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Quantifying polypharmacy in diabetes patients in the U.S.

Jing Tao
Virginia Commonwealth University

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QUANTIFYING POLYPHARMACY IN DIABETES PATIENTS IN THE U.S.

A thesis submitted in partial fulfillment of the requirements for the degree of Masters Science in Pharmaceutical Sciences at Virginia Commonwealth University.

by

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<td>Glycated hemoglobin</td>
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<td>AACE</td>
<td>American Association of Clinical Endocrinologists</td>
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<tr>
<td>ACE</td>
<td>American College of Endocrinology</td>
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<tr>
<td>ACE Inhibitor</td>
<td>Angiotensin-converting enzyme inhibitor</td>
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<tr>
<td>ARB</td>
<td>Angiotensin receptor blocker</td>
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<td>ADA</td>
<td>American Diabetes Association</td>
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<td>ADR</td>
<td>Adverse drug reaction</td>
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<td>AHRQ</td>
<td>Agency for Healthcare Research and Quality</td>
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<td>BMI</td>
<td>Body Mass Index</td>
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<td>CDC</td>
<td>Center for Disease Control and Prevention</td>
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<td>CHD</td>
<td>Coronary heart disease</td>
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<td>CVD</td>
<td>Cardiovascular disease</td>
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<td>CYP</td>
<td>Cytochrome system</td>
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<tr>
<td>DKA</td>
<td>Diabetic ketoacidosis</td>
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<tr>
<td>EASD</td>
<td>European Association for the Study of Diabetes</td>
</tr>
<tr>
<td>EMME</td>
<td>Eastern Mediterranean and Middle-East</td>
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<tr>
<td>ESRD</td>
<td>End-stage Renal Disease</td>
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<td>GDM</td>
<td>Gestational diabetes mellitus</td>
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<tr>
<td>GLM</td>
<td>Generalized linear model</td>
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<tr>
<td>HDL</td>
<td>High-density lipoprotein</td>
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<td>Abbreviation</td>
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<tr>
<td>HMG-CoA</td>
<td>3-hydroxy-3-methylglutaryl-coenzyme A</td>
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<td>HNC</td>
<td>Hyperosmolar Nonketotic Coma</td>
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<td>IDF</td>
<td>International Diabetes Federation</td>
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<td>IFG</td>
<td>Impaired Fasting Glucose</td>
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<td>IGT</td>
<td>Impaired Glucose Tolerance</td>
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<td>LA</td>
<td>Lactic Acidosis</td>
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<tr>
<td>LDL</td>
<td>Low-density Lipoprotein</td>
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<td>LEA</td>
<td>Lower-Extremity Amputation</td>
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<td>MEPS</td>
<td>Medical Expenditure Panel Survey</td>
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<td>MI</td>
<td>Myocardial infarction</td>
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<tr>
<td>MSA</td>
<td>Metropolitan statistical area</td>
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<td>NAMCS</td>
<td>National Ambulatory Medical Care Survey</td>
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<td>OLS</td>
<td>Ordinary Least Square</td>
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<td>OOP spending</td>
<td>Out-of-pocket (spending)</td>
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<td>PMED</td>
<td>MEPS Prescribed Medicines</td>
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<td>QALY</td>
<td>Quality-adjusted Life-year</td>
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<td>World Health Organization</td>
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ABSTRACT

QUANTIFYING POLYPHARMACY IN DIABETES PATIENTS IN THE U.S.

By Jing Tao, BPharm, M. S.

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science at Virginia Commonwealth University.

Virginia Commonwealth University, 2011.

Major Director: David A. Holdford, Ph.D.

Associate Professor, Department of Pharmacy

Objectives: To quantify polypharmacy and assess the socio-economic predictors of medication use and expenditure in diabetics.
Methods: This study analyzed adult diabetes patients using a nationally representative sample in Medical Expenditure Panel Survey in 2006. Top ten most highly utilized drug classes were identified. Descriptive statistics were used to portray the patients’ medication utilization and spending. Generalized linear models were conducted to assess the socio-economic variants in drug use and spending.

Results: On average, a diabetes patient had 45 prescriptions in 2006, for total annual spending of $3,161. A diabetes patient used drugs from 3.43 classes within top ten drug classes. Races and insurance coverage are associated with drug use and spending, holding other factors constant.

Conclusion: Diabetes patients use multiple classes of drugs. Insurance coverage and races are related with drug spending and utilization. More research is needed to evaluate the potential risks of drug-drug interactions due to polypharmacy.
CHAPTER 1
Introduction

1.1 Background

Diabetes mellitus is a group of chronic diseases characterized by hyperglycemia. According to the World Health Organization’s (WHO) definition, diabetes mellitus describes a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Generally, diabetes is categorized into four clinical classes: (1) Type 1 diabetes, (2) Type 2 diabetes, (3) Other specific types of diabetes, and (4) Gestational diabetes. Type 1 diabetes was previously called insulin-dependent diabetes because it usually strikes children and young adults. This form of diabetes results from destroyed pancreatic β-cell which is the only cells in the body that make the hormone insulin that regulates blood glucose. To survive, patients with Type 1 diabetes must have insulin delivered by injection or a pump. In adults, type 1 diabetes accounts for 5% to 10% of all diagnosed cases of diabetes \[1\]. Type 2 diabetes results from a progressive insulin secretory defect on the background of insulin resistance. Type 2 diabetes is by far the most common type of diabetes. In adults, type 2 diabetes accounts for about 90%-95% of all diagnosed cases of diabetes \[1\]. This form of diabetes was previously called noninsulin-dependent diabetes. It usually begins as insulin resistance, a disorder in which insulin is not used properly in the body. As the need for insulin rises, the pancreas gradually loses its ability to produce it. Type 2 diabetes is often associated with older age, obesity, family history of diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity. Other specific types of diabetes result from other causes such as infections, diseases of the exocrine
pancreas, surgery, and drug- or chemical-induced diabetes. This type of diabetes accounts for only 1% to 5% of all diagnosed cases \[1\]. Gestational diabetes mellitus (GDM) is a form of glucose intolerance that is newly diagnosed during pregnancy \[2\] \[3\]. This type of diabetes is more common among obese women and women with a family history of diabetes. During pregnancy, it requires treatment to normalize maternal blood glucose levels to avoid complications in the infant. Despite the difference in pharmaceutical treatment for type 1 and type 2 diabetes, both share similar complications. Diabetes is highly associated with cardiovascular complications such as coronary heart disease (CHD), large plaque burden and myocardial infarction (MI) \[4\]-\[6\]. Other diabetic-related complications include nephropathy, neuropathy, and retinopathy \[7\].

Diabetes has reached epidemic proportions in the United States. According to the most recent report from Center for Disease Control and Prevention (CDC), 25.8 million Americans have diabetes and an estimated 79 million adults have pre-diabetes \[2\]. The disease and its complications is one of the most expensive medical conditions in the US and ranks seventh as a leading cause of death in the nation \[2\]. Economically, diabetes imposes an increasing economic burden on national health care systems. Research has reported that the total costs of diagnosed diabetes in the United States in 2007 were $174 billion \[8\]. After adjusting for demographic differences, average medical expenditures among people with diagnosed diabetes were 2.3 times higher than for nondiabetics \[8\]. The increasing diabetes prevalence, the complexity of its complications, and the high cost of the treatment, presents challenges to diabetes management and cost control.

Pharmaceutical intervention plays an important role in preventing the progression of diabetes complications such as the cardiovascular disease \[9\]. Pharmaceuticals are used to provide tight
control of blood glucose levels, blood pressure, and cholesterol levels\textsuperscript{[10]}. Intensive glycemic control with insulin therapy in type 2 diabetes patients can delay the onset and progression of diabetic retinopathy, nephropathy and neuropathy\textsuperscript{[11]}. Similar benefits have been shown in therapies for individuals with type II diabetes\textsuperscript{[12]}. The UK Prospective Diabetes Study indicated that intensive control of blood pressure and blood glucose reduce the risk of complications in type 2 diabetes patients\textsuperscript{[13][14]}. A randomized placebo-controlled trial in UK reported that cholesterol lowering medication can significantly reduce the major coronary events, strokes and revascularisations\textsuperscript{[15]}. The STENO-2 study indicated that diabetes patients significantly benefit from an intensified, targeted intervention including using ACE Inhibitors or ARBs, smoking cessation and dietary interventions\textsuperscript{[16]}. The underlying pathology of cardiovascular diseases in diabetes patients is complicated and likely multi-factorial. Consequently, several therapeutic medications should be considered into the comprehensive diabetes care beyond glucose control.

Based on these results, clinical practice guidelines have recommended a more intensive form of diabetes care with multi-targets of medical care. Multiple drug therapy is generally required in the treatment for complications for patients with diabetes. For glycemic control, the American Diabetes Association (ADA) recommends that A1C targets be below or around 7\% for diabetes due to the strong association between A1C level and macrovascular complications\textsuperscript{[2]}. For hypertension, the blood pressure target has been lowered from 130/85 mmHg to 130/80 mmHg based upon ADA recommendations\textsuperscript{[10]}. The ADA also recommended that patients with high blood pressure ≥140/90 mmHg should receive pharmacologic therapy including either an ACE inhibitor or an angiotensin II receptor blocker (ARB), supplemented with a thiazide diuretic if necessary\textsuperscript{[2]}. For dyslipidemia in diabetes, statin therapy is recommended to achieve a LDL cholesterol level < 100mg/dl (2.60 mmol/l), regardless of baseline lipid levels\textsuperscript{[2]}. Additionally,
anti-platelet agents may also be considered as a primary cardiovascular risk prevention strategy for elderly diabetic patients. Recommended therapy includes aspirin (75-162 mg/day) for those who at increased cardiovascular risk or clopidogrel (75 mg/day) and aspirin for those who had an acute coronary syndrome history [2].

Each of the guidelines and clinical recommendations indicates the likelihood that comprehensive treatments of diabetic patients will involve several medications across different therapeutic drug classes. Hence, polypharmacy, which is defined as the prescriptions of multiple medications simultaneously [20], has become a salient consideration in the care of patients with diabetes. The major consequences of polypharmacy for diabetes patients include adverse drug reactions (ADRs), drug-drug interactions, increased drug costs, decreased medication adherence, potential duplicated therapy, as well as additional demands for health care services and decreased quality of life [17]. It is noted that with the accelerating rate of drug cost increasing, the financial burden of larger drug regimens may become particularly important for the society. It has been suggested that patients’ regimens should be regularly reviewed and evaluated in order to achieve optimum control of medical problems as well as to keep lower drug costs.

1.2 Objectives and specific aims

The aim of this research was to study the patterns of medication prescription in a nationally representative cohort of adult diabetic patients in 2006. The primary goal was to describe the number of prescriptions and drug classes used among diabetes patients on a personal level, and to quantify the spending on the diabetes-related medications. The secondary goal was to assess socio-economic variants in this patient population.

The study has following specific aims:
**Specific aim 1:** To list top ten drug classes by utilization among diabetes patients.

**Specific aim 2:** To describe the demographic characteristics (age, gender, and race) of the patient sample.

**Specific aim 3:** To calculate the average total drug cost, average out-of-pocket payment, and average number of prescriptions, and average number drug classes.

**Specific aim 4:** To evaluate the socio-economic predictors of medication use and drug spending among the diabetes patients, controlling for age, gender, race, geographic regions, marital status, general health perception and co-morbid diseases.

1.3 Significance

There is abundant evidence that tight control of glucose, blood pressure, and cholesterol levels decreases the risk of developing diabetes and its related macro- and microvascular complications and cardiovascular death [7][13][14][18][19]. On the other hand, the undesired consequences of multiple medications for diabetes have been described [20]-[23]. This includes adverse drug reactions, medication errors and increased risks of nonadherence and hospitalization rates.

The complexity of diabetes therapy on a personal level (number of medications undertaken) provides important implications for the safety of patients and quality of diabetes management as well as drug cost control. Documenting the average number of prescriptions and number of drug classes by each patient is important for public health concerns with respect to polypharmacy. Addressing the socio-economic inequalities regarding multi-pharmacy use and medication expenditures provides a better understanding for policy makers on strategies for diabetes management.
To our knowledge, however, there has been few study focused on detailed quantification of the level of complexity based on the therapeutic drug classes$^{[10][24]}$. The literature gap is discussed in Chapter 2. This study contributes to the literature that quantifies multiple therapeutic drug classes used on a patient level and its socio-economic determinants as they influence the patterns of patients’ medication utilization.
CHAPTER 2
Literature Review

2.1 Epidemiology of Diabetes

Current data show that we have been in the midst of a global epidemic of diabetes. Shaw and his colleagues, using the International Diabetes Federation (IDF) data, estimated that 285 million adults suffering from diabetes worldwide in 2010. This means that the global prevalence of diabetes is 6.4%, and it is predicted that the prevalence will reach 7.7% among adults by 2030 \[25\]. After adjusted for age and gender, the highest regional prevalence for diabetes in 2010 was for North America, followed by the Eastern Mediterranean and Middle-East (EMME) and South Asia \[25\]. The United States has the largest numbers of people with diabetes, followed by India and China, the two nations with the largest populations in the world \[25\].

According to the recent report from U.S. CDC, 25.8 million Americans have diabetes and 79 million adults have pre-diabetes. Pre-diabetes as defined by the American Diabetes Association as a condition in which blood glucose levels are higher than normal but not high enough to be diagnosed as diabetes\[^2\]. An estimated 90-95% of diagnosed diabetes is the noninsulin-dependent type 2 form of the disease which is characterized by insulin resistance, or the inability of cells to effectively use insulin \[^1\]. A report of the National Diabetes Fact Sheet for 2011 indicated that diabetes affects 8.3% of Americans of all ages and 11.3% of adults aged 20 years and above \[^26\].

Geography, age and race affect the prevalence of diabetes. In the U.S., there is a geographically coherent region of 15 southern states called the diabetes belt, where the prevalence of diagnosed diabetes is especially high \[^27\]. The prevalence of diabetes in the
diabetes belt was reported as high as 11.7% in 2007-2008 \cite{27}, compared to the national prevalence of 7.8% in the same year \cite{11}. Regionally, using the National Health and Nutrition Examination Survey (NHANES) database in 2003-2007, Danaei estimated that the lowest prevalence of diabetes was in the Midwest and the Northeast with the age-standardized prevalence ranging from 11.0% to 12.2% for men and 7.3% to 8.4% for women \cite{28}. The highest prevalence was in the southern and Appalachian states where age-standardized diabetes prevalence was 15.8% to 16.6% for men and 12.4% to 14.8% for women \cite{28}. Danaei also reported that age-standardized diabetes prevalence was higher in men than women in all states, with the largest differences in Minnesota, Colorado, Utah, and Maine, where prevalence in men was 32% to 38% higher than that in women (Figure 2.1) \cite{28}.

Racial variance in diabetes prevalence in adults has been shown where 7.1% of non-Hispanic whites, 8.4% of Asian Americans, 11.8% of Hispanics, and 12.6% of non-Hispanic blacks have diagnosed diabetes in 2007-2009 \cite{26}. Furthermore, compared to non-Hispanic white adults, the risk of diagnosed diabetes was 18% higher among Asian Americans, 66% higher among Hispanics, and 77% higher among non-Hispanic blacks \cite{26}.

The prevalence of diabetes increases with age. The prevalence of diabetes among individuals aged of 20-44, 45-64 and \geq 65 years old were 3.7%, 13.7% and 26.9%, respectively (Figure 2.2) \cite{2}. Compared to younger persons 44 years and younger, older patients over 65 years have more than 7 times the prevalence of diabetes.
Figure 2.1: Estimated prevalence of total diabetes by state, sex and age group (age-standardized to the 2000 U.S. population) [28]
2.2 Economic burden of diabetes

The growing number of diabetics and the costs of treatments for the disease and its complications have significant economic impact. The total estimated direct medical costs and lost productivity was $174 billion in 2007 in the United States. Direct medical costs attributed to diabetes include hospital inpatient care, diabetes medications and supplies, retail prescriptions to treat complications of diabetes, and physician office visits. Inpatient care accounts for 50% of total medical expenditures, followed by diabetes medication and supplies, which accounts for 12%. Indirect costs resulting from lost productivities due to diabetes were estimated as $ 58 billion, including absenteeism, reduced productivity while at work for the employed population, reduced productivity for those not in the labor force, unemployment from disease-related disability, and lost productive capacity due to early mortality. Averagely, people with diagnosed diabetes have medical expenditures that are up to 2.3 times higher than what
expenditures would be in the absence of diabetes\textsuperscript{[29]}. Other factors that are attributable to the economic burden of diabetes include higher insurance premiums paid by employees and employers, reduced earnings through productivity loss, and reduced overall quality of life for patients with diabetes and their families. On average, a US male diagnosed as having diabetes at age 40 years will lose almost 12 life-years and 19 quality-adjusted life-years (QALYs) compared with a person of the same age without diabetes. Similarly, a US female diagnosed as having diabetes at age 40 years will lose about 14 life-years and 22 QALYs\textsuperscript{[30]}.

Indeed, the burden of diabetes is imposed on all sectors of society. Much of the cost is preventable through improved diabetes management, initiated to reduce the prevalence of diabetes and costly complications.

2.3 Risk factors for diabetes population

While the prevalence of diabetes can provide information about the burden of disease in the community, prevalence rates do not capture individuals’ risks of developing diabetes. The variation in diabetes prevalence across states, ages and races indicates that diabetes is strongly affected by behavioral, cultural, and environmental factors clustered and overlaid on genetic susceptibility. Individual level of risk factors for diabetes include genetic predisposition, race/ethnicity, increased body mass index (BMI), physical inactivity, and some medical conditions associated with diabetes such as cardiovascular disease and obesity.

Individuals at higher risk for diabetes include: (1) those with impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG); (2) people over age 45; (3) those with a family history of diabetes; (4) people who are overweight; (5) people who do not exercise regularly; (6) people with low HDL cholesterol or high triglycerides, high blood pressure; (7) Certain racial and ethnic
groups such as NonHispanic Blacks, Hispanic/Latino Americans, Asian Americans and Pacific Islanders, and American Indians and Alaska Natives); and (8) women who had gestational diabetes, or who have had a baby weighing 9 pounds or more at birth [31].

Race is a strong independent risk factor for diabetes. Diabetes is over twice as prevalent among African-American adults as compared to their white counter-parts, with odds ratio (OR) =2.35 [32]. Some risk factors such as race, BMI, and socioeconomic status (SES) are associated with each other, presenting a combined impact on developing diabetes. A higher incidence of diabetes is reported among African American women in lower SES versus higher SES neighborhoods [33], increased BMI among women in areas of high unemployment relative to areas of low unemployment [34]. For overweight persons whose BMI was between 25-29.9, ethnic disparities worsened as diabetes prevalence increased 33% in Whites, compared to 60% in Blacks, and 227% in Mexican Americans [35]. Some investigations also indicate higher rates of diabetes in rural areas relative to urban centers [36][37], because socioeconomic factors such as education, income and health insurance status are strongly related to health and vary between rural and urban settings, and these factors contribute to health differences [37]. Health insurance status is important because it is related to income as well as health patterns. Lower income level contributes to a higher proportion of that is uninsured or poorer health insurance overages, resulting in lower level of access to the health care services.

Hence, a variety of factors contribute to the onset and management of diabetes disease, including demographic, geographic, socioeconomic factors and clinical information as well. Factors such as age, races/ethnicities, education, income, health insurance status, health perceptions, and lifestyles have impacts on the disease management and health care service
utilization. Understanding the diabetes epidemic and management must take into account a complex array of multiple risks such as individual, social, economic, and environmental factors.

2.4 Diabetes Complications

The population burden of diabetes complications is large in terms of mortality, morbidity, and loss of quality of life. Diabetes is such a serious disease in that it can result in blindness, kidney failure, peripheral neuropathy and arterial disease, cognitive impairment, and death\[38\]. The pathobiology of diabetic complications is generally featured as hyperglycemia-induced tissue damage, shown in Figure 2.3\[39\]. Although the damage process can be modified by both genetic determinants of individual susceptibility and independent accelerating factors such as hypertension, some cell types are particularly susceptible to be damaged by hyperglycemia because they are not efficient in reducing the transport of glucose inside the cell when they are exposed to hyperglycemia. These cell types include: capillary endothelial cells in the retina, mesangial cells in the renal glomerulus, and neurons and Schwann cells in peripheral nerves\[39\]. Hence, diabetes selectively damages cells such as endothelial cells and mesangial cells.
2.4.1 Morbidity

The morbidities of diabetes include cardiovascular disease, eye, kidney, and lower-extremity disease, acute metabolic complications and disability \[^{26}\][^{38}].

**Cardiovascular disease**

In the United States in 2004, heart disease and stroke were noted on 68% and 16%, respectively, of diabetes-related death certificates among people ages 65 years or older \[^{26}\]. In 2005-2008, 67% of adults aged 20 years or older with diabetes had hypertension, which is defined as blood pressure greater than or equal to 140/90 mmHg \[^{26}\]. The prevalence of ischemic heart disease among patients with diabetes varies by age groups.
The prevalence rate of heart disease was about 14 times the rate among those without diabetes in persons 18 to 44 years of age, 3 times as high in persons 45 to 64 years of age, and almost twice as high in those 65 years of age or older \[38\]. Other studies have shown that the rates of cardiovascular disease in diabetes patients are also different by patients’ gender. The absolute rates are reported to be higher in men than in women, while the relative risk is higher in women than in men, comparing those with and without diabetes \[41\] \[42\].

**Eye, Kidney, and Lower-Extremity Disease**

Diabetes retinopathy is the leading cause of new cases of blindness among adults \[26\] \[40\]. A cross-sectional study on a nationally representative sample of the National Health and Nutrition Examination Survey in 2005-2008 estimated a crude prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy was 28.5% and 4.4%, respectively, among older persons with diabetes aged above 40 years \[43\]. Vision loss due to diabetic retinopathy occurs through a variety of mechanisms, including retinal detachment, preretinal or vitreous hemorrhage, associated neovascular glaucoma, and macular edema or capillary nonperfusion \[44\]. Other cause of vision impairment among persons with diabetes include macular edema which is specific to diabetes, cataracts and glaucoma that are not specific to diabetes but occur more commonly in diabetic than in nondiabetic persons \[45\] \[47\].

Diabetes is the leading cause of end-stage renal disease (ESRD), nontraumatic lower-extremity amputations (LEAs) as well \[48\]. Diabetes is a major cause of chronic kidney disease (CKD) \[49\], and diabetic nephropathy accounted for 44% of all new cases of end-stage renal disease in 2008 \[26\]. The precise pathophysiologic basis for the association between deteriorating kidney function and diabetes disease is unclear. But it is suggested that poorly controlled glucose levels, blood
pressure, and cholesterol activate inflammatory mediators, and patients with a genetic predisposition may help progressing to advanced stage nephropathy\cite{49}. Lower-extremity disease, which includes peripheral neuropathy and peripheral arterial disease or both, results in elevated rates of lower-extremity amputations among persons with diabetes. More than 60\% of nontraumatic lower-limb amputations occur in people with diabetes\cite{26}. People with diabetes have been found to have 2 to 3 times the prevalence of either peripheral neuropathy symptoms or insensate feet\cite{50}.

**Acute Metabolic Complications**

The acute metabolic complications of diabetes consist of diabetic ketoacidosis (DKA), hyperosmolar nonketotic coma (HNC), lactic acidosis (LA) and hypoglycemia\cite{51}. DKA and HNC are related to insulin deficiency resulting in the metabolic outcome of very low levels of effective insulin action\cite{51,52}. DKA is clinically defined by absolute insulin deficiency with hyperglycemia, while HNC is defined by the presence of relative insulin deficiency. LA is usually related to other factors such as cardiovascular diseases, and hypoglycemia mostly results from the treatment of diabetes.

Only the incidence rate of DKA is available from population-based studies. It is estimated that DKA is more common in young diabetic people and may be more common in women than men\cite{51}. Except hypoglycemia, the other three metabolic complications of DKA, HNC, and LA require hospitalization for treatment and thereby result in increased use of health care resources and costs.

**Nervous System Disease**
Diabetic neuropathies are among the most frequent complication of long-term diabetes. About 60 to 70 percent of patients with diabetes have mild to severe forms of nervous system damage \cite{Diabetic Neuropathies}. The femoral nerve is commonly involved giving rise to symptoms in the legs and arms, and pain is the chief symptom that tends to worsen when patients are at rest. It is estimated that almost 30 percent of diabetes patients aged over 40 years old have impaired sensation in the feet \cite{Diabetic Neuropathies}. Furthermore, advanced femoral nerve disease is a major cause of lower extremity amputations.

**Other Diabetes Complications**

Other complications such as depression, susceptibility to other illnesses, are found higher rates among diabetes patients compared to other population. Depression is an independent risk factor for the onset of type 2 diabetes \cite{Depression and Type 2 Diabetes}. Not only can it complicate diabetes management, but also negatively affects the course of diabetes and is associated with increased risk of complications \cite{Depression and Diabetes Complications} \cite{Depression and Diabetes Complications}. There has been a growing call to understand the medical and psychosocial challenges that highlights the importance of concerning about mental health of the diabetes patients.

Besides, diabetes patients are found to be more susceptible to other illnesses, such as pneumonia and influenza. Most of the time, they have worse prognosis than patients without diabetes \cite{Diabetic Neuropathies}.

**2.4.2 Mortality**

Diabetes was the seventh leading cause of death based on U.S. death certificates in 2007 \cite{Diabetes Mortality}. This estimate is based on the 71,382 death certificates in which diabetes was the underlying cause of death \cite{Diabetes Mortality}. Furthermore, diabetes was a contributing cause of death in an additional
160,022 death certificates for a total of 231,404 certificates in the same year in which diabetes appeared as any-listed cause of death\textsuperscript{[26]}. Studies also suggested that death certificates underestimate the prevalence of diabetes among decedents\textsuperscript{[55]}.

2.5 Goals of drug therapy for Diabetes

Effective glycemic control is the main goal of diabetes therapy\textsuperscript{[2]}. However, the nonglycemic goals for diabetes management are of paramount importance as well, especially for the management for cardiovascular complications because they are the major cause of mortality in patients with diabetes\textsuperscript{[18]}.

2.5.1 Glycemic goals

The recognition of the efficacy in substantially reducing morbidity by achieving specific glycemic goals has made the effective treatment of hyperglycemia a priority in diabetes management\textsuperscript{[2][56][57]}. Intensive treatment strategies have been demonstrated to reduce complications of both type 1 and type 2 diabetes\textsuperscript{[7][13][14]}. The goals of glycemic control are set differently by different organizations. The American Diabetes Association suggested a general glycemic goal of lower than 7\% in glycated hemoglobin (A1C) level for nonpregnant adults\textsuperscript{[2]}, while the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) recommend A1C level of $\leq 6.5\%$\textsuperscript{[58]}. In general, studies have shown that maintaining glycemic levels as close to the nondiabetic range as possible has been demonstrated to have a powerful beneficial effect on reducing complications such as retinopathy, nephropathy, neuropathy, and cardiovascular disease (CVD) in diabetes patients\textsuperscript{[59]}.
Blood glucose-lowering medications are available for both type 1 and type 2 diabetes. However, oral blood glucose-lowering medications can only be used for patients with type 2 diabetes. These oral medications include sulfonylureas, meglitinides, the biguanide, metformin, thiazolidinediones, alpha-glucosidase inhibitors, and the oral dipeptidyl-peptidase-4 inhibitor sitagliptin\[60\]. The increased number of choices available to physicians and patients has heightened concern whether used alone or in combination with other blood glucose-lowering interventions are most appropriate for the individual patients\[59\][61\]. Overall, the ADA and the European Association for the Study of Diabetes (EASD) published a consensus statement that the main objective of hyperglycemia management is to achieve and maintain glycemic control and to change interventions when therapeutic goals are not being met \[2\].

2.5.2 Nonglycemic goals

The nonglycemic goals for diabetes management refers to the prevention and management of diabetes complications, among which cardiovascular disease is the major cause of morbidity and mortality for diabetes individuals and the largest contributor to the medical costs of diabetes. The genesis of cardiovascular complications is in pre-diabetic states, and studies have shown that strict glycemic control is effective in preventing and delaying the development of CVD \[18\]. The CVD treatments include controlling hypertension, elevated low-density lipoprotein (LDL), prothrombotic state and cigarette smoking. The goals of these treatments are listed in Table 2.1, according to the ADA statement on standards of medical care in diabetes 2010 \[2\][18\].

Other nonglycemic goals include nephropathy, retinopathy, neuropathy treatment and food care. ACE inhibitors or ARBs are recommended for the treatment of the nonpregnant patient with albuminuria, which is an early marker of chronic kidney disease (CKD) \[62\], and is
associated with a higher risk of renal function loss \cite{63}. The management of painful polyneuropathy is focused on symptom relief and positively improving the quality of life \cite{2}. For example, gastroparesis symptoms may improve with prokinetic agents such as metoclopramide or erythromycin; medications for erectile dysfunction may include phosphodiesterase type 5 inhibitors, intracorporeal or intraurethral prostaglandins \cite{2}.

| Table 2.1 Treatment goals for CVD in adult diabetes patients \cite{2} \cite{18} |
|----------------------------------|----------------------------------|
| Hypertension/blood pressure control | < 130/80 mmHg |
| Dyslipidemia control               | LDL cholesterol: < 100mg/dL |
|                                   | HDL cholesterol: >50 mg/dL |
|                                   | Triglycerides: < 150 mg/dL |
| Prothrombotic state control        | Aspirin therapy: 75-162 mg/day as primary prevention strategy in adult diabetes patients and macrovascular disease or for primary prevention in patients older than 40 years with diabetes or with more than one other CVD risk factor. |
| Cigarette smoking goal             | Cessation |

2.6 Polypharmacy Regimen for Diabetes and Literature Gap

Most diabetes patients take oral medications instead of insulin to control glucose level. It is estimated that only 12% adult patients with diabetes take insulin only, while 58% take oral medication only (Figure 2.4) \cite{26}.

Polypharmacy can be defined as the use of two or more medications simultaneously \cite{20}. The characteristics of diabetes and its complications often require a multiple medication regimen for diabetes, frequently using drugs from multiple therapeutic classes. However, the risks of polypharmacy and the potential inappropriate medication use must be considered and balanced against the benefits of multiple drug therapies. Simultaneous use of multiple medications is
often associated with drug-drug interactions, adverse drug reactions, medication errors, and increased risks of nonadherence to therapeutic regimens and higher hospitalization rates, especially for elderly patients who are suffering from decreased renal and hepatic functions \(^{[20]-[23]}\).

**Figure 2.4 Percentage of adults with diagnosed diabetes receiving treatment with insulin or oral medication, United States, 2007-2009**
*(Source: 2007-2009 National Health Interview Survey)* \(^{[26]}\)

Surprisingly, although the risks of multiple medication use are well recognized, most studies on polypharmacy have merely focused on the levels of adherence to the medication therapy \(^{[19]}\) \(^{[64]-[65]}\) and the association between the adherence level and clinical control of LDL, A1C, and blood pressure level \(^{[66]-[67]}\). An inverse relationship was evidenced between the number of drugs prescribed and patients’ adherence to diabetes-related medications, resulting a significantly lower A1C and total cholesterol level at the end of the study period \(^{[19]}\). Successful control of clinical targets depended highly on a subject’s baseline number of treatments. The number of medications among successful cases was 11 to 17 percentages lower than those failed to achieve
the clinical targets\textsuperscript{[67]}. However, these studies have typically not characterized the drug regimens in terms of a detailed description of therapeutic drug classes used to treat patients with diabetes.

Grant et al provided evidence that treatment related to diabetes care has grown more complex over time\textsuperscript{[24]}. Using the National Ambulatory Medical Care Survey (NAMCS), they characterized trends in the number of prescribed medicines, management of hyperglycemia, hypertension, and hyperlipidemia from 1991 to 2000. Significant increases were found in the number of prescription medicines reported at office visits over time (Figure 2.5). The unadjusted proportion of patients prescribed at least 5 medications increased in a linear trend from 18.2\% in 1991 to 29.9\% in 2000 (p<0.001), as shown in Figure 2.5. After controlling for age, gender, race/ethnicity, insurance status, physician type, the diabetes type and visit duration, the proportion of patient visits with 5 or more medicines increased by 10.1\% per year from 1991 to 2000 (95\% CI, 6.6\%-13.5\%; p < 0.001).

![Figure 2.5 Trends in the total number of prescribed medicines, 1991-2000\textsuperscript{[24]}](image)

Increases were also found in the use of medications for antihypertension and lipid level lowering (Figure 2.6). In similar regression models controlling for patient and physician...
characteristics and visit duration, the proportion of prescribing antihyperglycemia medications did not change significantly (p>0.05), but that of prescribing antihypertension and antihyperlipidemia medications resulted in significant increases, with an increase of 12.9% and 19.1% per year, respectively.

Figure 2.6 Trends in pharmaceutical treatment of hyperglycemia, hypertension, and hyperlipidemia, 1991-2000 [24]

However, this study was not able to provide a basic description of trends in the number of medications used by diabetes patients. The unit of the analysis was the visit instead of the patient, so the medication care at an individual level was not assessed. Furthermore, the study placed a cap on the total number of medications (5 medications) for each visit, so the average number of medications was not determined.

Huang et al assessed the trends in diabetes regimens from 1995 to 2003, using 30 managed care plans in Midwest and Southern regions [10]. To evaluate the complexity of medication regimens, they calculated the average number of medications and the proportion of patients receiving diabetes-related medications (blood glucose, blood pressure, and cholesterol control
agents). On a patient level, they noted a significant increase in the average total number of diabetes-related medications among patients with prescribed medications (from 2.96 to 3.70, p<0.01), with smaller increases seen for glucose lowering (from 1.45 to 1.65, p<0.01) and blood pressure lowering regimens (from 2.14 to 2.51, p<0.01). Regarding the proportion of patients on the three types diabetes-related medications, they reported a dramatic rise in the proportion on cholesterol lowering (18% to 39%, p<0.01) and antihypertension agents (51% to 62%, p=0.04), adjusted for age, age-squared, female and interactions of female with age variables (Figure 2.7) [10].

Compared with Grant’s study, Huang assessed the average number of medications and percentage of patients using three major drug categories of diabetes regimen. Nevertheless, the results of this study could not be generalized to the whole country because the study sample was not nationally representative. Besides, only three diabetes-related drug classes (cholesterol lowering, antihypertension and glucose lowering agents) were taken into account in this study. Even though cardiovascular diseases are important complications of diabetes, there are more treatments for diabetes patients in order to take care of other complications such as depression, neuralgia and kidney diseases. Thus, the complexity of regimen for diabetes patients needs to be comprehensively assessed. Moreover, they did not access to the actual risk factor levels, such as geographic, demographic, health insurance status, and other socio-economic factors. Our knowledge is sparse with respect to identifying individuals who are particularly prone to polypharmacy therapies. Overall, we do not know the extent of complexity of the regimens and financial burden of medical therapy in diabetes patients.
Based upon the prior literature, this study uses a recent and nationally representative dataset. The therapeutic drug classes among diabetes patients are broadened from 3 to top ten categories that are used among diabetes patients on patient level. Individual factors that have impacts on diabetes regimen and drug expenditures are evaluated as well, so as to give an extensive understanding of the complexity of diabetes treatment. The factors affecting individual’s medication use and drug expenditure are discussed in Section 2.7.
2.7 Socio-economic predictors of medication use and expenditure

Within the multicultural context of the United States, inequalities in health services utilization and consumption is a concern in this country. Differences in drug use and expenditures are based on race/ethnicity, gender, age, income, insurance status, geographic location, sexual orientation, occupation, or health behaviors. Disparities among the different segments of the population have been defined in terms of differences in health status, risk factors for disease and injury, access to and use of health care services, access to health insurance, and differences in the quality of care received [68]. Reasons for the inequalities in health care included differences in risk factors, lack of access to health care, inadequately targeted prevention messages, and cultural differences.

In the United States, the first national report on health care quality and disparity was released by the Agency for Healthcare Research and Quality (AHRQ) in 2003. It demonstrates a broad picture of the scope and characteristics of differences in health care quality and access associated with patient gender, age, race, ethnicity, income, education, and location [69][70]. They reported that racial and ethnic minorities and poor people often receive poorer quality of care and face more barriers when trying to access health care [70].

In this study, we focus on the demographic, geographic and related socio-economic variants in prescribed medication use and spending among adult patients with diabetes. These factors are overlapped and influence each other.

2.7.1 Demographic variants
The United States is an ethnically and racially diverse nation. The current population is approximately 67% non-Hispanic White, 12% black, 14% Hispanic, 1% American Indian/Alaska Native, and 4% Asian (Figure 2.8) [71].

There have been abundant studies reporting that racial/ethnic minorities and poor people use fewer medications and poorer quality of health care. Compared with whites, nonwhites including African Americans, Latinos, and Asian/Pacific Islanders often have poorer glycemic control [72]. Another study reported that the rates of medication underuse were highest among African Americans and Latinos [73]. The current proposed mechanisms for racial/ethnic disparities in medication use are physiologic, socioeconomic, cultural in nature. The median family annual income for non-Hispanic Whites and Asians is $20,000 to $25,000 higher than for Blacks, Hispanics, and American Indians/Alaska Natives in 1999 [71]. Hence, patients with higher education and income are able to purchase better health insurance coverage and to obtain more access to and high quality of healthcare services. The Hispanic population is estimated to be
much younger on average than the other demographic groups, with a median age of 25.8 years compared with 38.6 years for the white population in 2000. As a result, it is likely that Hispanics consume less health care than other groups and are underrepresented in research on the use and quality of health care. Besides, social determinants such as cultural beliefs in drug regimens and medical conditions may result in differences in medication adherence.

Gender may contribute to the difference in medication utilization and consumption. The imbalance between men and women exists with respect to health care utilization related costs. In general, women tend to use significantly more health care services and spend more health care dollars than men. An analysis of Express Scripts’ integrated database of medical and pharmacy claims demonstrated that women contribute to 60% of medical spending and consume 59% of the prescription volume.

Age has notable impacts on medication use as well. Elderly patients have higher risks of complications and side effects of medications due to their decreased liver and renal functions. Diabetes is such a chronic disease that the normal aging process can change the way medication are absorbed, metabolized and distributed in the body.

2.7.2 Geographic variants

Geographic factors influence not only the prevalence and incidence of diabetes, but the medication use among diabetes patients as well. Rural residents have disparities in access to care compared with urban residents because of distance to health care facilities. The impacts of geographic factors on medication use may overlap with that of race/ethnicity. Since Blacks or Hispanic populations tend to live in different areas from nonHispanic white populations, location matters in the measurement of health care disparities.
In this study, both geographic region and metropolitan statistical area (MSA) status are included to predict the variation in drug use and spending among adult diabetes patients.

2.7.3 Impacts of health insurance coverage

Health insurance coverage is an important determinant for medication use and spending, and it is strongly related to better clinical outcomes as well \[78\]. Health insurance status reflects a variety of social and economic status of the patients. Income level, employment status, citizenship status, and language play roles in disparities in insurance coverage, and thus impacts the access to care and quality of care \[79\].
CHAPTER 3

Methodology

3.1 Data Source

The data used in this study were derived from the 2006 Medical Expenditure Panel Survey (MEPS) Full Year Consolidated Data Files and the 2006 MEPS Prescribed Medicines (PMED) Files. The datasets were obtained from their official website which is maintained and co-sponsored by the Agency for Healthcare Research and Quality (AHRQ) and the National Center for Health Statistics (http://www.meps.ahrq.gov/mepsweb/).

MEPS, which was initiated in 1996, is a nationally representative longitudinal survey of families and individuals, their medical providers (doctors, hospitals, pharmacies, etc.), and employers across the United States [80]. MEPS is a survey of panel design, which is featured by five rounds of interviews covering two full calendar years [81]. The survey collects detailed information on health care utilization and expenditures, health insurance, and health status, as well as a variety of social, demographic, and economic characteristics for the civilian noninstitutionalized population. MEPS consists of two major components: household component (MEPS-HC) and insurance component (MEPS-IC). MEPS-HC collects data for each person on demographic characteristics, health conditions, health status, health insurance coverage, income, and employment. MEPS-HC data are available on MEPS Web site in data tables. MEPS-IC, which is also known as the health insurance cost study, collects data including the types of private insurance plans offered, premiums, contributions by employers and employees, and benefits associated with these plans. However, IC data files are not available for public release. In this study, we only used MEPS-HC data file.
Two data files were used from the household component: 2006 Full Year Consolidated Data File and 2006 Prescribed Medicines File. Data were obtained in Rounds 3, 4, and 5 of Panel 10 and Rounds 1, 2, 3 of Panel 11, covering calendar year 2006, as illustrated in Figure 3.1.

![Figure 3.1: Survey rounds for MEPS panels covering calendar year 2006](image)

The consolidated data file contains 1672 variables, pertaining to survey administration, demographics, employment, health status, disability days, quality of care, patient satisfaction, health insurance, income and person-level medical care use and expenditures. About 34,145 persons participated in MEPS Household Component of medical expenditure panel survey in 2006. This count includes all household survey persons who resided in eligible responding households. Of these persons, 32,577 persons were assigned a positive person-level weight. In this study, only the observations with positive person-level weight are used in the analysis. Observations with zero person-level weights were deleted.

In the prescribed medicine file, counts of prescribed medicine utilization are based entirely on household reports. Persons with no prescribed medicine use for 2006 are not included on this file. The prescribed medicine dataset contains 341,994 records of prescribed medicine. Of these prescribed medicine records, 336,109 records are associated with persons having positive
person-level weight. Diabetic supplies, such as syringes and insulin, are also included in the data of MEPS prescription drug expenditure and utilization. Each record on the prescription file includes an identifier for each unique prescribed medicine, national drug code (NDC), medicine name, selected Multum Lexicon variables, total expenditure and sources of payments. Multum Lexicon variables are derived from Multum Lexicon database at Cerner Multum. Inc, which is a global company, providing updated databases for drug information. We used Multum Lexicon variables to identify the drug classes that are used among the sample population.

In this study, the two data files were merged with each other by linking the unique person identifier, variable DUPERSID. By using the person-level weight variable (PERWT06F), the analyses were able to make estimates for the civilian noninstitutionalized U.S. population for 2006.

3.2 Study Sample

The study sample was nonpregnant diabetes patients who are older than 18 years of age. Patients were eligible for inclusion based on their answers to whether they have ever been diagnosed with diabetes (ICD-9-CM codes 249, 250)\textsuperscript{[81]} Patients with gestational diabetes were excluded. A total of 2,189 patients claimed to have been diagnosed as diabetes. These patients’ demographic information from consolidated data file was then linked with their prescribed medication records from prescribed medicine data file for analyses.

Information from the last rounds of Panel 10 and Panel 11 in the year 2006, in order to obtain the most accurate number of patients who have diabetes. Using the previous rounds information may exclude those patients who potentially have diabetes but were not diagnosed during the earlier rounds.
Due to the dataset limitation, we were not able to differentiate between patients with Type 1 and Type 2 diabetes. Albeit we were able to exclude part of the Type 1 diabetics by limiting only adult patients included in this study, we may still have some Type 1 diabetes who used insulin only without other oral anti-diabetic medications in our sample. Thus our estimates on medication use may be underestimated.

3.3 Variables

The MEPS database contains a wide range of demographic and clinical variables for analysis. These variables include age, gender, race, geographic region, metropolitan statistical area (MSA), marital status, education year, family income as percent of poverty line, family size, insurance coverage status, health perception, medical condition, medication use, and medication expenditure.

Categorical variables were created for some demographic information such as age groups, race/ethnicity, marital status, insurance coverage status, health perception and co-morbid diseases. For age groups, patients were divided into three categories: 18-44, 45-64 and 65-85 years of age, according to the age categorization of ADA \[2\]. Medication use among diabetic patients is age-related due to the progress of diabetes disease and complications. Patients over 65 years old are more likely to use multiple medications than younger individuals \[20\][62]. For the race/ethnicity variable, the study sample was categorized into seven groups: White Hispanic, White nonHispanic, Black, Asian, American Indian, Hawaiian and multiple races. Hispanic Nonwhite patients were differentiated from Hispanic White individuals on account of the fact that Hispanics share distinguished cultural beliefs, habits, income level, and education level from
non-Hispanic population. These racial/ethnic differences may contribute to variance in medication use among diabetes population.

The variable of health insurance coverage was categorized into Medicare Part D, Medicare non-part D, Medicaid, Private insurance coverage, and self-payers. Each patient was assigned to only one category of insurance type. A hierarchy according the primary payer was used for people who enjoyed coverage from more than one source. Medicare coverage had first place in this hierarchy. For instance, if a person was covered by Medicare and Medicaid or private insurance, he or she was categorized as having Medicare coverage regardless of any other coverage, because Medicare is the primary payer for his or her drug benefit. Same as other example, if someone had both Medicare non-Part D and private insurance, then the person was classified as having private insurance group as his primary payer is private insurance. The other two categorical variables that were created in this study were general health perception and co-morbid diseases. Both of these two clinical factors contribute to a variation in medication use and thus affect drug spending. Patients with poor health perception and more co-morbid diseases are more likely to experience polypharmacy.

Two indicator variables (family size, education year) were created to identify people who lived alone and who received at least a high school education. Family size and education are associated with medication compliance. Patients who live with their families have better adherence to their medications. Well-educated people are considered to have better knowledge about the therapeutic regimen and may enjoy higher income as well[71]. Hence, people who live with families and well educated are more likely to be adherent to prescriptions.

Twelve independent variables were used in a multivariable regression model to assess the impacts on the three study outcomes of medication use and costs (Table 3.1). As for the
variables of health perception and comorbiditites, only the information from the last rounds of Panel 10 and 11 (Figure 3.1) was used. As explained before, the health status and co-morbid diseases are progressing over time. In order to avoid the potential changes in health status and progress of comorbid diseases during the year, the information obtained at the end of the year was used in this study. The 12 independent variables and 3 dependent variables are listed in Table 3.1. In multivariate regression model, the largest group in each independent variable was set to be the reference group.

Table 3.1 – Variables in multivariate model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Independent variables</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>18-44, 45-64, 65-85</td>
</tr>
<tr>
<td>Gender</td>
<td>Male, Female</td>
</tr>
<tr>
<td>Race</td>
<td>White Hispanic, White nonHispanic, Black, Asian, American Indian, Hawaiian, Multiple race</td>
</tr>
<tr>
<td>Region</td>
<td>Northeast, Midwest, West, South</td>
</tr>
<tr>
<td>MSA status</td>
<td>MSA, NonMSA</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married, Widowed, Divorced, Separated, Never married</td>
</tr>
<tr>
<td>Family size</td>
<td>=1, &gt;1</td>
</tr>
<tr>
<td>Education Year</td>
<td>≤11 years, ≥12 year</td>
</tr>
<tr>
<td>Family income as percent of poverty line</td>
<td>Poor/negative, Near poor, Low income, Middle income, High income</td>
</tr>
<tr>
<td>Health Insurance Coverage</td>
<td>Medicare part D, Medicare nonpart D, Medicaid, Private insurance coverage, Self-pay</td>
</tr>
<tr>
<td>Health Perception</td>
<td>Excellent, Very good, Good, Fair, Poor</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Asthma, High cholesterol, Angina, Coronary heart disease, Heart attack, Other heart disease, Stroke, Arthritis, Emphysema, High blood pressure</td>
</tr>
</tbody>
</table>
Dependent variables

<table>
<thead>
<tr>
<th>Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total drug costs per person per year</td>
</tr>
<tr>
<td>Out-of-pocket payment per person per year</td>
</tr>
<tr>
<td>Number of therapeutic drug classes used per person per year</td>
</tr>
</tbody>
</table>

3.4 Identification of Top Ten Therapeutic Classes

Top ten therapeutic drug classes in total utilization with greatest number of prescriptions were identified among our study sample. The therapeutic classes have been identified by the Multum Lexicon variable: TCnSn, a therapeutic sub-classification variable [82]. As explained in the documentation for MEPS prescribed medicine file, the Multum Lexicon variables are derived from the Multum Lexicon database at Cerner Multum, Inc, which is a leading global company providing information management in healthcare [83]. Drugs are organized into three levels: therapeutic level (TCn), pharmacological level (TCnSn), and specific drug category level (TCnSn_n) [82]. The variable TCnSn is a sub-classification variable of TCn, assigning one or more sub categories to a more general therapeutic class category and sub-category given to a drug. For example, the TCn level category includes general therapeutic classes such as anti-infectives, then it is subdivided into pharmacological classes such as cephlosporins, penicillins, quinolones. Cephlosporins can be further subdivided into specific drug categories such as first to fourth generation cephlosporins (Figure 3.2).
3.5 Outcomes of Interest

This study aimed to assess the medication use and expenditure among diabetes patients in the year 2006. Medication use was defined at two levels: number of prescription filled and therapeutic drug class used in the defined year. At the prescription level, medication utilization was defined by prescriptions filled over the course of the year. At the therapeutic drug class level, medication use was defined as one or more purchases of a medication in a therapeutic class of the top ten drug classes. For this purpose, the assessed outcomes include: (1) the yearly average number of prescriptions filled per person; and (2) the yearly average number of drug classes used per person.

Medication expenditures were assessed with respect to (1) total drug cost per patient, and (2) out-of-pocket (OOP) spending per user. Out-of-pocket spending refers to the amounts paid by individual patients other than any insurance sponsors. Premiums for insurance were not included.
in OOP calculations in this study. Total drug cost included all payments by individuals (out-of-pocket payments), private insurance, Medicaid, Medicare, and other types of insurance.

Taking into account the risk factors in the prevalence of the diabetes as well as the patterns of drug use, socio-economic variables were evaluated in medication use of top ten drug classes and medication expenditures at the personal level. As introduced before, 12 independent variables were included in the multivariate regression model to examine the effects of each included factor on the outcomes of (1) total drug cost, (2) out-of-pocket, and (3) number of therapeutic drug classes used on an the patient level (Table 3.1).

3.6 Statistical Analysis

The top ten drug classes in utilization among diabetes patients were identified by sorting the number of prescriptions for each therapeutic drug class. We conducted descriptive analysis in evaluating medication utilization and expenditure on a patient level. For the drug expenditure, we calculated the averages of total drug cost, out-of-pocket spending per person per year. The total annual drug spending was charted for the top ten drug classes in 2006. The drug utilization per person per year was calculated based on the number of prescriptions and number of drug classes used by each patient. The percentages of patients using the top ten drug class were also calculated for each therapeutic class.

Generalized linear modeling (GLM) was used to conduct the multivariate regression. We had three dependent variables in terms of the drug spending (total spending and OOP) and top ten drug classes utilization. Due to the positively skewed distributions of the outcomes, we used a generalized Gamma distribution with a log link to fit the model, in order to obtain more unbiased estimates of the impact of the set of predictors. In the statistical model selection, the model
with a log link was superior to those with other functions of link such as reciprocal because it came out with the smallest deviance value, based upon the same degrees of freedom. In 2001, Manning and Mullahy suggested that the ordinary least square (OLS) estimates can be notably less precise and biased than some of the GLM alternatives, when the distribution is not bell-shaped or a skewed bell-shaped \cite{84}. Furthermore, the interpretation of the results is relatively straightforward using GLM, compared to OLS with log transformation.

To illustrate, the formula used in this study is shown below. The response variable $Y$ is linearly associated with values of the explanatory variables by:

$$Y = b_0 + b_1 Age + b_2 Gender + b_3 Race + b_4 Region + b_5 MSA + b_6 Marital + b_7 Familysize + b_8 Education + b_9 Povertylevel + b_{10} Insurance + b_{11} Healthperception + b_{12-21} (Comorbidities) + e$$

where the $e$ stands for the error term, while the relationship in the generalized linear model with log link is:

$$\log(mu_Y) = b_0 + b_1 Age + b_2 Gender + b_3 Race + b_4 Region + b_5 MSA + b_6 Marital + b_7 Familysize + b_8 Education + b_9 Povertylevel + b_{10} Insurance + b_{11} Healthperception + b_{12-21} (Comorbidities)$$

where $mu_Y$ stands for the expected value of $Y$. The log link function links the expected values of $Y$ to the regressors and determines the model.

All the data were weighted to reflect the drug utilization and expenditure of the whole population in the United States. Stata 10 was used to conduct all the analyses, using significance level of 0.05.
Chapter 4

Results

4.1 Study population

A total of 2,189 patients were identified in this study, representing 17.5 million diabetes patients in the United States in 2006. The mean age of patients was 63 years of age, 56.01% of the patients were women, and 49.06% were White-NonHispanic (Table 4.1). The majority of the study population was elderly patients, given that only 14.62% of the patients were younger than 45 years old. In our study sample, there were 12 patients who were diagnosed with diabetes but did not have any purchase records of prescription medicines. However, in order to obtain an accurate number of diagnosed diabetes patients and medication use patterns, these 12 patients were included into our analyses.

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Unweighted Frequency (%)</th>
<th>Weighted Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤44</td>
<td>320 (14.62%)</td>
<td>2,370,273.09 (13.51%)</td>
</tr>
<tr>
<td>45-64</td>
<td>1,043 (47.65%)</td>
<td>8,424,204.89 (48.03%)</td>
</tr>
<tr>
<td>≥65</td>
<td>826 (37.73%)</td>
<td>6,745,717.32 (38.46%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>963 (43.99%)</td>
<td>8,651,271.02 (49.32%)</td>
</tr>
<tr>
<td>Female</td>
<td>1,226 (56.01%)</td>
<td>8,888,914.27 (50.68%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White-Hispanic</td>
<td>501 (22.89%)</td>
<td>2,255,218.19 (12.86%)</td>
</tr>
<tr>
<td>White-NonHispanic</td>
<td>1,074 (49.06%)</td>
<td>11,352,405.40 (64.72%)</td>
</tr>
<tr>
<td>Black</td>
<td>468 (21.38%)</td>
<td>2,672,013.36 (15.23%)</td>
</tr>
<tr>
<td>Asian</td>
<td>74 (3.38%)</td>
<td>566,821.59 (3.23%)</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>32 (1.46%)</td>
<td>324,642.65 (1.85%)</td>
</tr>
<tr>
<td>Multiple Races</td>
<td>27 (1.23%)</td>
<td>243,241.93 (1.39%)</td>
</tr>
<tr>
<td>Native Hawaiian or Pacific Islander</td>
<td>13 (0.59%)</td>
<td>125,852.23 (0.72%)</td>
</tr>
<tr>
<td>Patient Characteristics</td>
<td>Unweighted Frequency (%)</td>
<td>Weighted Frequency (%)</td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noreast</td>
<td>333 (15.21%)</td>
<td>3,210,862.52 (18.31%)</td>
</tr>
<tr>
<td>Midwest</td>
<td>412 (18.82%)</td>
<td>3,698,500.68 (21.09%)</td>
</tr>
<tr>
<td>South</td>
<td>897 (40.98%)</td>
<td>6,968,094.42 (39.73%)</td>
</tr>
<tr>
<td>West</td>
<td>547 (24.99%)</td>
<td>3,662,737.66 (20.88%)</td>
</tr>
<tr>
<td><strong>MSA status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-MSA</td>
<td>480 (21.93%)</td>
<td>3,737,994.14 (21.31%)</td>
</tr>
<tr>
<td>MSA</td>
<td>1,709 (78.07%)</td>
<td>13,802,201.10 (78.69%)</td>
</tr>
<tr>
<td><strong>Education year</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤11</td>
<td>798 (97.06%)</td>
<td>4,741,580.24 (27.32%)</td>
</tr>
<tr>
<td>≥12</td>
<td>1,355 (62.94%)</td>
<td>12,611,139.80 (72.68%)</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>1,232 (56.28%)</td>
<td>10,378,177.10 (59.17%)</td>
</tr>
<tr>
<td>Widowed</td>
<td>371 (16.75%)</td>
<td>2,768,054.92 (15.78%)</td>
</tr>
<tr>
<td>Divorced</td>
<td>336 (15.35%)</td>
<td>2,658,680.2 (15.16%)</td>
</tr>
<tr>
<td>Separated</td>
<td>60 (2.74%)</td>
<td>379,034.63 (2.16%)</td>
</tr>
<tr>
<td>Never married</td>
<td>190 (8.68%)</td>
<td>1,356,248.42 (7.73%)</td>
</tr>
<tr>
<td><strong>Family size</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>=1</td>
<td>491 (22.43%)</td>
<td>4,088,380.98 (23.31%)</td>
</tr>
<tr>
<td>&gt;1</td>
<td>1,698 (77.57%)</td>
<td>13,451,814.30 (76.69%)</td>
</tr>
<tr>
<td><strong>Poverty level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>451(20.60%)</td>
<td>2,315,372.80 (13.20%)</td>
</tr>
<tr>
<td>Near poor</td>
<td>196 (8.95%)</td>
<td>1,137,674.62 (6.49%)</td>
</tr>
<tr>
<td>Low income</td>
<td>405 (18.50%)</td>
<td>2,794,879.61 (15.93%)</td>
</tr>
<tr>
<td>Middle income</td>
<td>584 (26.68%)</td>
<td>5,203,709.76 (29.67%)</td>
</tr>
<tr>
<td>High income</td>
<td>553 (25.26%)</td>
<td>6,088,558.49 (34.71%)</td>
</tr>
<tr>
<td><strong>Health Insurance Coverage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare part D</td>
<td>594 (27.14%)</td>
<td>4,215,645.81 (24.03%)</td>
</tr>
<tr>
<td>Medicare nonpart D</td>
<td>408 (18.64%)</td>
<td>3,815,136.68 (21.75%)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>203 (9.27%)</td>
<td>1,087,827.44 (6.20%)</td>
</tr>
<tr>
<td>Private insurance coverage</td>
<td>696 (31.80%)</td>
<td>6,852,033.68 (39.06%)</td>
</tr>
<tr>
<td>Self-pay</td>
<td>288 (13.16%)</td>
<td>1,569,551.68 (8.98%)</td>
</tr>
<tr>
<td><strong>General Health Perception</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>99 (4.52%)</td>
<td>921,799.06 (5.26%)</td>
</tr>
<tr>
<td>Very good</td>
<td>373 (17.04%)</td>
<td>3,443,171.32 (19.63%)</td>
</tr>
<tr>
<td>Good</td>
<td>778 (35.54%)</td>
<td>6,324,391.18 (36.06%)</td>
</tr>
<tr>
<td>Fair</td>
<td>645 (29.47%)</td>
<td>4,806,581.64 (27.40%)</td>
</tr>
<tr>
<td>Poor</td>
<td>293 (13.39%)</td>
<td>2,037,142.09 (11.61%)</td>
</tr>
</tbody>
</table>
4.2 Top ten therapeutic classes

The top ten drug classes in utilization among diabetes patients were: antihyperlipidemic agents, angiotensin converting enzyme inhibitors (ACE Inhibitors), beta-Adrenergic blocking agents, calcium channel blocking agents, diuretics, antihypertensive combinations, analgesics, antidiabetic agents, antidepressants, and proton pump inhibitors.

4.3 Annual drug utilization

On average, a diabetes patient had 45.34 (median=36) prescriptions (Table 4.2), and 3.43 (median=3) classes of drugs within the top ten drug classes (Table 4.3). However, the distribution of prescription counts was skewed. The maximum number of prescriptions was as high as 253 per person per year, using all of the top then drug classes throughout the year (Figure 4.1 and Figure 4.2).

| Table 4.2 – Description of number of prescription per person in 2006 |
|--------------------------|-----------------|-----|-----|-----|-----|
| Mean | Min | 25% | 50% | 75% | Max |
| 45.34 | 1 | 18 | 36 | 61 | 253 |

| Table 4.3 – Description of number of drug classes used per person in 2006 |
|--------------------------|-----------------|-----|-----|-----|-----|
| Mean | Min | 25% | 50% | 75% | Max |
| 3.43 | 0 | 2 | 3 | 5 | 10 |
Figure 4.1 Distribution of number of prescription used per person per year

Figure 4.2 Distribution of number of drug classes used per person per year
Regarding the top ten drug classes, about 83.9% of the patients used antidiabetic agents in 2006, and 52.6% used antihyperlipidemic agents, followed by analgesics, ACE inhibitors and Beta-blockers, with percentage of 39.6%, 37.4%, and 28.3%, respectively. Details are shown in Figure 4.3.

![Figure 4.3 - Percentage of Patients Using the Top ten Drug Class in 2006 (Weighted)](image)

### 4.4 Annual drug expenditure

On average, a diabetes patient incurred a total of $3,161 (sd = 4235.1) for prescribed medicines and spends $1,061 (sd = 1323.43) for out-of-pocket costs annually in 2006. The top ten categories accounted for 61.4% of the total drug spending for diabetics. Figure 4.4 shows
weighted annual total spending of the top ten drug classes. Antidiabetic and Antihyperlipidemic agents were the top two drug classes that cost the most, accounting for 24.1% and 13.5% of the total annual drug expenditure, respectively.

One outlier in the sample had 253 prescriptions used that cost a total of $117302.5. Out-of-pocket spending for this patient was $20076.29. This total was verified and the cause appeared to be due to significant analgesic use. This outlier was kept in the sample because the patient was alive on the last day of the study period and met the requirements for inclusion.

![Figure 4.4 – Annual total expenditure of top ten drug classes in 2006 (Weighted)
(Note: the numbers on the top of the bars are the percentage of each drug class spending out of total drug expenditure)](image-url)
4.5 Multivariate regression analysis outcomes

Tables A-1 to A-3 (Appendix) show the results from multivariate regressions. Race, marital status, and health insurance coverage were significant predictors in total drug spending among diabetes patients in year 2006. Compared to White-NonHispanic people, Asians spent 42% less, American Indians/Alaska Natives 39% less, and Native Hawaiians/Pacific Islanders 65% less total drug spending, all with p <0.05. Compared to married people, separated individuals spent 45.9% less on drugs, p=0.009. Differences in drug spending are also revealed with respect to health insurance coverage status. Compared to patients with Medicare Part D, patients with Medicare NonPart D, Private insurance coverage and those without drug coverage had lower total drug spending, accounting for 17%, 48%, and 74% less spending, respectively, each with p<0.01.

Out-of-pocket spending was associated with age, gender, race, and health insurance coverage among diabetes patients (Table A-2). Compared to elderly patients over 65 years, patients younger than 44 years old had 30.9% lower OOP payment (p=0.017), but patients between 45 years old and 64 years did not have significant difference in OOP payment from older adults. Males spent 14% less OOP than female patients, with p=0.016. Asians, American Indians/Alaska Natives, and Native Hawaiians/Pacific Islanders had lower OOP payment than White NonHispanic people. Asians were 61% lower, American Indians/Alaska Natives were 51% lower, people of multiple race background were 49% lower, and Native Hawaiians/Pacific Islanders were 97% lower than the comparison group, respectively, all with p<0.05. For health insurance coverage, self-payers spent 40.89% more OOP than Medicare Part D beneficiaries (p=0.003), while Medicaid beneficiaries had 26.5% lower OOP payments compared with Medicare Part D enrollees.
Regarding the number of top ten drug classes used per person per year, predictors of age, gender, race, and health insurance coverage showed significant variances among diabetes patients (Table A-3). Compared with older adults over 65 years, patients younger than 44 years old used 10.6% fewer drug classes, while patients between 45 to 64 years old used 9.09% more drug classes, both with p<0.05. Male patients used 5.3% fewer drug classes than females, p=0.016. This is supported by findings that females tend to use more medicine than males [74][75]. Compared to White NonHispanic patients, White Hispanics used 9.2% fewer drug classes, p = 0.008. Regarding health insurance coverage, not surprisingly, patients with private insurance and those without drug coverage used fewer drug classes than patients with Medicare Part D, 20.7% and 33.2% fewer, respectively, p<0.001, holding everything else constant. The number of drug classes used by patients was associated with the total drug costs and out-of-pocket payments. Patients without drug insurance tend to use fewer drug classes, spent less on total drug spending but had to pay more by themselves than Medicare Part D beneficiaries. Private insurance beneficiaries spent less on total drug spending, took fewer medications than Medicare Part D beneficiaries, but their out-of-pocket payments did not have significant difference.
Chapter 5

Discussion

5.1 Main findings

Diabetes is a progressive and complex metabolic disorder with a set of complications that make it necessary to undertake polypharmacy for patients. In this nationally representative cross-sectional study, we identified the top ten drug classes used most by diabetes patients. These drug classes include Antihyperlipidemic agents, Angiotensin converting enzyme inhibitors (ACE Inhibitors), Beta-Adrenergic blocking agents, Calcium channel blocking agents, Diuretics, Antihypertensive combinations, Analgesics, Antidiabetic agents, Antidepressants, and Proton pump inhibitors. This finding is in line with the strategies of prevention and treatment of diabetes and diabetes-related complications such as vascular and neuropathic diseases.

Among the top ten therapeutic drug classes, antidiabetic agents were used by 83.9% of diabetes patients, and accounted for 24.1% of the total spending on drugs among diabetics in 2006. Antidiabetic medications, also called antihyperglycemic agents, treat diabetes mellitus by lowering blood glucose levels. Generally, patients are required to undertake monotherapy or combination of antidiabetic agents in order to achieve the goal of blood glucose lowering to a clinically safe range, as recommended by the clinical guidelines [2]. A large body of evidence have demonstrated that combination therapy appear to be more effective than monotherapy in glucose control [85][86]. Traditional antidiabetic agents include sulphonylureas, biguanides, thiazolidinediones, meglitinide analogues, and alpha-glucosidase inhibitors, that control hyperglycaemia through one or more sites of action [76]. Newer drugs mimic or potentiate the activities of incretin hormones, including GLP-1 (glucagon-like peptide-1) mimetics and DPP-4
(dipeptidyl peptidase-4) inhibitors\textsuperscript{[18]}. Despite the benefits of combination therapy of glucose control, concurrent use of multiple pharmaceuticals of this drug class may raise the risk of adverse effects of poor adherence and drug-drug interactions, especially for drugs that are metabolized by the cytochrome P450 (CYP450) system. For instance, it has been confirmed that thiazolidinediones (TZD), meglitinide analogues, and sulphonylureas are subject to potentially interfere with drugs metabolised with the CYP450 system\textsuperscript{[87][88]}, and may lead to worse outcomes of cardiovascular complications\textsuperscript{[89]}.

Antihyperlipidemic agents are another major group of medications for diabetes patients, ranking second amongst the top ten therapeutic drug classes in utilization and expenditure for patients in 2006. Diabetes patients tend to have a characteristic dyslipidemia, making them 2 to 4 times more likely to develop cardiovascular disease than those without diabetes\textsuperscript{[90]}. Even when effective glycemic control is achieved with antidiabetic treatment, dyslipidemia persists in many patients with diabetes, especially type 2 diabetes\textsuperscript{[86]}. Antihyperlipidemic agents are used to control lipid levels. Major antihyperlipidemic medications include HMG-CoA reductase inhibitors (statins), niacin, fibrates, and bile acid sequestrants\textsuperscript{[91]}. Many statins, except pravastatin, are primarily metabolized by the cytochrome P450 system\textsuperscript{[87][88]}, and may thus induce drug-drug interactions based on this mechanism.

There are concerns about multiple medication regimens for diabetes patients. On average, a diabetes patient used 3.43 drug classes out of the top ten drug classes in this study. Furthermore, significant variance exists in the number of drug classes used by each patient. About 25\% of the patients in this study used more than 5 drug classes, and 10\% used more than 6 drug classes in 2006. The number of concurrent medications may be even larger than these number of drug classes, because many patients take combination therapy of antidiabetic agents. Earlier studies
have shown that treatment with two or three drugs may not result in medication problems, but when the number of drugs exceeds four, patients are exposed to significant risks such as medication errors, medication noncompliance, and higher rates of hospitalization \[92] [93].

On one hand, it is apparent that an increase in the number of co-medications tends to decrease the adherence of patients to their treatment regimens, and this may result in a more severe adverse reaction, higher rates of hospitalization and related healthcare costs. On the other hand, drug-drug interactions are a concern when patients are taking multiple drugs. Studies have found a positive association between the number of concurrent medications used and the potential for clinically relevant or potentially serious drug-drug interactions \[94] [95]. As mentioned before, drugs that undergo metabolism by CYP 450 isoenzymes system, such as statins, TDZs are subject to induce drug-drug interactions if they are administered with some calcium channel blockers such as verapamil and diltiazem, which inhibit CYP 3A4 \[96]. For diabetes patients, the medications used to treat the complications may adversely affect the control of glucose. For example, thiazide diuretics may be useful to treat mild to moderate hypertension but may induce glucose intolerance by diminishing insulin sensitivity \[97]. Other drugs for hypertension, such as Beta-blockers, may inhibit beta-adrenergic stimulation of insulin secretion and mask some symptoms of hypoglycemia \[76]. Especially, we found that 38% of our study population is of 65 years age or older. Older adults are more fragile to these risks of multi-medication regimens. Physiological changes associated with aging, such as decreased renal and hepatic function, decreased total body water and decreased lean body mass, requires special consideration in terms of the dosage and combination of the medications for elderly patients \[20] [76].

The patterns of medication use among diabetes patients are potentially influenced by a web of factors. Indeed, some of these factors are health status related, but demographic and socio-
economic statuses are also important. In this study, we explored the predictive effects of race/ethnicity and health insurance overage on the medication use patterns with consideration of other covariates mediating these effects. After adjusting for other socio-demographic and geographic factors, including age, gender, education, marital status, family size, region, MSA, and poverty level, two predictors have demonstrated significant differences with regard to medication use among diabetes patients. Generally, minorities have profoundly lower drug spending and use a lower number of drug classes than NonWhite-Hispanics. One possible explanation for this variation is cultural difference. Ethnic culture affects our beliefs about health, illness, and medications, and it also influences how we comply with prescribed medications. Studies indicated that Asian patients are more cautious about American medications and often initiate downward dosage adjustments to avoid potential adverse drug reactions. Secondly, certain race or ethnic groups seem to be closely linked to disadvantaged socioeconomic position in terms of income, education and wealth. The lower medication use and spending may somewhat reflect reduced access to health care, limited social support, or local discriminatory practices. As for health insurance status, apart from the health conditions and aging factors, moral hazard could be an explanation for the disparities. Patients with generous pharmaceutical benefits who have more access to medications may have incentive to use more drugs. In this study, we used a hierarchy classification of the insurance coverage. Medicare enrollees, even if they have supplemental coverage from private insurance, are categorized into Medicare group. Hence, patients with Medicare Part D have comparatively more generous benefits for prescribed medications. These patients seem to have more total drug spending while less out-of-pocket payments than patients with other coverage, especially those
with private insurance only and without drug insurance. Meanwhile, Medicare Part D enrollees are found to use more drug classes than private insurance patients and self-payers.

Compared to previous studies, the results of this study add greater depth to the picture of diabetes therapy complexity. We identified ten therapeutic drug classes that are mostly used among diabetes patients. Apart from three major components of diabetes therapies such as antidiabetic antihyperlipidemic, and antihypertensive agents, other agents, such as analgesics, PPIs, antidepressants, and diuretics are identified into the top ten drug classes that are used most often among diabetics, so that we obtained more detailed and comprehensive information about the medication use among diabetes patients. Instead of using the visit as the unit of analysis, we used the person as the unit of analysis. We calculated not only the medication use with regards to number of prescriptions and therapeutic drug classes in a year, but also the economic burden for individuals in terms of annual total drug spending and out-of-pocket payment. We also provided evidence that the prescribed medication uses among diabetes patients vary across different races/ethnicities and different insurance coverage, after adjusting for other socio-economic factors. This heterogeneity in medication use and spending may reflect differences in the health care environments and indicates the importance of implementing individualized treatment strategies for diabetes patients.

5.2 Limitations

This is a cross-sectional study on a representative sample. We described the relationship of the socio-economic variables with our study outcomes. However, we were not able to establish causal relationships or obtain reliable perspectives on the outcomes from this study. Secondly, we used a nationally representative survey dataset to gather demographic information and related
prescribed medicine records. Some questions cannot be solved, given the limited information available in the database. For example, we have one outlier in our sample with an extremely large amount of drug spending and usage, but we have no idea about the reason for these large values. Furthermore, the sample sizes of certain minorities were too small to be stable.

In addition, prescribed medication use is a crude measure in this study. We can only obtain the total number of drug classes that are used in the year span. However, we cannot distinguish between switches and addition of the drugs. For instance, if a diabetes patient used drug class A and switched to class B later, we count the number of drug classes used as 2. Meanwhile, when a diabetes patient used drug class A and added class B into his/her regimen later, we still count 2 drug classes used by this patient. Furthermore, we were unable to ascertain each patient’s health insurance status change. We used the insurance coverage status on the last day of the year for each patient, which is imprecise. For some people, insurance coverage changes over the year due to some reasons such as unemployment or retirement. It is complex to grab and take into account all of these changes.

Last but not least, we studied on the prescribed medication in this project with no regards to other medicines such as OTC and herbal drugs. MEPS collects drug data prompted to look at prescribed medicines only. However, this information is important as well. Some analgesics are OTC drugs, and diabetes patients may not report this information in the survey. Excluding these medications may provide conservative estimates as well as underestimates of cost and complexity of diabetes treatment. More importantly, the effects of prescribed medication therapies may be affected because of drug-drug interactions or changes in the metabolism of the prescribed drugs \[20\] [105], which is a potential threat for drug safety.
5.3 Implications and future directions

The findings in this study are enlightening for patient care purposes. The number of drug classes that are used by most of the diabetes patients are reaching or already exceeding the threshold for increased risks of falls, hypoglycemia, and other adverse drug events \[10\]. Hence, despite the fact that intensive treatment goals and multiple medications may bring benefits for diabetes patients, polypharmacy is likely to raise the concern of the risks of ADRs, nonadherence and drug-drug interactions for clinicians and patients with diabetes. More efforts are needed on investigating how to optimize the clinical diabetes regimens in purpose to simultaneously increase the benefits and minimize the undesired consequences of polypharmacy.

Our results are also potentially useful for health policy planning. Heterogeneous medication use and spending makes it prudent to focus health care quality improvement efforts on patients with poorer drug coverage or those who are at lower socio-economic positions. For this purpose, more research is needed on a larger span of study periods, by which we may obtain the trends of the variance in medication use and spending across different socio-economic positions over time.

5.4 Conclusions

In summary, diabetes patients used multiple therapeutic drug classes in 2006. Antidiabetic and antihyperlipidemic agents were two classes that were mostly used by diabetes patients and had higher costs than other categories of medications. We also found significant impacts of racial/ethnic and insurance coverage status differences on medication utilization and expenditure, after adjusting for other pertinent covariates among individuals with diabetes mellitus. Knowledge about the complexity of diabetes therapy and the characterization of the socio-economic variations will enable quality improvement of diabetes care.


[73] Tseng CW, Tierney EF, Gerzoff RB, Dudley RA, Waitzfelder B, etal. Rce/ethnicity and economic differences in cost-related medication underuse among insured adults with diabetes:


the translating research into action for diabetes study. *Diabetes Care.* 2008 February; 31(2): 261-266.


Appendix

Detailed Multivariate Regression Results
Table A-1  Weighted multivariate regression in total drug spending per person in 2006

<p>| Independent Variables | Coef. (95% CI) | P&gt;|z| |
|-----------------------|---------------|-----|
| <strong>Age</strong>               |               |     |
| 65-85                 | Referent      |     |
| 18-44                 | -0.21 (-0.44, 0.02) | 0.074 |
| 45-64                 | 0.17 (-0.015, 0.36) | 0.071 |
| <strong>Gender</strong>            |               |     |
| Female                | Referent      |     |
| Male                  | -0.058 (-0.16, 0.043) | 0.258 |
| <strong>Race</strong>              |               |     |
| White nonhispanic     | Referent      |     |
| White hispanic        | -0.14 (-0.31, 0.021) | 0.086 |
| Black                 | -0.13 (-0.28, 0.013) | 0.073 |
| Asian                 | -0.42 (-0.69, -0.14) | 0.003* |
| American Indian or Alaska Native | -0.39 (-0.74, -0.032) | 0.033* |
| Native Hawaiian or Pacific Islander | -0.65 (-1.23, -0.069) | 0.028* |
| Multiple race         | 0.16 (-0.27, 0.59) | 0.47 |
| <strong>Region</strong>            |               |     |
| South                 | Referent      |     |
| Northeast             | 0.11 (-0.03, 0.25) | 0.125 |
| West                  | -0.053 (-0.20, 0.09) | 0.47 |
| Midwest               | -0.11 (-0.24, 0.021) | 0.100 |
| <strong>MSA status</strong>        |               |     |
| MSA                   | Referent      |     |
| NonMSA                | 0.13 (0.0004, 0.24) | 0.049* |
| <strong>Education Year</strong>    |               |     |
| ≤ 11                  | Referent      |     |
| ≥ 12                  | 0.054 (-0.065, 0.173) | 0.376 |
| <strong>Marital status</strong>    |               |     |
| Married               | Referent      |     |</p>
<table>
<thead>
<tr>
<th>Marital status</th>
<th>Widowed</th>
<th>-0.073 (-0.25, 0.11)</th>
<th>0.423</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Divorced</td>
<td>-0.063 (-0.23, 0.10)</td>
<td>0.447</td>
</tr>
<tr>
<td></td>
<td>Separated</td>
<td>-0.46 (-0.81, -0.11)</td>
<td>0.009*</td>
</tr>
<tr>
<td></td>
<td>Never married</td>
<td>0.065 (-0.15, 0.28)</td>
<td>0.549</td>
</tr>
<tr>
<td>Family size</td>
<td>=1</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 1</td>
<td>0.10 (-0.051, 0.25)</td>
<td>0.193</td>
</tr>
<tr>
<td>Poverty level</td>
<td>Middle income</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poor</td>
<td>-0.034 (-0.21, 0.14)</td>
<td>0.702</td>
</tr>
<tr>
<td></td>
<td>Near poor</td>
<td>-0.072 (-0.29, 0.14)</td>
<td>0.514</td>
</tr>
<tr>
<td></td>
<td>Low income</td>
<td>-0.09a (-0.25, 0.066)</td>
<td>0.255</td>
</tr>
<tr>
<td></td>
<td>High income</td>
<td>0.050 (-0.075, 0.17)</td>
<td>0.435</td>
</tr>
<tr>
<td>Health Insurance Coverage</td>
<td>Medicare part D</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medicare nonpart D</td>
<td>-0.17 (-0.31, -0.02)</td>
<td>0.024*</td>
</tr>
<tr>
<td></td>
<td>Medicaid</td>
<td>0.24 (-0.024, 0.51)</td>
<td>0.075</td>
</tr>
<tr>
<td></td>
<td>Private insurance coverage</td>
<td>-0.48 (-0.68, -0.28)</td>
<td>0.000*</td>
</tr>
<tr>
<td></td>
<td>Self-pay</td>
<td>-0.74 (-0.97, -0.50)</td>
<td>0.000*</td>
</tr>
<tr>
<td>General Health Perception</td>
<td>Fair</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Excellent</td>
<td>-0.40 (-0.64, -0.17)</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Very good</td>
<td>-0.19 (-0.33, -0.038)</td>
<td>0.014*</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>-0.20 (-0.33, -0.080)</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>Poor</td>
<td>0.17 (-0.00063, 0.34)</td>
<td>0.051</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Asthma</td>
<td>0.35 (0.20, 0.50)</td>
<td>0.000*</td>
</tr>
<tr>
<td></td>
<td>High cholesterol</td>
<td>0.29 (0.19, 0.39)</td>
<td>0.000*</td>
</tr>
<tr>
<td></td>
<td>Angina</td>
<td>0.012 (-0.20, 0.22)</td>
<td>0.911</td>
</tr>
<tr>
<td></td>
<td>Coronary heart disease</td>
<td>0.25 (0.077, 0.43)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Effect Size</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Heart attack</td>
<td>-0.11 (-0.30, 0.071)</td>
<td>0.229</td>
<td></td>
</tr>
<tr>
<td>Other heart disease</td>
<td>0.16 (0.017, 0.30)</td>
<td>0.028*</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>0.024 (-0.16, 0.21)</td>
<td>0.797</td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>0.12 (0.016, 0.23)</td>
<td>0.025*</td>
<td></td>
</tr>
<tr>
<td>Emphysema</td>
<td>0.17 (-0.087, 0.42)</td>
<td>0.198</td>
<td></td>
</tr>
<tr>
<td>High blood pressure</td>
<td>0.34 (0.23, 0.45)</td>
<td>0.000*</td>
<td></td>
</tr>
</tbody>
</table>

This model included race/ethnicity, health insurance coverage status as main predictors. The remaining variables were included as covariates (age, gender, education, region, MSA status, marital status, family size, poverty level, general health perception, and comorbidities). “Referent” refers to the comparison group. “*” Statistically significant at p<0.05.
<p>| Independent Variables | Coef. (95% CI) | ( P&gt;|z| ) |
|-----------------------|----------------|----------|
| <strong>Age</strong>               |                |          |
| 65-85 Referent        |                |          |
| 18-44 -0.31 (-0.56, 0.058) | 0.017*       |
| 45-64 0.028 (-0.17, 0.23) | 0.788        |
| <strong>Gender</strong>            |                |          |
| Female Referent       |                |          |
| Male -0.14 (-0.25, -0.026) | 0.016*       |
| <strong>Race</strong>              |                |          |
| White nonhispanic Referent |            |          |
| White hispanic -0.094 (-0.28, 0.09) | 0.326       |
| Black -0.078 (-0.24, 0.086) | 0.353       |
| Asian -0.61 (-0.92, -0.29) | 0.000*       |
| American Indian or Alaska Native -0.51 (-0.91, -0.11) | .0013* |
| Native Hawaiian or Pacific Islander -0.97 (-1.62, -0.32) | 0.004* |
| Multiple race -0.49 (-0.95, -0.026) | 0.038* |
| <strong>Region</strong>            |                |          |
| South Referent        |                |          |
| Northeast -0.0016 (-0.16, 0.15) | 0.984       |
| West -0.0017 (-0.16, 0.16) | 0.984       |
| Midwest -0.15 (-0.29, -0.0058) | 0.041*      |
| <strong>MSA status</strong>        |                |          |
| MSA Referent          |                |          |
| NonMSA 0.11 (-0.026, 0.25) | 0.111       |
| <strong>Education Year</strong>    |                |          |
| ( \leq 11 ) Referent |            |          |
| ( \geq 12 ) 0.15 (0.014, 0.28) | 0.030*      |
| <strong>Marital status</strong>    |                |          |
| Married Referent      |                |          |</p>
<table>
<thead>
<tr>
<th>Status</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Widowed</td>
<td>0.527 (-0.14, 0.26)</td>
<td>0.527</td>
</tr>
<tr>
<td>Divorced</td>
<td>-0.23 (-0.42, -0.047)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Separated</td>
<td>-0.35 (-0.74, 0.037)</td>
<td>0.076</td>
</tr>
<tr>
<td>Never married</td>
<td>-0.056 (-0.29, 0.18)</td>
<td>0.645</td>
</tr>
</tbody>
</table>

### Family size

<table>
<thead>
<tr>
<th>Family size</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>=1</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>&gt; 1</td>
<td>0.010 (-0.16, 0.18)</td>
<td>0.910</td>
</tr>
</tbody>
</table>

### Poverty level

<table>
<thead>
<tr>
<th>Poverty level</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middle income</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>poor</td>
<td>-0.14 (-0.34, 0.054)</td>
<td>0.156</td>
</tr>
<tr>
<td>Near poor</td>
<td>0.031 (-0.21, 0.27)</td>
<td>0.802</td>
</tr>
<tr>
<td>Low income</td>
<td>0.013 (-0.16, 0.19)</td>
<td>0.885</td>
</tr>
<tr>
<td>High income</td>
<td>-0.029 (-0.17, 0.11)</td>
<td>0.689</td>
</tr>
</tbody>
</table>

### Health Insurance Coverage

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare part D</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>Medicare nonpart D</td>
<td>0.11 (-0.050, 0.27)</td>
<td>0.177</td>
</tr>
<tr>
<td>Medicaid</td>
<td>-0.27 (-0.60, 0.038)</td>
<td>0.087</td>
</tr>
<tr>
<td>Private insurance coverage</td>
<td>-0.021 (-0.24, 0.20)</td>
<td>0.846</td>
</tr>
<tr>
<td>Self-pay</td>
<td>0.41 (0.14, 0.67)</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

### General Health Perception

<table>
<thead>
<tr>
<th>Perception</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>-0.34 (-0.60, -0.071)</td>
<td>0.013*</td>
</tr>
<tr>
<td>Very good</td>
<td>-0.13 (-0.30, 0.039)</td>
<td>0.134</td>
</tr>
<tr>
<td>Good</td>
<td>-0.065 (-0.21, 0.08)</td>
<td>0.362</td>
</tr>
<tr>
<td>Poor</td>
<td>0.29 (0.10, 0.49)</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

### Comorbidities

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>0.32 (0.15, 0.49)</td>
<td>0.000*</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>0.24 (0.13, 0.36)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Angina</td>
<td>0.14 (-0.096, 0.37)</td>
<td>0.250</td>
</tr>
<tr>
<td>Condition</td>
<td>Odds Ratio (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>0.14 (-0.057, 0.34)</td>
<td>0.161</td>
</tr>
<tr>
<td>Heart attack</td>
<td>0.029 (-0.18, 0.24)</td>
<td>0.784</td>
</tr>
<tr>
<td>Other heart disease</td>
<td>0.16 (0.0041, 0.32)</td>
<td>0.044*</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.013 (-0.17, 0.22)</td>
<td>0.901</td>
</tr>
<tr>
<td>Arthritis</td>
<td>0.043 (-0.081, 0.17)</td>
<td>0.497</td>
</tr>
<tr>
<td>Emphysema</td>
<td>0.12 (-0.17, 0.40)</td>
<td>0.419</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>0.30 (0.18, 0.43)</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

This model included race/ethnicity, health insurance coverage status as main predictors. The remaining variables were included as covariates (age, gender, education, region, MSA status, marital status, family size, poverty level, general health perception, and comorbidities).

“Referent” refers to the comparison group.

“*” Statistically significant at p<0.05.
<p>| Independent Variables | Coef. (95% CI)         | P&gt;|z| |
|-----------------------|------------------------|---|
| Age                   |                        |   |
| 65-85                 | Referent               |   |
| 18-44                 | -0.11 (-0.20, 0.0092)  | 0.032* |
| 45-64                 | 0.091 (0.012, 0.17)    | 0.024* |
| Gender                |                        |   |
| Female                | Referent               |   |
| Male                  | -0.053 (-0.096, -0.0098) | 0.016* |
| Race                  |                        |   |
| White nonhispanic     | Referent               |   |
| White hispanic        | -0.092 (-0.16, -0.024) | 0.008* |
| Black                 | -0.030 (-0.091, 0.031) | 0.336 |
| Asian                 | -0.09 (-0.21, 0.028)   | 0.133 |
| American Indian or Alaska Native | -0.15 (-0.30, -0.0015) | 0.048* |
| Native Hawaiian or Pacific Islander | -0.24 (-0.48, -0.0046) | 0.05* |
| Multiple race         | -0.085 (-0.26, 0.089)  | 0.338 |
| Region                |                        |   |
| South                 | Referent               |   |
| Northeast             | -0.0164 (-0.074, 0.041) | 0.574 |
| West                  | 0.020 (-0.038, 0.078)  | 0.508 |
| Midwest               | 0.011 (-0.044, 0.066)  | 0.692 |
| MSA status            |                        |   |
| MSA                   | Referent               |   |
| NonMSA                | 0.020 (-0.031, 0.71)   | 0.442 |
| Education Year        |                        |   |
| ≤ 11                  | Referent               |   |
| ≥ 12                  | 0.032 (-0.018, 0.082)  | 0.204 |
| Marital status        |                        |   |</p>
<table>
<thead>
<tr>
<th>Marital Status</th>
<th>Referent</th>
<th>Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Married</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>-0.12 (-0.19, -0.040)</td>
<td>0.003*</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>-0.087 (-0.15, -0.019)</td>
<td>0.012*</td>
<td></td>
</tr>
<tr>
<td>Separated</td>
<td>-0.069 (-0.22, 0.079)</td>
<td>0.360</td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>0.020 (-0.068, 0.11)</td>
<td>0.659</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Family size</th>
<th>Referent</th>
<th>Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>=1</td>
<td></td>
<td>0.093 (0.029, 0.16)</td>
<td>0.005*</td>
</tr>
<tr>
<td>&gt; 1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Poverty level</th>
<th>Referent</th>
<th>Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middle income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>0.045 (-0.028, 0.12)</td>
<td>0.224</td>
<td></td>
</tr>
<tr>
<td>Near poor</td>
<td>0.061 (-0.030, 0.15)</td>
<td>0.187</td>
<td></td>
</tr>
<tr>
<td>Low income</td>
<td>0.014 (-0.051, 0.079)</td>
<td>0.668</td>
<td></td>
</tr>
<tr>
<td>High income</td>
<td>0.011 (-0.041, 0.064)</td>
<td>0.667</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Health Insurance Coverage</th>
<th>Referent</th>
<th>Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare part D</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare nonpart D</td>
<td>-0.011 (-0.071, 0.050)</td>
<td>0.724</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>-0.039 (-0.15, 0.072)</td>
<td>0.488</td>
<td></td>
</tr>
<tr>
<td>Private insurance coverage</td>
<td>-0.21 (-0.29, -0.12)</td>
<td>0.000*</td>
<td></td>
</tr>
<tr>
<td>Self-pay</td>
<td>-0.33 (-0.43, -0.23)</td>
<td>0.000*</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>General Health Perception</th>
<th>Referent</th>
<th>Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>-0.092 (-0.19, 0.0064)</td>
<td>0.067</td>
<td></td>
</tr>
<tr>
<td>Very good</td>
<td>-0.08 (-0.14, -0.020)</td>
<td>0.009*</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>-0.037 (-0.089, 0.015)</td>
<td>0.164</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>0.015 (-0.057, 0.087)</td>
<td>0.690</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Referent</th>
<th>Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>0.10 (0.039, 0.16)</td>
<td>0.002*</td>
<td></td>
</tr>
<tr>
<td>High cholesterol</td>
<td>0.32 (0.28, 0.36)</td>
<td>0.000*</td>
<td></td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Odds Ratio (CI)</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>0.11 (0.027, 0.20)</td>
<td>0.010*</td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>0.22 (0.14, 0.30)</td>
<td>0.000*</td>
<td></td>
</tr>
<tr>
<td>Heart attack</td>
<td>0.027 (-0.05, 0.11)</td>
<td>0.505</td>
<td></td>
</tr>
<tr>
<td>Other heart disease</td>
<td>0.14 (0.085, 0.20)</td>
<td>0.000*</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>-0.0091 (-0.086, 0.068)</td>
<td>0.817</td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>0.11 (0.064, 0.15)</td>
<td>0.000*</td>
<td></td>
</tr>
<tr>
<td>Emphysema</td>
<td>-0.047 (-0.15, 0.059)</td>
<td>0.384</td>
<td></td>
</tr>
<tr>
<td>High blood pressure</td>
<td>0.46 (0.41, 0.51)</td>
<td>0.000*</td>
<td></td>
</tr>
</tbody>
</table>

This model included race/ethnicity, health insurance coverage status as main predictors. The remaining variables were included as covariates (age, gender, education, region, MSA status, marital status, family size, poverty level, general health perception, and comorbidities). “Referent” refers to the comparison group. “*” Statistically significant at p<0.05.
Vita

Jing Tao was born in Shanghai, China on April 29th, 1981. She is a Chinese resident currently living in Richmond, Virginia. She obtained her Bachelor of Science Degree in Pharmacy in 2003 from Fudan University in Shanghai, China. From Aug 2003 till Jun 2008, she worked as a pharmacist in Shanghai Ruijin Hospital, which is one of the top hospitals in China. Her major duties included statistical analyses and reports for Shanghai Antimicrobial Drugs Use Monitoring Network, ADR case collection and reports, and individualized therapy design of immunosuppressants for patients in Renal Transplantation Center in Ruijin Hospital. In August 2009, she started her graduate study in Pharmacotherapy and Outcome Science at Virginia Commonwealth University, School of Pharmacy, where she worked as a teaching assistant. In the two-year program training, she accomplished three projects with her advisor. Currently she is pursuing a Master’s Degree with the thesis research related with database analyses on diabetes therapy.
EDUCATION

Aug, 2009 - Aug, 2011  MS in Pharmacotherapy and Outcome Sciences, Department of Pharmacotherapy and Outcome Science, Virginia Commonwealth University.

Sep, 1999 - Jul, 2003  B.Sc.Pharm, School of Pharmacy, Fudan University.

PROFESSIONAL EXPERIENCE

Aug, 2009 – Aug 2011  Teaching assistant at School of Pharmacy, Virginia Commonwealth University

Jun, 2005 – Jun, 2008  Clinical pharmacist at Clinical Pharmacology Laboratory, Shanghai Ruijin Hospital

Aug, 2003 – May, 2005  Rotation pharmacist in Shanghai Ruijin Hospital

CONFERENCE PRESENTATIONS


Tao J, Zhang JX.  Is good insurance bad for antibiotic prescribing: the case of acute respiratory tract infections in adult primary care. AcademyHealth's Annual Research Meeting (ARM), Boston, MA, USA, June 2010 (Poster presentation)
Tao J, Zhang JX. Antibiotic prescribing for acute respiratory tract infections in adult primary care: Is good insurance bad for antibiotic prescribing? International Society for Pharmacoecconomics and Outcome Research (ISPOR) 15th Annual International Meeting, Atlanta, GA, USA, May 2010 (Poster presentation, Finalist Award)

Zhang JX, Tao J. Market concentration and its cross-linkage with consumption of ACE Inhibitors and ARBs. International Society for Pharmacoecnomics and Outcome Research (ISPOR) 12th Annual European Congress, Paris, France, October 2009 (Podium presentation)