to be higher than reported in the literature secondary to the exclusion of cases without recorded hA1C values. The relationships between glycemic control and diabetes disease severity, polypharmacy (total numbers of different medications and therapeutic drug subclasses took daily), and total number of comorbid conditions are significant, indicating that homebound individuals with Type 2 diabetes aged 65 years and older are less likely to have optimal glycemic control in the presence of multiple morbidities and polypharmacy, providing support for the study hypothesis. It is important to state that the results of the bivariate and correlation analyses describe the association between the variables not cause and effect. The results appear to be

consistent with the literature on glycemic control and homebound individuals with Type 2 diabetes aged 65 years and older. Within the regression model, the presence of polypharmacy negatively influences glycemic control. Although the likelihood of an association between glycemic control and therapeutic drug subclasses is significant, the number of therapeutic drug subclasses is not significant in predicting optimal glycemic control. After controlling for potentially confounding variables, the lack of diabetic manifestations has a significant and positive influence on optimal glycemic control; but the influence of comorbid conditions is not significant in the model. Likewise, the likelihood of an association between glycemic control and number of therapeutic drug categories took daily is not significant. These results may be due to sample size. However, I suspect the level of disease severity may influence the association between optimal glycemic control and comorbid conditions, therapeutic drug subclasses and categories secondary to the number of medications it takes to manage the level of manifestations of the principle condition. Comorbid conditions that are asymptomatic require less aggressive medical management compared to those with manifestations, and of longer duration, to achieve target treatment goals.

The results of the study further indicate that antidiabetic therapy is a strong predictor of optimal glycemic control. Those individuals with a treatment regimen of oral agents, singular and in combination are more likely to achieve optimal glycemic control than those on insulin agents or combination therapies of oral and insulin agents. Consistent with previous research (Willey et al., 2006), the highest (84%) proportion of the sample with optimal glycemic control took a single oral agent compared to the lowest (40%) proportion which took 3 oral agents.

Only 40% of those individuals in this study using insulin treatment analogs achieve optimal glycemic control.

Another significant finding of the study is the low level of adverse clinical outcomes; diabetes associated emergent care and/or hospitalizations. Only 2.6% (6) of the entire study population (5% of the sample) experienced unscheduled emergent care secondary to hypoglycemia or hyperglycemia, diabetes out of control, preventing full exploration of the likelihood of an association between glycemic control and adverse clinical outcomes. However, this finding is important since there are significant drug to drug interactions present in the sample population with an increased potential of drug-associated hypoglycemia and/or hyperglycemia.

The proportion of the sample that could potentially have moderate drug to drug interaction is 92.5%, which is consistent with previous research (Ibrahim, King, & Dansky, 2005). As shown in Table 5.1, concomitant with administration of oral antidiabetic agents and/or insulin, the highest proportion (95.8%) of drugs taken by this population, are cardiovascular agents; with 60% taking beta-blockers (β-blockers), 49.2% take angiotensin-converting enzyme (ACE) inhibitors, and 43.3% take diuretics; followed by central nervous system agents at 91.7%, with 60.8% taking non-steroidal anti-inflammatory agents (NSAIA). The antidiabetic therapies, especially monotherapy consisting of the insulin secretagogues (sulfonylureas) or insulin, as well as the combination therapies, sulfonylureas plus metformin, or sulfonylureas plus metformin plus insulin, all have a high risk of hypoglycemia (Salem, Fathallah, Hmouda, & Bouraoui, 2011; Munger, 2010; Ibrahim, King, & Dansky, 2005; Chelliah & Burge, 2004; Chutka, Evans, Fleming, & Mikkelson, 1995). Among the cases with diabetes-associated adverse clinical

outcomes, 4 of 6 took insulin and 2 took sulfonylurea monotherapy. The concomitant administration of β-blockers and sulfonylureas may inhibit some of the normal physiologic response to hypoglycemia (Chelliah & Burge, 2004), preventing patients from recognizing the symptoms of hypoglycemia in time to take corrective action. The efficacy of insulin secretagogues (sulfonylureas) may be potentiated by ACE inhibitors which may increase the risk of hypoglycemia by enhancing insulin sensitivity (Munger, 2010). NSAIA may stimulate insulin secretion or increase plasma concentration of insulin secretagogues by displacing them from plasma protein binding sites and/or inhibiting their metabolism, resulting in hypoglycemia (Salem, Fathallah, Hmouda, & Bouraoui, 2011). Diuretics interfere with the hypoglycemic effect of insulin and oral antidiabetic agents possibly as a result of potassium depletion, increasing the risk for hyperglycemia (Salem, Fathallah, Hmouda, & Bouraoui, 2011). One explanation for the low incidence of diabetic-associated adverse clinical outcomes may be a lower level of functional impairment of the gastrointestinal tract, liver and kidney. These systems are primarily responsible for the absorption, detoxification and excretion of medications, age-associated changes or disease processes in renal and hepatic clearance may increase the likelihood of adverse drug reactions. Another explanation may be the timing of medication dosages, decreasing the potential of drug to drug interactions.

Table 5.1

AFHS Pharmacologic Therapeutic Categories and Subclasses: Frequency Distribution in Sample Population

		n	%
Drug Categories	Drug Subclasses		
Anti-infective Agents		14	11.7
Anti-neoplastic Agents		8	6.7
Autonomic Drugs		29	24.2
Blood Formation, Coagulation, and Thrombosis		35	29.2
Cardiovascular Drugs		115	95.8
	Beta blockers	72	60.0
	ACE inhibitors	59	49.2
	Calcium Channel Blockers	44	36.7
	Antilipemics	82	68.3
Central Nervous System Agents		110	91.7
	NSAIA	73	60.8
	Opiates	55	45.8
	Analgesics	18	15.0
	Antidepressants	36	30.0
Electrolytic, Caloric, and Water Balance		105	87.5
	Diuretics	52	43.3
Respiratory Tract Agents		8	6.7
Gastrointestinal Drugs		60	50.0
	Antiulcer	54	45.0
Hormones and Synthetic Substitutes			
	Anti-diabetic Agents		
	Oral agents	98	81.7
	Insulin	62	51.5
	Thyroid hormones	32	26.7
Smooth Muscle Relaxers		10	8.3
Miscellaneous Therapeutic Agents		16	13.3

Note: N = 120. AFHS = American Hospital Formulary Service.

Practice and Policy Implications

The results of this study support the premise that health-related factors of multiple chronic conditions and complex medication regimens to manage those conditions do have a

significant impact on glycemic control among homebound individuals with Type 2 diabetes aged 65 years and older. Challenges for home health agencies in managing the care of elderly Type 2 diabetics include difficulty obtaining comprehensive assessments; effectively monitoring changes in health status; working within existing reimbursement and policy constraints; and coordinating care from a mix of providers through periods of acuity, transition, rehabilitation, and maintenance. To mediate these challenges and facilitate evidenced-based practice patterns and effective coordination of care, it is necessary to identify the primary provider responsible for comprehensive care management, the medical care home. Study results highlight the need for a thorough analysis of the medication regimens and the potential outcomes associated with the use of multiple therapeutic drug subclasses. An interdisciplinary approach to care will involve consistent, effective communication and coordination of the principal providers, providing close clinical monitoring to assess for periods of undetected hypoglycemia, and drug-drug interactions.

Previous research has identified the addition of an exercise program, aerobic and resistance training to improve glycemic control (Dutton, Tan, Provost, Sorenson, Allen, & Smith, 2009; Albright, Franz, Hornsby, Kriska, Marrero, Ullrich, & Verity, 2010). The introduction of physical therapy for the homebound individual with Type 2 diabetes starts with a comprehensive assessment of functional motor performance and the identification of contraindications and or limitations for exercise. To effectively train individuals for lifestyle modifications, and promote adherence to a physical activity/exercise program, physical therapists must become more adept in discussing medications, dosing intervals and compliance; symptom management and corrective actions; relationship between meals, snacks

and blood glucose levels and physical activity/exercise during treatment sessions. The presence of polypharmacy and the potential of drug to drug interactions, as well as exercise induced hypoglycemia signal the need for increased glucose monitoring associated with exercise, patient education regarding the signs and symptoms of hypoglycemia and the appropriate corrective actions to eliminate or reduce the effects of symptoms. Communication and coordination with nursing and the medical care home is important since hypoglycemia and hyperglycemia can occur up to 24 hours after exercise and medication adjustments may be required to prevent adverse reactions.

Recommendations for Future Research

Multiple comorbid conditions and polypharmacy are associated with poor glycemic control. In order to better understand the interplay of glycemic control, comorbid conditions and polypharmacy, future research should focus on the severity of the conditions, examining the influence of age-associated changes (organ/system impairment) and the increased potential for drug to drug interactions with concomitant antidiabetic therapy among individuals aged 65 years and older. The presence of multiple organ/system impairment secondary to aging and multiple disease processes may impact the absorption, distribution, and excretion of medications, increasing potential for adverse drug reactions and poor blood glucose regulation. Both the ADA (2010) and the American Association of Clinical Endocrinologists (AACE, 2011) recommend increased hA1C (7% to 8%) target levels for individuals with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long duration of Type 2 diabetes when aggressive measures have not been successful. To date there has been limited research on the relationships with

clinical outcomes in this population. The ability to achieve optimal glycemic control with increased hA1C targets may reduce the potential of adverse clinical outcomes, poor blood glucose control and drug-drug interactions in this population.

Limitations

Several limitations of the study should be mentioned. The population studied is from a single home health agency serving one large geographic area, and the results may not be generalized to other agencies or locations. The scales in the OASIS data set have been validated; however, the responses are based on the clinical judgment of the registered nurse and may be subjective, the initial and discharge documents are not completed by the same clinician in all cases, measurement error is possible. Medical records of home health agencies are not comprehensive. There are inconsistencies between the documented comorbid conditions and the prescribed medications; the medication profile suggests the presence of conditions not previously identified. Data obtained from medication profiles consisted of prescription medications and over-the-counter non-steroidal anti-inflammatory agents only, limiting complete analyses of drug to drug interactions, and potentially suppressing the associations between glycemic control and therapeutic drug subclasses and categories.

Of particular concern is the number of excluded cases for analyses which limits the complete exploration of the relationships between the variables. Optimal glycemic control is the principal outcome measure for the study, 112 cases (48.3%) did not have recorded hA1C laboratory values. It is beyond the scope of this study to explore why this information is not in the home health medical record, but questions to consider:

1. What is the primary objective of diabetes disease management from the physician's perspective? And, which treatment protocol for Type 2 diabetes does he/she employ? And, how does he/she assess the efficacy of the antidiabetic therapy regimen?
2. What is the most effective communication tool to share information between the physician's office and the agency for coordination of care?

Whatever the reasons, current medical protocol has identified the hemoglobin A1C as the definitive measure of glycemic control. In order to adequately assess blood glucose control and the efficacy of the antidiabetic therapy regimen, it is necessary to obtain the results of the hemoglobin A1C, and incorporate that information as part of the plan of care. Home health services are an extension of the medical care home, as such agency professionals have a responsibility to effectively manage the care of the homebound individual by improving care coordination and communication.

Conclusion

The results of this study further demonstrate that polypharmacy and comorbid conditions are significant risk factors associated with poor glucose control in homebound individuals with Type 2 diabetes aged 65 years and older. There continues to be a need for scientific research in this population cohort; and the dose-response association between antidiabetic therapy interventions designed to lower blood glucose levels in the presence of chronic disease and polypharmacy. The implementation of evidenced-based practices within the current reimbursement scheme for chronic disease management requires development of

innovative strategies, and comprehensive coordinated care plans involving formal and community-based informal care providers to successfully manage this population cohort.

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