MEDICATION USE AND HEALTHCARE OUTCOMES IN DEVELOPMENTALLY DISABLED MEDICAID ADULTS WITH TYPE 2 DIABETES: A QUANTITATIVE RACE BASED ANALYSIS

by

Isha B. Patel

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Dissertation Committee:

**Associate Professor Rajesh Balkrishnan, Chair
Professor Richard P. Bagozzi
Associate Professor Cleopatra Caldwell
Associate Professor Steven R. Erickson
Clinical Assistant Professor Susan Woolford**

Dedication

Mam, Gadi dada, Kau ba, Pappa, Joiti Ba, Chatur Dada

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List of Abbreviations

ICD-9-CM   International Classification of Disease, 9th Division, Clinical Modifications

IRB   Institutional Review Board

OLS   Ordinary Least Squares regression

GLS   General Least Squares regression

HBM   The Health Belief Model

AHRQ   Agency for Healthcare Research and Quality

US   United States

Hba1c   Glysolated hemoglobin

OHA   Oral hypoglycemic therapy

HMO   Health Maintenance Organization

UKPDS   United Kingdom Prospective Diabetes Study

TZD   Thiazolidinediones

LDL   Low density lipid

BMI   Body Mass Index

NHANES   National Health and Nutrition Examination Survey

MPR   Medication Possession Ratio

NDC   National Drug Code

FDA   Food and Drug Administration

ER   Emergency room visit

ANOVA   Analysis of variance

ESS   Explained sum of squares

CI   Confidence Interval

LR   Likelihood Ratio

ID   Intellectual Disability

DD   Developmental Disability

SSDI   Social Security Disability Insurance

Abstract

Background:

The prevalence of diabetes mellitus is high among patients with developmental disabilities (Cerebral palsy, Autism, Down's syndrome and Cognitive disabilities). Developmentally disabled (DD) individuals experience delays in detection of chronic comorbidities such as diabetes, obesity, high blood pressure, arthritis, CVD and chronic pain. They also have poor disease management, poor healthcare utilization and low quality of care. Very few studies have looked at the diabetes related health outcomes in DD adults.

Objective:

This study examines the racial health disparities in medication adherence and medication persistence in DD adults with type 2 diabetes enrolled in Medicaid. This study also determines the association of race, medication adherence and its interaction with healthcare utilization and healthcare costs in Medicaid enrollees with DD and type 2 diabetes.

Methods:

This was a retrospective cohort study based on the Health belief model and Aday Anderson's model of healthcare utilization. The dataset used for this study was the MarketScan® Multi-State Medicaid Database. Adults aged 18-64 years with a prior diagnosis of a developmental disability (cerebral palsy/autism/down's/cognitive disabilities) and a new diagnosis of type 2 diabetes enrolled in Medicaid from January 1, 2004 and December 31, 2006, were included. Adults were included if they had a continuous enrollment for at least 12 months and were

excluded if they were dual eligible. Anti-diabetic medication adherence and diabetic medication persistence were measured using multivariate logistic regression and the Cox-proportional hazard regression respectively. Probabilities of anti-diabetic healthcare utilization (inpatient, outpatient and emergency department visits) in DD adults were measured using multivariate logistic regression models. Multivariate negative binomial regression was used to measure the rate of change of type 2 diabetes related healthcare utilization in DD patients. Multivariate linear regression with log-transformation was used to determine type 2 diabetes related healthcare costs in DD Medicaid enrollees.

Results:

The study population comprised of 1529 patients. After controlling for covariates, African Americans had significantly lower odds (25%) of adhering to anti diabeticmedications compared to Caucasians (OR = 0.75, 95% CI = 0.58-0.97, p<0.05). Also, after controlling for other covariates, the hazard was higher in African Americans compared to Caucasians (Hazard Ratio = 1.03, 95% CI = 0.91-1.18, p<0.629). After controlling for all the covariates, compared to DD Caucasians, DD African Americans were more likely to have type diabetes related inpatient (OR=1.71; 95% CI, 1.02-2.85, p<0.05) and emergency department visits (OR, 1.67; 95% CI, 1.03-2.73) respectively.

Conclusion:

Racial disparities exist in healthcare outcomes in DD Medicaid patients with type 2 diabetes. The needs of the developmentally disabled individuals are somewhat different than the needs of individuals without disabilities. Policy recommendations should focus on increasing the number of outpatient centers, culturally competent healthcare providers, and primary caregivers who can collaborate with other specialized healthcare professionals to enhance the overall quality of care

for the patients. There should be a focus on designing culturally appropriate health prevention and health promotion interventions for minorities.

Chapter 1 Introduction

1.1 Risk and Burden of type 2 diabetes in DD patients

Research shows that adults with developmental disabilities (DD) tend to have a more sedentary lifestyle, do not exercise often and tend to consume high calorie diet (McGuire 2007, Temple 2003, Ewing 2004). These practices can lead to obesity which is a risk factor for type 2 diabetes. Also, adults with DD have a higher life expectancy compared to a few decades back and this increase in the life expectancy is accompanied by a vulnerability to the development of a number of age related comorbid chronic conditions, including type 2 diabetes (Merrick 2004, Sohler 2009). Diabetes management requires screening for various chronic disease conditions (Shiremen 2010). A study conducted in DD population residing in Canada showed that even though 94% of the study population visited their general practitioner on a regular basis, only 52% and 44% had blood glucose and cholesterol measured respectively and only 29% and 19% were screened for diabetic retinopathy and microalbuminaria respectively. This shows that the screening rates for chronic diseases is quite low in the DD population as compared to the recommended national guidelines. Active engagement of the DD population in health education interventions and health screening interventions is not always possible which makes the management of chronic comorbid conditions challenging (Shiremen 2010).

1.2 Medication adherence and outcomes in adults with DD

Individuals with DD face many issues that make the care process for them complex. These issues include accelerated aging and consequences of long term medication and systems issues like access to experienced caregivers and continuity of care. About 76% of individuals with DD reside at home and around 25% of them are cared for by family members who are 60 years or older. Increase in life expectancy also increases the care giving responsibility of families. Families of individuals with DD strive on a continuous basis to support DD patients to attain and maintain a certain degree of independence (Heller 2010). In many ways, the medication management issues of aging individuals with DD may be similar to that of older adults. However, there are many issues unique to their condition and require additional medication management considerations. Taking this into account, Healthy people 2020 adds nine new objectives to those of Healthy people 2010 to deal with appropriate medication management among older adults with disabilities (Healthy People 2020).

In individuals with DD, many health complications may emerge with increasing age. In individuals with Down syndrome (DS) and Cerebral Palsy (CP), these complications may include obesity, accelerated aging and its interaction with accompanying secondary medical aspects, and long term medication use (Saxon 2010). Adult individuals with DD face increased risk of developing chronic conditions at a younger age, which may be rooted in not only biological factors but also in lack of appropriate healthcare, lifestyle and environmental issues. They may be more prone to health issues related to dental, respiratory, and cardiac health conditions, paricularly non-atherosclerotic heart disease. They may be also prone to issues such as problems with eating/swallowing, diabetes, hypercholesterolemia, hypertension, reduced mobility, bone demineralization, and osteoporosis.

Many factors contributing to non-adherence among adults with DD are similar to those in general aging population. However, for adults with DD desiring to achieve good health and maintain some degree of independence, factors contributing to medication non-adherence are also compounded by issues related to communication, vision, hearing, dexterity, and cognitive limitations (Ince 2009). Some of the common causes of non-adherence among adults with DD are fragmentation of care, comorbidity, polypharmacy, and considerations of medication side effects (Ince 2009).

In order to increase medication adherence among aging individuals with DD, it is important to develop medication and treatment goals centered towards the need of the individual, coupled with careful assessment and understanding of the role of the caregiver and family based care (Heller 2011). Family and professional caregivers play an important role in supporting individuals with DD. However, in many situations they may be ill prepared to meet the needs of the patient's needs (Marks 2010). This may have negative influence over the quality of care and may have other negative consequences. For example, caregivers may make erroneous assessment of client's need for medication and thus negatively influence prescribing. Therefore, it is very important to increase health literacy and awareness among caregivers about issues related to aging process and unique medication needs of individuals with DD (Lau 2010). Another problem faced by adults with DD, especially those whose care is publicly funded, is the occurrence of disruptive health events like inpatient visits and transition to another care unit. This leads to fragmentation of care and causes issues related to care continuity, whereby the individual has restricted access to caregivers and providers familiar with his/her specific needs. Issues related to communication and sharing of health information among health networks further complicate this problem. Due to the special and somewhat unique needs of individuals with DD, it is important

to consider that care transition is not restricted only to the systems and healthcare providers but also should take into account the transition of care between physicians, patients, and caregivers.

1.3 Importance of looking at comorbidities in Medicaid patients

Medicaid enrollees have twice the prevalence rate of diabetes compared to the general US population. Almost 15% of the Medicaid enrollees had diabetes in 2005. These enrollees account for a big portion of the Medicaid expenditure, associated with many micro and macro vascular complications related to diabetes (Cohen 2007, Smith 2006). Comorbidities in patients with diabetes are quite common and a majority of the patients have at least one comorbidity (Druss 2001). Comorbidity leads to increase in morbidity and mortality and can be a source of financial burden on the patients and the federal healthcare system. Comorbidity management also entails increase in the use of healthcare resources and failure to procure the same can increase the probability of poor patient outcomes.

Debilitating comorbidities in diabetic patients can make the process of medication adherence challenging since more the conditions that the patient has, the more are the medications and more complex is managing several conditions at the same time. About 40% patients with diabetes have as many as three comorbidities (Maddigan 2005). Patients with DD who already have impaired physical and mental functioning face an additional burden in performing self-care tasks for managing diabetes and other associated comorbidities such as depression, CVD and arthritis (Bayliss 2003, Kerr 2007, Noel 2005). Some studies show that increase in the number of comorbidities leads to an increase in medication adherence. Some of the reasons that can be attributed to the above finding are that that the patients procure information about diabetes leading to more awareness about its management or the patients are motivated to manage

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diabetes due to their perception about its severity and the perceived susceptibility towards the occurrence of diabetes related comorbidities. Researchers also posit that medication adherence and other clinical outcomes are characteristic of the primary disease condition and its related comorbidities (Kerr 2007, Piette 2004, Piette 2006).

Comorbid conditions also have an impact on clinical practice. While treating patients with multiple comorbidities, physicians face several challenges since the treatment becomes more complicated, several treatment guidelines need to be taken into consideration and at the same times adhering to different treatment guidelines might not be possible. Also, increase in the risk of adverse drug events due to chronic physical and behavioral comorbidities in patients can impact physician's perception of delivering care and patient's perception of accepting care and this is turn can affect healthcare utilization, clinical outcomes such as survival and economic outcomes such as cost of care (Ford 2004). Lack of management of comorbid conditions can increase disease severity, impair quality of life and physical and mental functioning in the patients and lead to higher risk of mortality.

Medicaid population is a highly vulnerable population since majority of the enrollees belong to a low income group and have multiple chronic comorbidities, disabilities, severe mental disorders and substance abuse problems compared to enrollees in Medicare or other commercial healthcare plans (Adelmann 2003). Hence medication adherence and healthcare utilization patterns might be very different from the enrollees in Medicare or commercial plans (Higashi 2007, Desai 2002, 2004, Goldberg 2007). Studying the impact of comorbid conditions on diabetes care and accordingly designing interventions for provision of comprehensive and cost effective care should be the objective of healthcare providers and policy makers.

1.4 Multiple medication adherence

Nearly 44% of the US population has at least 1 chronic disease condition and almost 33% of these people have 3 or more chronic disease conditions. Ageing will increase this percentage in the future as it increases the risk of development of chronic disease conditions. 50% of the people aged 60 years and more take at least 3 medications and 10% of this population take at least 7 or more medications (Paez 2009). Hayes (1979) defines adherence to medications, diet or lifestyle as a process that is directed by health or medical advice. Perceptions related to medication intake and medication related expenditures can play an important role in adhering to medications for patients with multiple chronic conditions. The list of medications that patients with a number of chronic conditions have to consume can be quite long and different conditions require patients to adhere to different medication therapies. As medication adherence decreases, medication failure rates increase and the severity of the multiple disease conditions also increases (Paez 2009). Taking or refilling medications only when symptoms become severe, refilling only those medications which are affordable or talking alternate doses of the medications that are more expensive might be some of the factors that can be attributed towards lower adherence.

1.5 Adherence improves healthcare outcomes in type 2 diabetes

Medication adherence provides several advantages such as reducing healthcare costs, patient suffering, and HbA1c level by less than 8% and the risk of mortality by half (Gibson 2010, Simpson 2006, Ruelas 2009). Even though medication adherence improves health and clinical outcomes by reducing the risk factors related to chronic disease conditions such as diabetes, non-adherence is an issue witnessed not only in developing countries but also in developed countries

(Lehane 2009, DiMatteo 2002, Ruelas 2009, Simpson 2006). Medication adherence rates in the developed countries are as low as 50% and in the developing countries; the numbers are lower than 50% (WHO 2003). Non adherence is a problem seen not only with diabetes but with many other conditions and it presents challenges in making the treatment prescribed by physicians a success (Lehane 2009). A systematic review conducted by Cramer et al (2004) which included 20 studies dated 1966 to 2003, showed that adherence rates that impacted blood glucose levels varied and were suboptimal. Identifying barriers to medication adherence and designing interventions to reduce them can improve adherence to chronic disease medication therapies.

1.6 Significance of the study

Medicaid covers uninsured and unemployed individuals, mainly comprising of pregnant women, children, adults with physical and developmental disabilities, elderly and frail individuals. Individuals with disabilities make up just 14% of all the Medicaid enrollees and yet are accountable for 42% of the total Medicaid expenses. Research has shown that people with disabilities have higher rates of diabetes characteristic of the type of disability (McDermott 2007, McDermott 2006). Among people with disabilities, rates of diabetes in patients with sensory or psychiatric disabilities are 31.6% and 24.7% respectively compared to 15.8% in patients without sensory or psychiatric disabilities. Diabetes is seen in only 10.4% patients with DD. However, the rates of obesity are 67% in patients with DD, sensory and psychiatric disabilities (McDermott 2006). Adults with DD experience disparity in receipt of healthcare due to their physical and mental chronic comorbidities (Havercamp 2004, Fisher 2004, Parish 2006, Phillips 2002). Limited information exists about the prevalence and management of type 2 diabetes in adults with DD. Chronic disease conditions including diabetes, are not managed properly in patients with DD (Beange 1995). So far, two studies have been conducted in Kansas Medicaid

patients with DD and diabetes. Results from one study state that the quality of care received by DD patients with diabetes was poorer compared to the national recommended standards (Shiremen 2010). The other study showed that adults with physical disabilities and diabetes had better screening rates for chronic disease conditions compared to the national recommended rates (Reichard 2012). There is not a single study to date that has looked at the medication intake patterns, healthcare utilization and costs in adults with DD and type 2 diabetes. The life expectancy of adults with DD has increased in recent decades but the additional years brought along by the increase in life expectancy have also increased the burden of morbidity. There is a national concern about the health of adults with DD. They possess a higher risk for developing type 2 diabetes, need special accommodations for getting the appropriate care and face a number of challenges in accessing healthcare. Hence, this study looks at the fulfillment of type 2 diabetes needs in terms of medication adherence and healthcare utilization in adults with DD enrolled in Medicaid.

1.8 Objectives and hypotheses

Objective 1: To describe select patient characteristics (sociodemographic factors and medication-related factors) of Medicaid-enrolled DD patients with a diagnosis of type 2 diabetes and examine the predictors of medication adherence in Medicaid-enrolled DD patients with a diagnosis of type 2 diabetes, after adjusting for select confounders. (Manuscript 1)

Hypothesis 1: Compared with Caucasian DD patients with type 2 diabetes, African American DD patients with type 2 diabetes will have lower medication adherence, after adjusting for select confounders. (Manuscript 1)

Objective 2: To examine the predictors of medication persistence in Medicaid-enrolled DD

patients with a diagnosis of type 2 diabetes, after adjusting for select confounders. (Manuscript 1)

Hypothesis 2: Compared with Caucasian DD patients with type 2 diabetes, African American DD patients with type 2 diabetes will have lower medication persistence after adjusting for select confounders. (Manuscript 1)

Objective 3: To examine the effect of race, medication adherence, and the combined effects of race and medication adherence on type 2 diabetes related health resource utilization (outpatient visits, inpatient visits and emergency room (ER) visits) in Medicaid enrolled DD patients with a diagnosis of type 2 diabetes after adjusting for select confounders. (Manuscript 2)

Hypothesis 3: DD African-American patients with type 2 diabetes with lower medication adherence have a higher type 2 diabetes related inpatient visits and ER visits but lower outpatient visits, after adjusting from select confounders when compared with three other groups: DD Caucasian patients with type 2 diabetes and lower medication adherence, DD Caucasian patients with type 2 diabetes and higher medication adherence and DD African-American patients with type 2 diabetes and higher medication adherence. (Manuscript 2)

Objective 4: To examine the effect of race, medication adherence , and the combined effects of race and medication adherence on type 2 diabetes related costs (medication costs, medical costs and overall costs) in Medicaid enrolled DD patients after adjusting for select confounders. (Manuscript 2)

Hypothesis 4: Among Medicaid enrollees, African American DD patients with type 2 diabetes and lower medication adherence will have higher type 2 diabetes related costs (medication costs, medical costs and overall costs) compared to three other groups: DD Caucasian patients with

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type 2 diabetes and lower medication adherence, DD Caucasian patients with type 2 diabetes and

higher medication adherence and DD African-American patients with type 2 diabetes and higher

medication adherence, after adjusting for select confounders. (Manuscript 2)

Chapter 2 Literature review

2.1 Diabetes Mellitus

2.1.1 Prevalence and economic burden of Diabetes:

Diabetes Mellitus, a serious metabolic disorder is a seventh leading cause of death in the United States (US) (CDC 2011). According to the Centers for Disease Control and Prevention (CDC) 2011 estimates, 25.8 million children and adults out of 311 million have diabetes and out of these 25.8 million, there are about 7 million people who have undiagnosed diabetes. In 2009, the number of diabetic people were 23.6 million so in just 2 years, this number has increased by 2.2 million. The number of people with pre-diabetes is also very high and it amounts to about 79 million adults and children (CDC 2011, U.S. Census Bureau). Diabetes is a leading cause of morbidity, mortality, functional disability, reduced quality of life and several micro and macro vascular complications such as cardiovascular illness and blindness (Norris 2011, Gregg 2002). There are three forms of diabetes mellitus:

a) Type 1 diabetes: This type is seen generally among 5% of the population, mostly children and young adults and insulin injection or pump is the preferred form of treatment. The causes of type 1 diabetes can be attributed to autoimmune, genetic or environmental factors.

b) Type 2 diabetes: This type is seen among the remaining 95% of the adult population. The common forms of treatment include diet control, exercise and medications which can

help either delay the onset or control the symptoms of type 2 diabetes.

c) Gestational diabetes: This occurs in about 2%-10% pregnant females. Women diagnosed with gestational diabetes have a 35%-60% risk of developing type 2 diabetes in 10-20 years. Also the newly born has an increased risk of developing type 2 diabetes (Hunt 2007, Dabelea 2011, Kitzmiller 2007).

Age and race are risk factors for developing type 2 diabetes. Adults older than 65 years have a seven times higher risk of developing type 2 diabetes compared to adults aged 20-44 years (Diabetes Report Card 2012). The prevalence of diagnosed diabetes in the US from 2007-2009 was 2.6% among adults aged 20-44 years, 11.7% among adults aged 45-64 years and 18.9% among adults aged 65 years and older respectively. Diabetes disproportionately affects racial minorities in the US and they have an increased risk of developing diabetic complications at a much younger age compared to non-Hispanic Caucasians. American Indians and Alaskan Indians are diagnosed with diabetes at a rate twice compared to non-Hispanic Caucasians (Geiss 2011). In 2007-2009, the age estimated numbers stated that adults diagnosed with diabetes aged 20 years or more constituted 16.1% American Indians and Alaskan Natives, 12.6% non Hispanic African Americans, 11.8% Hispanics, 8.4% Asian Americans and 7.1% non Hispanic Caucasians (CDC 2011). One of the main reasons for the increased incidence of diabetes can be attributed to the increasing incidence of obesity. Management of diabetes can be achieved by both pharmacologic treatment such as treating glycemia and non-pharmacologic treatment such as patient education, evaluating and minimizing micro and macro vascular risks (Qaseem 2012).

It is estimated that the worldwide incidence of diabetes will increase from 171 million in 2000 to 366 million in 2030. The numbers in the US are also estimated to rise to 44.1 million (diagnosed

and undiagnosed patients) out of a population of 386 million in 2034 and to 48.3 million (diagnosed patients) out of a population of 439 million respectively (Wild 2004, U.S Census Bureau, Huang 2009, Deshpande 2008, Narayan 2006). The cost of diabetes related healthcare places a huge burden on the US economy with treatment costs and loss of productivity accounting for $174 billion in 2007. These costs are estimated to rise to $336 billion in 2034 (CDC 2011, Deshpande 2008, Huang 2009, Narayan 2006, Wild 2004, Huang 2009). There is a need to design and implement interventions that can mitigate the complex and expensive healthcare needs related to diabetes (American Diabetes Association).

2.1.2 Disease progression to type 2 diabetes

The symptoms of type 2 diabetes are not very alarming upon their occurrence which is one of the reasons for its late detection. Pre-diabetic patients do not show symptoms of diabetes. However, if pre-diabetic people get their blood glucose checked on a regular basis, it is possible to know that the blood sugar level is above normal but not as high as diabetic patients. Long term damage to the circulatory and cardiovascular system starts to occur in pre-diabetic stage. As severity of the condition increases, occurrence of micro vascular and macro vascular problems such as retinopathy, coronary artery disease, cerebrovascular disease, neuropathy, peripheral vascular disease and nephropathy also increase (ADA website, Diabetes Report Card 2012).

The estimates of the development of micro vascular conditions in patients with type 2 diabetes are as follows:

a) Severe kidney disease and end stage renal disease in 10%-40% patients

b) Number one cause of diabetic retinopathy in patients aged 20-74 years

c) Mild to severe nervous system damage in 60%-70% patients

d) Non traumatic lower limb amputations in more than 60% patients with comorbid severe nerve disease (National Diabetes Information Clearinghouse 2008).

The estimated occurrence of macro vascular conditions which are more common and which are the leading cause of deaths in 80% patients with type 2 diabetes are as follows:

a) Ten times higher risk of co-occurrence of cardiovascular diseases in patients aged less than 45 years (Vijan 2004).

b) Two times higher cardiovascular mortality rate in male patients and four times higher cardiovascular mortality rate in female patients (Winer 2004).

2.1.3 ADA treatment guidelines

The American Diabetes Association (ADA) publishes evidence based guidelines for screening, diagnosis and therapy of patients with diabetes on an annual basis. The ADA guidelines assist clinicians, patients, researchers, payers, and other interested individuals with designing and providing diabetes treatment that can improve patients' health outcomes, achieve treatment goals and establish diabetes quality of care standards (ADA 2008). Type 2 diabetes is a complex condition with many related comorbidities and therefore ADA has mentioned several guidelines for the overall management of the disease. Some of the most important recommendations necessary for the initiation and maintenance of type 2 diabetes management therapy are: HbA1c < 7.0%, blood pressure < 130/80 mmHg, and low-density lipoprotein (LDL) cholesterol < 100 mg/dl, diet modification, initiation of metformin therapy, taking additional OHAs if blood sugar levels do not subside, and eventually initiating insulin therapy if all the above fail. The above comprehensive standards of care are evidence based and are regularly upadated. They consist of recommendations to diagnose, and delay or prevent pre-diabetes, diagnose diabetes, initiate and

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maintain medication therapy, screen for diabetes related comorbid conditions and begin lifestyle modifications for long term management of diabetes. The ADA recommends, given the evidence in large sample randomized controlled trials showing association of medication therapy and reduction in micro vascular and macro vascular risk, that diabetes therapy should be formulated and changed with regards to the characteristics of type 2 diabetes patients (ADVANCE 2007, ACCORD 2008, Duckworth 2009, UKPDS 1998). Measuring glycosylated hemoglobin A1c is of prime importance since the HbA1c level remains consistent over several months and is a strong indicator of diabetes complications (Sacks 2002, Knowler 2002, Sttraton 2000). Hence the HbA1c test should be done initially while making the diagnosis and later at regular intervals in diabetic patients (ADA 2008). Research states that a 1 percent reduction in mean HbA1c level is correlated with a 21 percent reduction of risk of micro vascular complications, myocardial infarction, amputation and stroke (UKPDS 1998, Sttraton 2000).

Evidence about the association of mortality and intensive treatment in diabetes patients is inconclusive. Results of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study indicate that among the two groups that aimed to reduce CVD with intensive interventions targeting a HbA1c level of less than 6 versus a HbA1c level of less than 7-7.9 percent respectively, the group that aimed achieving a HbA1c level of less than 6 showed higher CVD mortality (Gerstein 2008). Two other trials, the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial, and the Veterans Affairs Diabetes Trial had different interventions than the ACCORD trial and both the trials showed no CVD mortality in patients aiming for an HbA1c level of 6.5 percent unlike the ACCORD study (Patel 2008). There is also evidence showing improvement in CVD outcomes as a result of intensive glycemic control. Cheung et al (2009) analyzed the National Health and Nutrition

Examination Survey data to study the 1999-2006 national trends in achieving diabetes therapeutic goals, mainly looking at diabetes prevalence, treatment, and management. The study looked if the 17,306 study participants aged 20 years or older met ADA standards of medical care by achieving HbA1c level of less than 7 percent, blood pressure of 130/80 mmHg and LDL less than 100 mg/dl. Study results showed that from 1999-2006, the prevalence of diabetes increased from 6.6% to 7.8%, number of overweight people with HbA1c level of less than 7 percent significantly increased from 43.1% to 57.1%, number of people with blood pressure of 130/80 mmHg increased from 39.2% to 45.5% and the number of obese people with LDL less than 100 mg/dl increased from 36.1% to 46.5%. The number of patients achieving all the three targets increased from 7% to 12.2%. Difficulty in achieving all the three target goals at the same time was evident from the fact that only one in every eight study participant could do it (Cheung 2009, Kuritzky 2011). The main goal of diabetes management is providing affordable and effective treatment to the patients with minimum risk of side effects. In a meta-analysis study looking at the impact of adding a third OHA to the medication regimen of type 2 diabetes patients who were already on a metformin and a sulfonylurea and had HbA1c of more than 7 percent, the results indicated that HbA1c reduced by 0.7 percent and 1.08 percent for acarbose and insulin users respectively, hypoglycemic episodes doubled in frequency with insulin intake, weight increased by 2.84 kg and 4.25 kg with insulin and thiazolidinedione intake and weight reduced by 1.63 kg with glucagon-like peptide-1 agonist intake respectively. The researchers concluded that addition of a third OHA was not of significant benefit and if a third OHA was added, then the decision should be governed by patient preference and clinical characteristics (Gross 2011).

Enforcing of stringent A1c goals through treatment intensification should be done with caution in children, patients with severe hypoglycemia, and patients with comorbid conditions such as CVD, stable micro vascular complications, short life expectancy and long standing diabetes (ADA 2008). Research states that intensive glycemic control is not very beneficial in functionally impaired elderly patients with multiple comorbidities so treatment intensification or A1c reduction should be based on clinical judgment, the existent treatment plan and need for appropriate care (Nathan 2009, Huang 2008). According to the ADA recommendations, the frequency of A1c testing in patients with glycemia under control should be twice annually whereas in patients with unstable glycemia or patients managed with highly intensive therapy such as pregnant women with type 1 diabetes, the frequency should be four times annually (ADA 2008).

2.1.4 Treatment of type 2 diabetes

2.1.4.1 Lifestyle interventions:

People in general, are at a risk of developing chronic disease conditions if they do not lead a healthy lifestyle. Statistics such as one in every 3 Americans developing diabetes over their lifetime, even though surprising, indicate the need to proactively adopt healthy eating habits, be physically active and have optimal weight (Narayan 2003). This proactive approach known as "primordial prevention" consists of preventive measures to alleviate the risk factors of chronic disease conditions by modifying the environmental factors and social values that shape people's health behavior. Primordial prevention is effective in people with a low risk of developing chronic disease conditions but in people with a high risk of developing chronic disease conditions such as diabetes i.e. among the pre diabetic, older and overweight/obese people whose

blood glucose levels are impaired, there is a need for more intensive lifestyle interventions. Such interventions are part of "primary prevention" and involve incurring costs, screening of high risk individuals, and using medications to delay or prevent the early onset of diabetes. Many randomized controlled trials conducted worldwide have attested to the delay or prevention of early onset type 2 diabetes as a result of intensive lifestyle interventions involving diet, exercise and medication usage (Pan 1997, Tuomilehto 2001, Knowler 2002, Ramachandran 2006, Chiasson 2002, Gerstein 2006).

The National Diabetes Education Program (NDEP) has a number of educational materials that consists of interventions to prevent the progression of pre diabetes to type 2 diabetes for people belonging to racial minorities such as African Americans and Latinos who are at a higher risk of developing type 2 diabetes (NDEP website (c,d)). To reduce the incidence of micro and macro vascular complications associated with type 2 diabetes especially cardiovascular conditions, the NDEP, ADA and AACE (American Association of Clinical Endocrinologists)/ACE (American College Of Endocrinology) recommends the achievement of the following goals: A1c levels less than 7, blood pressure of 130/80, low density cholesterol less than 100 and high density cholesterol more than 40 (NDEP website (a,b)). Lifestyle interventions for preventing or delaying the transition of pre diabetes to type 2 diabetes are recommended by healthcare providers, insurance providers and employers. A randomized controlled trial "Diabetes Prevention Program" (DPP) conducted over a period of 3 years showed that a 16-week intensive lifestyle counseling intervention comprising of instructions on consuming the right diet and performing physical activity contributed to an average weight loss of 5.6 kg. About half the participants of the trial lost 7% of their initial body weight and the transition of pre diabetes to type 2 diabetes reduced by 58%. When the participants of the DPP trial were followed for

another 7 years, 85% of the participants who remained in the trial did regain about 5 kg of the lost weight. Compared to the placebo group, there was a reduction in the transition from pre diabetes to type 2 diabetes by 34% and 18% among the participants in the intensive lifestyle group and the metformin group respectively (Knowler 2009). The results of another randomized controlled multicenter trial AHEAD (Action for Health in Diabetes) showed that during a period of 4 years, patients with type 2 diabetes who were provided education, support, diet restricted in calories and who exercised regularly lost 6.15% weight compared to the control group patients with type 2 diabetes who received only support and education and lost only 0.88% weight. In addition, changes such as reduction in A1c levels, blood pressure and triglyceride levels and increase in the high-density lipoprotein cholesterol levels were seen in the participants in the intensive treatment group (Wing 2010). The ADA and AACE/ACE guidelines for the patients with pre diabetes and diabetes recommend strength training two times per week, medical nutrition therapy for weight loss and dyslipidemia, 150 minutes per week moderate physical activity, smoking cessation and loosing 7% of the body weight for overweight/obese patients. The last recommendation is in response to the findings of the DPP study (Handelsman 2011, ADA 2011).

2.1.4.2 Medications:

Medication therapy in type 2 diabetes helps in achieving the optimum glycemic control and also controlling the related micro and macro vascular complications (UKPDS 33 1998, Stratton 2000). Two decades ago, the favored therapy of choice for type 2 diabetes comprised of proper diet control, frequent exercising, using sulphonlyurea as medication and injecting insulin if the medications failed to work (Scheen 1998). Overall, oral hypoglycemic agents (OHAs) do help in reducing glycemic levels in diabetic patients but the choice of the right OHA is governed by a

number of factors such as the duration of type 2 diabetes, previous therapy, clinical and biochemical markers and baseline glycemia. Selection of a particular OHA or a class of OHAs or decision to change OHAs is primarily linked to obtaining the desired level of glycemic control (Peters 1996, Krentz 2005). In order to achieve the desired glycemic control, the dosing of OHA is individualized for every type 2 diabetes patient based on a variety of factors like side effects of OHAs, ease of use, tolerance, long term adherence and cost of OHAs (Nathan 2009). Often, in type 2 diabetes patients newly starting OHA therapy, OHAs are initiated at a lower dose and the dosing is adjusted accordingly upon regularly monitoring the HbA1c levels (Krentz 2005). The National Diabetes Statistics estimated by the 2007-2009 National Health Interview Survey show that among US based adults with either type 1 or type 2 diabetes, 58% consume only oral medications, 14% take both insulin and oral medications, 12% take only insulin and the remaining 16% do not take either of the two (National Diabetes Statistics 2011). Type 2 diabetes patients have insulin deficiency. Initiating diabetes medication therapy is based on the accurate judgment of either insulin resistance or defective insulin secretion. If the HbA1c levels are more than 8.5%, OHAs with rapid glucose lowering effects or a combination dose are recommended compared to patients with new onset of type 2 diabetes who have HbA1c level less than 7.5% and in whom OHAs with slower glucose lowering effect that can be recommended (Peters 1996). As type 2 diabetes progresses with worsened glycemic control, the dosage and the number of OHAs are increased accordingly (Nathan 2009).

OHAs can be categorized into three groups on the basis of their mechanism of action:

(a) insulin secretagogues: OHAs that increase insulin secretion

(b) α-glucosidase inhibitors: OHAs that delay absorption and digestion of carbohydrates

(c) insulin sensitizing agents: OHAs that have direct effect on insulin responsive tissues.

Table 2.1: Pharmacologic Therapy to Type 2 Diabetes Patients

A) Initiate monotherapy when HbA1C levels are 6%-7%

Options include:

Metformin
Thiazolidinediones
Secretagogues
Dipeptidyl-peptidase 4 inhibitors
a-Glucosidase inhibitors
Monitor and titrate medication for 2-3 months
Consider combination therapy if glycemic goals are not met at the end of 2-3 months

B) Initiate combination therapy when HbA1C levels are 7%-8%

Options include:

Secretagogue + metformin
Secretagogue + thiazolidinedione
Secretagogue + a-glucosidase inhibitor
Thiazolidinedione + metformin
Dipeptidyl-peptidase 4 inhibitor + metformin
Dipeptidyl-peptidase 4 inhibitor + thiazolidinedione
Secretagogue + metformin + thiazolidinedione
Fixed-dose (single pill) therapy
Thiazolidinedione (pioglitazone) + metformin
Thiazolidinedione (rosiglitazone) + metformin
Thiazolidinedione (rosiglitazone) + secretagogue (glimepiride)
Thiazolidinedione (pioglitazone) + secretagogue (glimepiride)
Secretagogue (glyburide) + metformin
Rapid-acting insulin analogs or premixed insulin analogs may be used in special situations
Inhaled insulin may be used as monotherapy or in combination with oral agents and long-acting insulin analogs
Insulin-oral medications; all oral medications may be used in combination with insulin; therapy combinations should be selected based on the patient's self-monitoring of blood glucose profiles
Initiate/intensify combination therapy using options listed above when HbA1C levels are 8%-10% to address fasting and postprandial glucose levels

C) Initiate/intensify insulin therapy when HbA1C levels are >10%

Options include:

Rapid-acting insulin analog or inhaled insulin with long-acting insulin analog or NPH
Premixed insulin analogs

(a)Insulin secretagogues:

(i)Sulfonylureas:

Sulfonylureas have been used as OHAs since 1950s. Tolbutamide belonging to the class of sufonlyureas is an insulin secretagogue and was the first OHA introduced in 1956 (Scheen 1998). Besides tolbutamide, some other older and first generation sulfonylureas that have been since the last four decades are acetohexamide, chlorpropamide and tolazamide. Compared to the first-generation sulfonylureas, the second generation sulfonylureas were prescribed in smaller doses since they had higher potency with lower side effects (Luna 2001). The third generation sulfonylureas are glipizide (brand names Glucotrol® and Glucotrol XL®), glyburide (Micronase®, Glynase®, and Diabeta®), and glimepiride (Amaryl®). All drugs under the sulfonylurea class have a similar mode of action. They stimulate secretion of insulin from pancreas, thereby reducing the concentration of blood glucose. Sulfonylureas are well tolerated, have simple dosing; are inexpensive and are given as first line therapy once or twice per day before meals to patients in whom non pharmacologic attempts have failed to achieve glycemic control. Though the mode of action among the different drugs belonging to sufonlyurea class is similar, the side effects differ with regards to the method of intake and the interaction with other drugs. Sulfonylureas are compatible with all classes of OHAs except with insulin secretagogues. Sulfonylureas are potent, safe and cost effective OHAs for diabetes management but they have certain side effects which include hypoglycemia, hypoglycemic coma, secondary failure, weight gain, cutaneous sensitivity reactions and severe hypoglycemia (with long acting sulfonylureas) (Luna 2001, Chipkin 2005, Riddle 1999).

(ii)Meglitinides:

Derivatives of meglitinides and phenylalanine used in patients with type 2 diabetes are repaglinide and nateglinide respectively. Repaglinide and nateglinide were introduced in the

market in 1998 and 2001 respectively and are non-sulfonylurea secretagogues. Their mode of action is similar to sulfonylureas but their half life is just 1 hour which is much shorter compared to sulfonylureas. They are directed to be consumed before or during meals. Since repaglinide and nateglinide are similar to sulpohnlyureas, there is no added advantage taking them in addition to sulphonlyureas (Luna 2001, Quillen 2002, Chipkin 2005). Repaglinide and nateglinide offer several advantages. Both the drug classes are preferred by people who do not follow a regular schedule of eating meals or people who generally forget to eat their meals. They can be taken as monotherapy, are associated with a low risk of hypoglycemia and do not lead to weight gain compared to sulfonylureas. Repaglinide and nateglinide are also preferred in patients with renal insufficiency since they are metabolized and excreted by hepatic mechanism. On the downside, repaglinide and nateglinide have to be taken a number of times during the day since they do not sustain high levels of insulin and they are also more expensive than sulfonlyureas (Luna 2001, Chipkin 2005, Riddle 1999).

(b) Insulin sensitizing agents:

(i)Biguanides:

Phenformin was released in the US in 1976 but was withdrawn due to high risk of fatal lactic acidosis. Then in 1994, another biguanide metformin (brand name Glucophage®) was released. Metformin improves insulin sensitivity and lowers blood glucose levels. It does not cause hypoglycemia. For metformin to be clinically effective, insulin should be present since it does not stimulate insulin release. It reduces blood glucose level by increasing the insulin sensitivity of the muscle tissue, thereby improving glucose absorption and by decreasing glucose production from the liver. Metformin acts in presence of beta-cell function and is not related to age or duration of diabetes or weight of the patient. Metformin is a drug of choice in obese or

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overweight type 2 diabetes patients since it leads to a slight weight loss by acting as an appetite suppressant. It is a cheap OHA, used as monotherapy or in combination with other OHAs or insulin, has a favorable lipid and antihypertensive effect and works effectively in patients with normal weight. Research has shown reduction in the risk of myocardial infarction in overweight patients taking metformin (UKPDS 34, 1998). Metformin is contraindicated in patients with renal impairment and liver disease. Renal impairment can lead to a rare life threatening occurrence of lactic acidosis caused by intake of metformin with mortality rates as high as 50% (Qullien 2002, Luna 2001, Chipkin 2005, Riddle 1999). Other side effects of metformin include gastrointestinal (GI) problems such as diarrhea and bloating, metallic taste in the mouth and changes in the vitamin B12 levels (Luna 2001, Chipkin 2005, Riddle 1999).

(ii)Thiazolidinediones (TZD):

Troglitazone was the first thiazolidinedione (TZD) introduced in the US in 1997, followed by rosiglitazone and pioglitazone in 1999. Troglitazone, unlike rosiglitazone and pioglitazone was withdrawn from the market due to hepatotoxicity in 2000 (Vasudevan 2004, Bailey 2000, Krentz 2000, Quillen 2002). TZDs act via various modes. They improve insulin sensitivity by the stimulation of a nuclear receptor PPARγ. TZDs do not stimulate insulin production by pancreas but improve insulin sensitivity by increasing the GLUT-1 and GLUT-4 glucose transport proteins and up-regulating insulin responsive genes. Genes involved in lipid and carbohydrate metabolism are activated by TZDs as a result of gene regulation. TZDs increase skeletal muscle sensitivity and enhance glucose and fatty acid uptake by adipose tissues leading to increased lipogenesis, glycolysis, and glucose oxidation. In liver, there is decreased gluconeogenesis, glycongenolysis and increased lipogenesis (Vasudevan 2004). TZDs are expensive, can cause weight gain, fluid retention, decrease in hemoglobin concentration causing edema or anemia, and

can be used as monotherapy or in combination with metformin, sulfonylureas and insulin. Substitution of TZD with sulfonylurea or metformin is not preferred (Riddle 2005). Rosiglitazone and pioglitazone are contraindicated in patients with liver disease, cardiovascular diseases, congestive heart failure or other fluid overloaded diseases and both the drugs reduce portion of smaller atherogenic low density lipid (LDL) cholesterol (Lago 2007, Singh 2007). Anti-atherogenic actions of TZDs and its association with the risk of CVD can have important clinical implications and the related research is being conducted currently through clinical trials. Rosiglitazone leads to a rise in the total cholesterol concentration for upto three months of initiating the TZD therapy whereas pioglitazone decreases triglyceride concentrations and the effectiveness of oral contraceptives (Roberts 2003, Luna 2001, Chipkin 2005, Riddle 1999).

(c) alpha-glucosidase inhibitors:

These OHAs have a non systematic mode of action. They block the breakdown of starches in the intestine, inhibit the α-glucosidase enzyme which converts carbohydrates to glucose and leads to a delay but not prevention in the absorption of carbohydrates and complex sugars. There are three types of alpha-glucosidase inhibitors available for treatment, out of which two are available in the US market: acarbose (brand name Precose®) and meglitol (Glyset®). The third alpha-glucosidase inhibitor unavailable in the US is voglibose. These OHAs are a bit on the enpensive side and can be used individually or in combination. Some advantages of alpha-glucosidase inhibitors are that they do not cause weight gain and have plasma triglyceride concentration lowering ability (Ogawa 2004, Chiasson 2004). They target postprandial hyperglycemia and therefore are suitable for use in patients consuming complex carbohydrates since they have slightly raised basal glucose concentration. Acarbose leads to hepatic toxicity and hence meglitol is preferred comparatively. Side effects of alpha-glucosidase inhibitors consist of gastrointestinal

discomfort; mostly flatulence, diarrhea, and bloating (Kuritzky 1999). Hence, they are contraindicated in patients with limited gastrointestinal tolerance or with chronic intestinal diseases (Luna 2001, Chipkin 2005, Riddle 1999).

2.1.4.3 Insulin therapy:

In case of type 2 diabetes patients, in whom the medication therapy does not help in controlling blood glucose levels, insulin therapy is recommended (DeFronzo 1999). Insulin therapy is generally used in patients when one medication or a combination of medications alone fail to lower blood glucose level or in pregnant patients or in patients with severe hepatic or renal impairment. Insulin therapy is not widely used in type 2 diabetes patients due to potential disadvantages such as hypoglycemia, weight gain, and non-adherence to complicated insulin therapy (Brunton 2006, Riddle 2002). Besides the above disadvatnages associated with insulin therapy, patients feel anxious due to use of needles, pain caused by injection, social stigma associated with insulin intake, difficulty in administration, perceived severity of the disease condition and frequent dosing (Polonsky 2004, Korytkowski 2002, Peyrot 2003). Insulin therapy does have several benefits. Not only does it improve insulin sensitivity and causes reversal of insulin resistance in type 2 diabetes patients, it also improves HbA1c levels when used in combination with OHAs (Andrews 1984, Scarlett 1982, YkiJarvinen 2000).
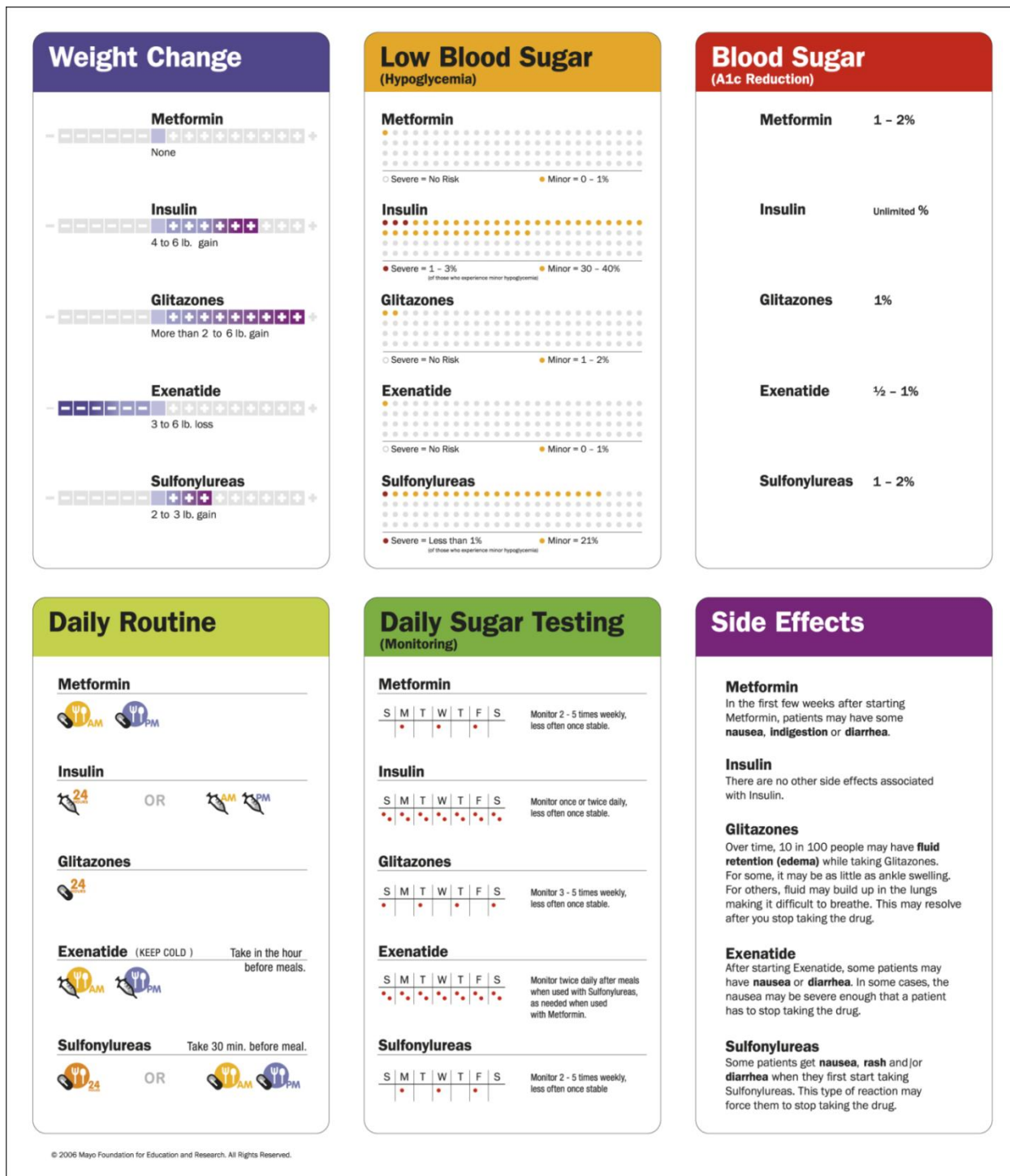
Figure 2.1: The Diabetes Mellitus Medication Choice Aid (Mullan 2009)

2.1.5 Medication adherence in patients with type 2 diabetes

2.1.5.1 Impact of medication adherence on type 2 diabetes outcomes:

Medication adherence is a crucial part of the treatment process; non-adherent behavior may create bottlenecks that may limit the effectiveness of medication and care provided by the healthcare system. In the context of diabetes, this bottleneck is evident in poor adherence rates to diabetes medication (36% to 93%) that limit the effectiveness of newly developed drugs and therapies (Cramer 2004). This may also explain, to some extent, the low proportion (43%) of diabetes mellitus patients with acceptable HbA1c levels of below 7%, recommended by American Diabetes Association (Saaddine 2002, Kerr 2004, ADA, 2008).

In context of diabetes, medication adherence has been found to be related with a wide range of outcomes, both medical and non-medical. Adherence has been associated with enhanced blood glucose control (Rozenfeld 2008, Ho 2006, Krapek 2004, Lawrence 2006, Schectman 2002, Pladevell 2004), and reduced mortality (Ho 2006). Among economic and administrative outcomes, adherence has been associated with fewer inpatient visits (Lau 2005) and lower health-care costs (Sokol 2005, Hepke 2004).

Various adherence studies in the context of diabetes have focused on glycemic control, economic burden (Abegunde 2007, Pohar 2007), complications associated with diabetes (UKPDS 1998) and medication cost-effectiveness (Salas 2002, Valentine 2007). A study in a managed care setting demonstrated higher glycemic control among adherent patients and found that high OHA medication adherence was associated with lower HbA1c levels. Using baseline HbA1c and therapy regimen as controls, the study found that with each 10% increase in OHA medication adherence, HbA1c levels decreased by 0.1% (Rozenfeld 2008). Similarly, in a study by Krepek

(2004), higher adherence levels were associated with a 10% reduction in HbA1c (Krapek 2004). Looking at economic and administrative outcomes, another study of 57,687 diabetic patients in an HMO showed that those with increased OHA medication adherence had fewer emergency department visits, fewer inpatient admissions, and decreased medical care costs (Hepke 2004). In a retrospective cohort (N = 11 532) analysis by Ho and colleagues, 62 non-adherent diabetic patients had higher all cause inpatient visits and all-cause mortality than adherent diabetes patients (Ho 2006). In a range of studies, low medication possession ratios (MPRs), an indicator of poor medication adherence, were generally associated with higher costs among patients with type 2 diabetes. A study by Balkrishnan et al (2003) reported a 10% increase in anti- diabetic medication adherence to be associated with 8.6% reduction in total annual healthcare costs (Balkrishnan 2003). Another study by Wagner reported that the mean annual costs for Medicaid patients with baseline HbA1c<8 were \$4475, whereas mean annual cost for patients with HbA1c>10 were \$8088 (Wagner 2001). Connecting these findings with the previous findings associating adherence and HbA1C levels, it can be argued that since adherence levels are inversely proportional to HbA1c levels, mean annual costs will be higher for non-adherent patients who are more likely to have higher HbA1C levels.

2.1.5.2 Barriers to medication adherence in type 2 diabetes patients:

WHO classifies the factors impacting pharmacologic and non-pharmacologic adherence to type 2 diabetes as:

A) Treatment and disease characteristics:
This factor consists of three components, namely complexity of treatment, duration of disease and delivery of care. Higher OHA adherence is associated with single medication intake or less

frequent dosage intake (Paes 1997, Dailey 2001). Longer duration of diabetes is associated with less likelihood to take insulin or perform physical activity and higher likelihood of consuming inappropriate food (Glasgow 1987, Jarosz 2000). Cost of care affects access to care which in turn impacts metabolic control. Diabetic patients visiting their physicians for diabetes rather than for an acute condition have a higher probability of receiving counseling on adherence to diet and medications (Yawn 2001, Kern 2001).

B) Intra-personal factors:

These factors consist of age, gender, self-esteem, self-efficacy, stress, depression and alcohol abuse. Older age, being a female, positive self-esteem and higher self-efficacy are associated with higher adherence to diabetes self-care including insulin administration, monitoring blood glucose, performing physical activity, higher life satisfaction and medication adherence (Andersen 1997, Stetson 2000, Kneckt 2001, Plotnikoff 2000, Senecal 2000, Ott 2000, Aljasem 2001). On the other hand, stress, emotional problems, depression and alcohol abuse are associated with poor adherence to OHAs, diet and self-care, worsened glycemic control, more diabetes complications and less frequent glucose monitoring (Andersen 1997, Peyrot 1999, De Groot 2001, Lustman 2000, Ciechanowski 2001, Johnson 2000).

C) Inter-personal factors:

Two important inter-personal factors such as a positive patient physician relationship and availability of social support can lead to better adherence to OHAs (Ciechanowski 2001), diet and insulin administration (Ruggieron 1990) and regular monitoring of blood glucose level (Anderson 1997).

D) Environmental factors:

These factors comprise of high-risk situations and environmental systems. High risk situations

are situations that lead to reduced adherence. Such situations can arise at home, at work or in public. Some of the high risk situations that are associated with poor adherence to diabetes self-care are over eating and under eating, loneliness, social events, time pressure, holidays, eating out and competing priorities (Schlundt 1994 (a), Schlundt 1994 (b), Schlundt 1989). Environmental factors such as economic, agricultural, political, healthcare related, geographical, ecological and culture related affect people over a longer course of time rather than impacting immediately or in a shorter duration (Ramlogan 1997, Miller 2002).

Table 2.2: Factors affecting adherence to diabetes therapy for the control of diabetes and interventions for improving it (WHO 2003):

Diabetes	Factors affecting adherence	Interventions to improve adherence
Socioeconomic-related factors	(-)Cost of care, patients aged over 25 years, environmental high-risk situations,(+) social support , family support , patients aged less than 25 years	Mobilization of community-based organizations; assessment of social needs; family preparedness
Healthcare team/health system-related factors	(-)Poor relationship between patient and physician	Multidisciplinary care; training of health professionals on adherence; identification of the treatment goals and development of strategies to meet them; continuing education; continuous monitoring and reassessment of treatment; systems interventions: health insurance for nutrition therapy, telephone reminders to patients, chronic care models
Condition-related Factors	(-)Depression; duration of disease	Education on use of medicines
Therapy-related Factors	(-)Complexity of treatment, (+) Less frequent dose; monotherapy with simple dosing schedules; frequency of the self-care behaviour	Patient self-management; simplification of regimens ; education on use of medicines
Patient-related Factors	(-)Depression; stress and emotional problems; alcohol abuse, (+)Positive self-esteem/self-efficacy	Behavioural and motivational interventions, assessment of psychological needs

(+) factors having a positive effect on adherence; (–) factors having a negative effect on adherence.

2.1.5.3 Different measures of medication adherence:

Diabetes treatment is a multidimensional process that involves elements like medications, dietary controls and other behavioral and lifestyle changes. However, one of the frequently used adherence measure focuses on medication adherence and is considered one of the most important adherence measures. Nonadherence specific to medication has been associated with increased economic burden and adverse health conditions (Hearnshaw 2006, Dunbar-Jacob 2001, Lau 2004, Lee 2006, Sokol 2005). Medication adherence measures are being used as part of the Healthcare Effectiveness Data and Information Set (HEDIS) quality measures to assess plan quality and plan payment systems, and since Medicare provides Medication Therapy Management (MTM) services, many MTM providers develop and validate adherence measures to evaluate MTM services (Touchette 2006, Christensen 2003).

In 2001–2003, 57% of diabetic patients were using oral medications, whereas only 12% patients were using a combination of oral medications and insulin (CDC 2005). Since diabetes is a chronic disease and medication adherence plays an important role in its management, standardizing adherence calculations for diabetic patients has become an important objective. Use of administrative claims data is emerging as one of the most prominent sources for adherence calculations. Though adherence measures based on administrative claims data are highly likely to overestimate adherence due to their inability to access consumption, and also pose issues in cases where multiple medications are being procured from multiple pharmacies by the patient, they tend to provide a practical, unobtrusive, relatively inexpensive and effective way of collecting data for large populations. Anderson et al (1997) demonstrated that out of 136 studies using administrative claims data for adherence calculations, about 57% used MPR and related measures, 43% used switching and discontinuation, and around 10% used medication

gaps. Adherence measures using pharmacy claims data have been validated when used with other measures such as patient reports, pill counts, questionnaires, and interviews (Garber 2004, Choo 1999, Cook 2005, Grymonpre 2006, Kwon 2003, McKenzie 2000).

Some of more common adherence measures are Medication possession ratio (MPR), Medication refill adherence (MRA), and Continuous measure of medication acquisition (CMA), Proportion of days covered (PDC), days between fills adherence rate (DBR) and refill compliance rate (RCR), Compliance ratio (CR), Medication possession ratio modified (MPRm), Continuous measure of medication gaps (CMG) , Continuous multiple interval measure of oversupply (CMOS) and Continuous, single interval measure of medication acquisition (CSA). Out of these measures, MPR, MRA, and CMA seem to be similar and yield equivalent values. Similarly, DBR and RCR measures provide equivalent values. Karve et al (2008) found most medication adherence measures to be significant predictors of inpatient admission; RCR, CR, and CSA were the measures that did not predict inpatient admission significantly. Among the rest of measures considered in the study, PDC, MPR, CMOS, and CMG were the best predictors of future inpatient visits (any cause and diabetes related). While predicting any cause inpatient visits, MPR and CMOS were similar to PDC and CMG; they were also the second best predictors of inpatient visits due to diabetes. PDC, MPR, CMOS, and CMG were found to be better predictors of inpatient visits than other measures, and PDC and MPR both provided higher values for more compliant patients. Overall, measures using the entire index period of 365 days as denominator in the formula predicted inpatient visits better than measures using period between first and last refill in the denominator.

Table 2.3: Formulae for measuring adherence (Karve 2008)**:**

Adherence measure	Formula
Medication possession ratio (MPR)	Number of days supply in index period/number of days in the study period (365 days)
Medication refill adherence (MRA)	[number of days supply in index period/number of days in the study period (365days)]×100
Continuous measure of medication acquisition (CMA)	Number of days supply/total days to next fill or end of observation period (365 days)
Proportion of days covered (PDC)	[Number of days supply in index period/ number of days in the study period (365 days)] ×100 capped at 1
Refill compliance rate (RCR)	(Number of days supply/last claim date -index date) × 100
Days between fills adherence rate (DBR)	1 – [(last claim date - index date) - total days supply/last claim date] index date] x 100
Compliance ratio (CR)	Number of days supply in the index period - last days supply/last claim date - index date
Medication possession ratio modified (MPRm)	[Number of days supply/(last claim date- index date + last days supply)] × 100
Continuous measure of medication gaps (CMG)	Total days of treatment gaps/total days to next fill or end of observation period (365 days)
Continuous multiple interval measure of oversupply (CMOS)	Total days of treatment gaps (+) or surplus (-)/ total days to next fill or end of observation period (365 days)
Continuous, single interval measure of medication acquisition (CSA)	Days supply obtained at the beginning of the interval/days in interval

2.1.5.4 Measuring medication adherence in type 2 diabetes patients:

Though compliance has been of interest to researchers for a long time, there is no standard way to define and measure compliance (Cleemput 2002). Compliance essentially is the level to which a patient follows the medication regimen prescribed by the healthcare provider (Osterberg 2005). Some researchers prefer to use the term 'adherence' instead of 'compliance' because the use of latter term seems to imply passivity on the part of the patient. The term 'adherence' is an

indicator of the more active role that the patient plays in the treatment process and implies a patient centric conceptualization of the treatment process (Tabor 2004).

One of the key problems for compliance researchers is the variability in compliance measurement methods (Murray 2004). The lack of standardized compliance measurement may be primarily due to the range of variation in the nature of health problems and medication regimens. Diseases with multimodal treatment regimen may need different measures than diseases with simple medication regimens (Kyngas 2000). For example, in a multimodal regimen consisting of medication and behavioral therapy, it may be hard to identify compliance for each component and associate them with the health outcomes. In other words, compliance with one component of the regimen may not be appropriate when the success is caused by other components, or by the interaction of all the components of the regimen.

Existing methods for measuring compliance can be categorized into two types; direct methods, and indirect methods. Direct methods mostly involve medical testing such as assessment of blood, urine and saliva to determine drug concentration levels. Though these provide relatively objective, reliable and quantifiable data, the cost and resources involved in such measurements may prove barriers to their widespread use in real life medical settings (Kyngas 2000). Indirect methods are based on collecting information that may be considered a predictor of compliance; such information may include patient reports, pill counts, refill adherence, and electronic monitoring using microchip technologies. Though indirect methods are more viable in terms of resources and costs involved, they also suffer from various limitations to their reliability. For example, pill counting takes the consumption over a period of time into account and cannot measure the timing of the dosage; this not only limits the reliability but also makes the method vulnerable to 'pill dumping' by the patients. Similarly, Medication Event Monitor System

(MEMS), a relatively expensive method than pill counting, provides a better compliance measurement but is not able to ensure if the patient takes the medication or not. Another indirect method used at the pharmacy level is refill adherence that involves tracking of patient medication refills using computerized prescription records. There are two commonly used measures of refill adherence; Proportion of days covered (PDC), and Medication possession ratio (MPR). PDC is calculated by dividing the number of days of drug coverage by the number of days in the refill interval; it avoids double counting of days and provides a value between 0 and 1. MPR, on the other hand, involves counting the number of days supplied by the prescriptions filled during the period. Though more viable in terms of costs and resources, refill adherence methods suffer from limitations similar to 'pill counting': it is not possible to get data about actual medication consumption on a daily basis.

In previous studies, medication adherence has been found to display a wide range of variations. A systematic review study conducted from 1966 to 2003 using adherence data for oral hypoglycemic agents (OHAs) and insulin reviewed 20 reports looking at correlations between adherence and glycemic control (Cramer 2004). The findings showed that adherence to OHAs reported by retrospective studies ranged from 36% to 96% (among patients on medication for 6-24 months), whereas prospective studies using electronic monitoring devices showed adherence rates ranging from 67% to 87%. The review indicated that electronic-monitoring devices may be more effective in measuring adherence and may capture medication consumption missed by retrospective studies.

Table 2.4 Methods for measuring medication adherence (Osterberg 2005):

Methods	Advantages	Disadvantages
Direct Methods		
Directly observed therapy	Most accurate	Patients can hide pills in the mouth and then discard them; impractical for routine use
Measurement of the level of medicines or metabolite in blood	Objective	Variations in metabolism and "white-cost adherence" can give a false impression of adherence; expensive
Measurement of the biologic maker in blood	Objective	Requires expensive quantitative assays and collection of bloody fluids
Indirect Methods:		
Patient questionnaires, patient self-reports	Simple; inexpensive; the most useful method In the clinical setting	Susceptible to error with increases in time between visits; results are easily distorted by the patient
Pill counts	Objective, quantifiable, and easy to perform	Data easily altered by the patient (e.g., pill dumping)
Rates of prescription refills	Objective; obtain easy to data	A prescription refill is not equivalent to ingestion of medication; requires a closed pharmacy system
Assessment of the patient's clinical response	Simple, generally easy to perform	Factors other than medication adherence can affect clinical setting
Electronic medication monitors	Precise; results are easily quantified; tracks patterns of taking medication	Expensive; require return visits and downloading data from medication vials
Measurement of physiologic markers (eg: heart rate in patients taking beta-blockers)	Often easy to perform	Marker may be absent for other reasons (e.g., increased metabolism, poor absorption, lack of response
Patient diaries	Help to correct for poor recall	Easily altered by the patient
When the patient is a child, questionnaire for caregiver or teacher	Simple; objective	Susceptible to distortion

2.1.6 Burden of type 2 diabetes and related resource utilization in Medicaid patients

Chronic diseases place a substantial disease burden on the society. From a clinical perspective, a secondary analysis of the Medical Expenditure Panel Survey (MEPS) by Druss et al (2001)

showed that around 50% of the overall U.S. healthcare expenditures can be accounted for by one or more of the five conditions that affects about one quarter of the U.S. population. These conditions are mood disorders, diabetes, heart disease, asthma, and hypertension. Comorbidity was found to be most common among diabetics and infections, microvascular and macrovascular diseases accounted for a large portion of clinical and economic burden of diabetes.

From the economic burden standpoint, a secondary data analysis of the 2002 National Survey of America's Families by Shen et al (2006) analyzing out-of-pocket spending on healthcare reported that health insurance did not necessarily reduce the financial healthcare burden. This was demonstrated by the fact that a substantial number of two million people experiencing medical bankruptcy in 2002 had health insurance. In spite of having insurance, medical costs did create financial constraints, which were experienced more severely by people from low-income group and affected their usage of medication and emergency services. Insured people in low-income groups with serious health issues spent less on healthcare than people in high-income groups. Another secondary study of the 2000-2004 Medical Expenditure Survey (MEPS) by Banerjee et al (2010) showed that among adults enrolled in Medicaid, after controlling for employment and health status, individuals with more than one transition in health insurance status were more likely to have higher rates of healthcare utilization than those with one or no transition. Among people without continuous Medicaid coverage, the use of emergency department and office visits and inpatient visits increased by 10% and 36%, whereas the use of prescription medications decreased by 19%.

Financial constraints may reduce access to prescriptions and may lead to non-adherence that may increase overall economic burden. A pre-post study of 36 patients with lower socioeconomic status enrolled in a program providing free medical care and medications showed that inpatient

charges dropped from $838,145 to $459,962 from 6 months prior to the study to 6 months during the study (NyKamp 2000). The costs of drugs were $27,588 for the program and the cost avoidance was $378,183. This cost was avoided due to decrease in inpatient visit rates by 39.5% and increase in outpatient visits by 64.4%. This shows that though among under or uninsured people, the economic burden for chronic disease management is high (Banerjee 2010, Bogner 2010, Druss 2001, Shen 2006), focus on increasing adherence may restrict hospital and emergency department visits and may result in overall cost saving.

This relationship between adherence and utilization of healthcare service has been examined by numerous studies. A review of 37 studies by Asche et al (2011) analyzed the association between adherence and glycemic control, healthcare resource utilization, quality of life and mortality among diabetic patients. In 23 out of 37 studies examining glycemic control and adherence, 57% patients reported a positive relationship. Seven of the eight studies examining relationship between adherence and inpatient visits reported that higher level of adherence was associated with decrease in inpatient visit rates. Two of the three studies examining adherence and emergency department visits reported that increased adherence was associated with decrease in emergency department visits. A study by Lu et al (2004) used the administrative claims data from 2000 to 2001 for studying type 2 diabetes patients. The study reported that patients' non-adherent (MPR<80%) to antihyperglycemic agents in 2000 faced greater risk of inpatient visits in 2001.

Though adherence may reduce inpatient visits and emergency visits, it may not always result in reduction of overall medical care expenditures. A prospective cohort study by Hepke et al (2004) used insurance claims to examine the association between adherence to pharmaceutical therapy and well being and total associated costs for diabetes treatment. The researhers found increased

adherence to be associated with decreased inpatient and emergency department visits. However, the researchers also found that even though increased adherence was associated with decreased medical care costs, it was not associated with reduction in overall healthcare costs as high medication costs offset the decrease in medical care costs. Similarly, Sokol et al (2005) conducted a large retrospective cohort observation study to examine the association between adherence and healthcare utilization. Sample population included patients that were continuously enrolled in medication and prescription plans for two years (June 1997 to May 1999). The study looked at medication adherence, cost, and utilization in patients with four chronic conditions: diabetes, hypertension, hypercholesterolemia, and congestive heart failure. The study reported lower inpatient visit rates for patients with high adherence for all four chronic conditions. However, though they found that for diabetes and hypercholesterolemia, high adherence was associated with lower disease related medical costs, medical care cost savings were offset by higher medication costs.

2.1.7 Healthy People 2020:

Racial disparities are one of the key public health challenges faced by health policy makers. According to Healthy People 2010, health disparities are differences in health indicators and outcomes based on gender, race, education, income, disability, geographic location, or sexual orientation. One of the primary focus areas for health disparities is diabetes, which occurs disproportionately in certain ethnic populations (Flegal 1991;Healthy people 2020; Vinicor 1994). African Americans, Hispanics, American Indians, certain Pacific Islander and Asian American populations are affected disproportionately by diabetes compared to Caucasians. This disparity is also observed among economically disadvantaged and older populations. American Indians are affected 2 to 5 times more than Caucasians. Similarly, African American adults are

1.7 times more likely and Mexican American/Puerto Rican adults are 2 times more likely to be affected by diabetes respectively, compared to non-Hispanic Caucasians of similar age. Minority groups constitute 25 percent of type 2 diabetes patients in United States and account for majority of child and adolescent type 2 diabetes patients. Diabetes can lead to serious consequences such as amputation and death and can cause hyperglycemia and other comorbid conditions that may increase the disease related burden and severely impact the quality of life of patients (Shenolikar 2006). Diabetes can lower life expectancy upto 15 years and increase the risk of heart diseases by two to four times (Healthy People 2020).

One of the key issues to address diabetes related disparities is that of access to healthcare system and awareness of options available to patients. Various diabetes services like self-management training programs and eye-retina exams can be helpful in addressing diabetes and its associated conditions. However, many vulnerable populations lack access to these services for various reasons, one primary reason being systems problems such as vulnerable populations living in medically underserved areas (Healthy People 2020, Shenolikar 2006).

In light of these disparities, Healthy people 2020 initiative by government proposes a multidimensional approach to address health disparities and attain long term national health objectives (Healthy People, 2020). The initiative proposes to involve academicians, practitioners, government agencies, and public in a concerted effort to attain nationwide health objectives over a period of 10 years. The key objective of the program is to enhance quality and duration of life across the society. More specifically, the key goals of the initiative are four-fold; 1) enhancing quality and duration of life by controlling preventable diseases and other key health threats such as disability, injury and premature deaths, 2) attaining overall health improvement across society by eliminating health disparities, 3) promoting environments conducive to promotion of good

health across communities, and 4) promoting healthy behaviors and development in order to enhance quality of life. The approaches to be used to attain these objectives focus on better assessment of health priorities, increasing public awareness about factors contributing to health related quality of life, use of measurable goals and objectives at national, state and local levels, involving multiple stakeholders in policy making and practice improvement, and identifying critical areas for research, evaluation and data collection. Based on the objectives and approaches presented above, the Healthy people 2020 proposes four health measures; 1) general health status, 2) health-related quality of life, 3) determinants of health, and 4) disparities.

In Healthy People 2020, diabetes is one of the key health areas due to its impact on quality of life and the degree of health disparity observed in diabetes occurrence. The focus is on understanding diabetes and the nature of disparities in order to develop effective solutions. The initiative identifies four transitions points in diabetes healthcare, which present opportunities for addressing the disease. These transition points are; 1) primary prevention, 2) early diagnosis, 3) access to care to everyone, and 4) improved quality of healthcare. These points focus not only on disease related issues but also intend to address access barriers that have been identified as one of the key systems problems. Some examples of the focus on disparities involve identification of vulnerable populations, introduction of new diagnostic criteria, and implementation of prevention oriented community based interventions.

2.1.8 Racial disparities in medication adherence and healthcare utilization in patients with diabetes mellitus:

Racial health disparities in diabetes control are observed through a wide range of health indicators. Poorer glycemic control is observed among non-Hispanic blacks and Mexicans

compared to non- Hispanic whites. Both African American and Hispanics are significantly more likely to have borderline or poorly controlled hypertension, diabetes associated neuropathy, retinopathy, and diabetes-related amputations than non-Hispanic whites (Bonds 2003, Ness 1999,Harris 1998).   Similarly, micro vascular complications of the eyes, nerves, kidneys, and lower extremity amputations are more frequent among African-Americans and Hispanic Americans compared to non-Hispanic Caucasians (Haffner 1988, Franklin 1990, Haffner 1989, Resnick 1999, Cowie 1989).

According to Adams et al (2005), African Americans were more likely to have increased Hba1c in a HMO setting, after adjusting for baseline Hba1c, Body Mass Index (BMI), age, types of diabetes medications, diabetes-related inpatient visits, number of Hba1c tests, physician visits, and non-diabetes medications. In African American males with previously diagnosed diabetes, Hba1c levels were higher than white men by 0.11 units. Similarly, in African-American women previously diagnosed with diabetes, the adjusted average Hba1c was 0.30 units higher than white women. Among newly diagnosed African American men, the observed average Hba1c levels were 0.49 units higher than white men whereas no significant difference was observed in Hba1c levels by race among women (Adams 2005).

African Americans are more likely to be affected by poor blood pressure and poor glycemic control than whites (Konen, 1999). African American men are more likely to suffer from blurred vision and hypertension but are less likely to suffer from peripheral atherosclerotic disease (Konen 1999). African American women are more likely to be affected by constipation and hypertension but are less likely to be affected by peripheral vascular disease (Konen 1999). Though the contributing factors to these disparities need a deeper understanding, some factors might be rooted in genetic predispositions and other factors increasing disease severity and

burden of disease among minority populations might be lower level of health awareness, and inadequate access to care and disease prevention programs.

Socioeconomic factors emerge as an important indicator of health disparities. Socioeconomic barriers comprise of financial inadequacy and problems with housing, education, family and access to care (Hill-Briggs 2002). Paying for healthcare and prescriptions may compete with other basic needs and priorities and may create strong bottlenecks for access and adherence. Exploring the nature of these bottlenecks, a study by Heisler et al (2005) found that non whites were twice as likely to cut down on necessities and incur debt in order to cope with medication costs compared to the white respondents (Heisler, 2005). A comparison between prescription use among eligible Medicare beneficiaries in 10 states showed lower rates of filled prescriptions and pharmacy costs among African Americans in 8 states (Schore 2003). A study based on 2000 Behavioral Risk Factor Surveillance System data demonstrated that uninsured diabetic patients were more likely to have low incomes; African Americans and Hispanic patients were also more likely to be uninsured. Uninsured patients were less likely to report having annual dilated eye exams, foot examinations, Hba1c tests, and glucose monitoring than those with private health insurance (Nelson 2005). In another study of diabetic individuals based on the 3rd National Health and Nutrition Examination Survey (NHANES), Harris et al (1999) found that among those aged 20-64 years, higher proportion of non-Hispanic whites and non-Hispanic blacks were insured compared to Mexican Americans. Non-Hispanic whites (81%) had highest rate of private insurance coverage, followed by non-Hispanic blacks (56%) and Mexican-Americans (45%) (Harris 1999). Another study exploring relationships between access to diabetes care and health outcomes demonstrated that patients with restricted access to healthcare had higher HbA1c levels than those using acute care facilities and patients without a usual source of care reported

significantly higher Hba1c levels than patients receiving care at doctor's clinics (Rhee 2005). It has to be noted that the interaction of access issues and systems factors is not straight forward and more nuanced understanding of these factors need to be developed. A study found that in the context of diabetes, though access to healthcare is important, provider specialty (endocrinologist/primary care physician) might not have as much impact on quality of care (Greenfield 1995). Another study by Harris et al (2000) based on The National Health and Nutrition Examination Survey (NHANES) data found that high healthcare access and utilization rates for diabetes patients do not necessarily predict satisfactory health outcomes (Harris 2000), and factors such as health literacy, knowledge about disease management and trust in healthcare system may also play a significant part**.**

2.2 Developmental Disabilities (DD):

2.2.1 Introduction:

Developmental disabilities (DD) are a group of conditions that begin during the developmental period, and may result in physical, learning, language, or behavioral impairments. These conditions, affecting around one in six children in U.S., may impact a person's everyday functioning, and usually last through a person's lifetime (Boyle 2011).

Factors causing these disabilities are not specifically known. However, complex mix of factors such as genetics, parental health and behaviors during pregnancy, mother/child health during pregnancy/birth, exposure to toxins like lead, are thought to predispose individuals to developmental disabilities. According to recent estimates, about 15%, of children aged 3 through 17 years have one or more developmental disabilities. These disabilities include ADHD, autism,

cerebral palsy, hearing loss, intellectual disability, learning disability, vision impairment and other developmental delays (Boyle 2011).

2.2.2 Cerebral Palsy:

Cerebral palsy (CP), the most common childhood motor disability, affects a person's ability to move and maintain balance and posture. CP is caused by brain impairments affecting a person's ability to control his or her muscles. A person with severe CP may not be able to move at all, but someone with mild CP may be able to move, though slightly awkwardly, without special assistance. The manifestation of CP may vary depending upon the area of the brain being affected. These manifestations may include spasticity or stiff muscles, dyskinesia or diminished control over movement, and ataxia or poor control over balance and coordination (American Academy of Pediatrics Healthy Children website). Almost 40% of children with CP have intellectual disability (Kirby 2011).

According to CDC, the lifetime cost to care for an individual with CP is nearly $1 million (2003) dollars (CDC 2004). CP has no cure but early treatments may restrict the severe consequences to some extent. The available treatment options include medicines, surgery, braces, and physical, occupational, and speech therapy. Oral medications such as diazepam, baclofen, dantrolene sodium, and tizanidine are generally used to facilitate muscle movement and control. These drugs, in many cases, may have to be used in quantities that may cause side effects such as drowsiness, upset stomach, high blood pressure, and possible liver damage as a result of long-term use (National Institute of Neurological Disorders and Stroke website).

2.2.3 Down syndrome:

Down syndrome is a condition involving physical and mental problems that occurs when a child

is born with an extra copy of chromosome instead of the normal 46 chromosomes. This extra copy influences physical and mental development patterns and leads to physical and mental problems. Some usual physical signs of Down syndrome are: a flat face slanted towards the eyes, short neck, small ears, large tongue, small hands and feet, white spots on iris, a single crease across the palm of the hand, a small pinky finger curved towards the thumb, and poor muscle tone (National Center on Birth Defects and Developmental Disabilities website).

According to CDC estimates, in U.S., around 6000 babies are born each year with Down syndrome (Parker 2010). The manifestation of Down syndrome varies across children; some children with Down syndrome may have serious birth defects whereas some people with Down syndrome grow to adulthood and are relatively less affected. One of the key factors identified to be associated with Down syndrome is the mother's age; children born to mothers 35 years or older are more likely to have Down syndrome (Besser 2007). Though there is no known way to cure or prevent Down syndrome, therapy regimens including speech, occupational, and physical therapy are found helpful in infants and children (National Center on Birth Defects and Developmental Disabilities website(b)).

2.2.4 Autism:

Autism spectrum disorders (ASDs) refer to a group of developmental disabilities caused by some unidentified problem with the brain. Autistic people may not look different from people without ASD but they may be different in terms of learning, communication and behavior. The thinking and learning abilities among people with ASD may vary across a wide range, ranging from gifted to severely challenged. Besides, autistic disorder, one of the more commonly known ASDs, there are other less known ASDs such as "pervasive developmental disorder-not otherwise specified"

(PDD-NOS) and Asperger Syndrome (National Center on Birth Defects and Developmental Disabilities website(a)).

According to CDC, about 1 in 88 children in U.S. is affected by ASD, which is five time more common among boys than girls starting in early childhood, ASDs last through a person's lifetime (CDC 2012). People with ASD have higher medical expenditure than those without ASDs. Considering mean expenditure, the difference is $4,110-$6,200/year; the mean expenditure for people with ASDs is 4.1-6.2 times greater than those without ASDs. Similarly, difference in median expenditure between those with ASDs and those without ASDs is $2,240-$ 3,360 per year; median expenditure for those with ASDs being 8.4-9.5 times greater than those without ASDs (Shimabukuro 2008).

Available treatments for ASDs include therapy and training and some FDA approved medications. Therapies and training may involve a wide range of options depending on the symptoms. Some examples include auditory training, discrete trial training, vitamin therapy, anti-yeast therapy, facilitated communication, music therapy, occupational therapy, physical therapy, and sensory integration (Reichow 2009, Rogers 2008, Myers 2007, the National Institute of Mental Health website). The only two FDA approved medications for ASDs are antipsychotics risperidone (Risperdal) and aripripazole (Abilify) that can reduce irritability, aggression and the chances of individuals with ASDs harming themselves. Off label medications are prescribed by doctors if the medications have been approved to treat disorders with ASD like symptoms. (The National Institute of Mental Health website)

2.2.5 Intellectual disabilities:

Intellectual disability (ID)/cognitive disability, formerly known as mental retardation is a

condition that limits an individual's ability to develop and function at an expected level. The severity of ID varies in children and this creates challenges for them to express themselves or communicate their needs on a daily basis. The physical development and learning is delayed in individuals with ID compared to their peers without ID ((National Center on Birth Defects and Developmental Disabilities website(c)). ID is the most commonly occurring developmental disability. About 6.5 million people have ID in the US. 1 in 10 children receiving special education in the US has ID. In 2003, 7,98,345 Medicaid enrollees were disabled and out of these disabled enrollees, 13% had diabetes (National Dissemination Center for children with disabilities). In 2008, the Medicaid expenditure associated with disability was $136.61 billion (Cohen 2007). ID can be caused due to genetic mutation (Downs syndrome, fragile X syndrome, phenylketonuria), problems at birth (lack of oxygen during labor), health issue (whooping cough, the measles, or meningitis), malnutrition, exposure to poisons (lead, mercury), drinking during pregnancy, rubella infection in pregnant women and improper development of the fetus in mother's womb. (National Dissemination Center for children with disabilities website) ID can occur in individuals anytime before the age of 18 (American Association on Intellectual and Developmental Disabilities website). Children with ID might learn to talk, walk and run much later than other children of their age. They might also have trouble understanding social norms, rules, consequences of their actions and solving problems. ID can be diagnosed by healthcare professionals through intellectual functioning and through adaptive behavior. To measure intellectual functioning, the child's IQ is tested and to measure adaptive behavior, the abilities of the child with ID are compared with other children without ID ((National Center on Birth Defects and Developmental Disabilities website(c)).

Table: 2.5 Levels of intellectual/cognitive disabilities (Rocha 2013):

Mild	Moderate	Severe	Profound
• IQ 50-70 • Slower than normal in all areas • No unusual physical signs • Can learn practical skills • Reading and math skills up to grades 3-6 • Can conform socially • Can learn daily task skills • Functions in society	• IQ 35-49 • Noticeable delays, particularly speech • May have unusual physical signs • Can learn simple communication • Can learn elementary health and safety skills • Can participate in simple activities and self-care • Can perform supervised tasks • Can travel alone to familiar places	• IQ 20-34 • Significant delays in some areas; may walk late • Little or no communication skills, but some understanding of speech with some response • Can be taught daily routines and repetitive activities • May be trained in simple self-care • Needs direction and supervision socially	• IQ <20 • Significant delays in all areas • Congenital abnormalities present • Needs close supervision • Requires attendant care • May respond to regular physical and social activity • Not capable of self-care

2.2.6 Barriers and facilitators influencing access to care and healthcare utilization in patients with DD:

A) Availability:

There is a dearth of primary care physicians available to assist minority patients with DD residing in rural areas due to insufficient training. Among the few primary care health professionals willing to assist DD patients, the main reason for insufficient availability of health professionals is often attributed to the fact that their only source of payment is Medicaid. Factors such as low Medicaid reimbursements, need for prior reauthorization, long treatment duration, tiring paperwork, challenging process to coordinate services, rampant failure to treatment compliance, transportation issues for patients residing in rural areas, and poor follow up upon treatment completion limit access to primary care for DD patients.

a) *Provider availability:*

Many physicians do not possess the knowledge to treat patients with DD (Scott 1993). It is often challenging for minority families to find trustworthy physicians, specialists and auxiliary healthcare providers to treat DD patients (Caudle 1993, Cornelius 1993, Friedman 1994, Kindig 1993). Often families have to hunt for competent physicians that can treat DD patients (Reichard 2004).

b) *Coordination of healthcare:*

Coordinating care for treating minority patients with DD is often challenging in absence of case managers and at times families of such patients tend to rely on friends and acquaintances for procuring services of the appropriate healthcare providers (Reichard 2004).

c) *Information and referral systems:*

Information and referrals are often obtained from community based developmental disability organizations which are part of the state Medicaid, family members/caregivers of minority patients with DD also seek advice from social workers, family support workers and friends (Reichard 2004).

d) *Distance and transportation*:

Patients with DD residing in rural areas have to travel long distances or wait for a long duration in a physician's office to access specialized services. Caregivers who are family members, might, at times, have to miss work to take such patients for their physician visits. In case of adults with DD who cannot drive independently, lack of transportation limits access to healthcare services, physical

activity and recreation as well as attending health appointments and social exclusion (Rask 1994, Smith 1996, Crain 1998, Harbaugh 1998).

e) *Continuity of care*:

Continuity of care in minority patients with DD is associated with several factors such as presence of trust, good bedside mannerisms, affordability of care, good referrals, improvement in patient's health, absence of the need to explain patient history repeatedly by family members and specialty providers avoiding moving the health records of the DD patient every time they change a primary healthcare provider. Patients with DD have special needs which their primary care provider might understand with whom they share a unique relationship. DD patients often have acute illnesses and a new primary care provider might be unable to view their pain or distress in the light of their chronic condition (Lubin 2012).

B) Affordability:

Lower Medicaid reimbursement rates for physicians, enrollee inability to pay out of pocket expenditures, lifetime of spending caps, presence of administrative barriers and narrow eligibility standards are some of the issues that make it difficult for patients with DD to get access to the care that they need (Bolden 1993, Kopac 1998, Hughes 1996' Palfrey 1994). The basic care that is reimbursable for people eligible for Social Security Disability Insurance (SSDI) is often limited. For low income developmental disability patients who have other chronic conditions or disorders, often the cost of healthcare not covered by SSDI inhibits their access to care.

C) Accessibility:

Accessing care is often tough for non-English speaking patients (Woloshin 1995) and for

patients with cultural values different than the physicians' (Riddick, 1998, Vasquez 1991, Woloshin 1995).

a) Clinical logistics:

Apart from linguistic barriers, minority patients with DD tend to face physical barriers such as lack of wheel chair friendly examination rooms. Such patients might not be able to use the standard height examination table which might result in them wasting time changing tables during their visit; this may also make it difficult for the physician to properly position and examine the patient. Minority patients with DD might also have difficulty performing their daily activities at their homes without additional facilities such as enlarged door frames, ramps or additional bathroom equipment (Reichard 2004, Lubin 2012).

b) Emotional support:

Patients with DD with less community integration and lack of emotional support tend to feel isolated. The National Core Indicators Survey conducted among patients with DD residing in North Carolina in 2001 and in New York in 2009 have shown that adults with DD feel that they receive inadequate social support almost seven times more than their peers without DD and many of them have no thriving social circles with no friends or dates (Havercamp 2004, NYS Core Indicators Report, 2009).

c) Competency of healthcare provider:

I)Knowledge:

Physicians and other healthcare providers should possess general knowledge about what constitutes disability, different types of DD, clinical knowledge of DD including causes, symptoms, characteristics, and the natural history of DD, as well as the specific comorbidities associated with developmental disabilities. In addition to knowing about the theoretical aspect of the different conditions that constitute DD, knowledge about providing actual care by means of performing diagnostic testing and developmental screening, providing psychotropic medications, designing behavioral interventions and using adaptive equipment for the management of the different conditions is also necessary for healthcare providers. Providing referrals to healthcare agencies and community resources to support DD patients and knowledge about the eligibility criteria to get access to care can impact the healthcare utilization and quality of care delivered among DD patients.

II)Skills:

(i) Patient healthcare practitioner relationship/communication

The unique and complex medical condition of DD patients requires more specialized considerations from physicians as well as the health delivery system including insurance and Medicaid. The relationship between patients and Healthcare practitioners is restricted, in many cases, by the inability of the patient to articulate his problems and needs and also by the assumption of the providers

that it is patients' responsibility to advocate and communicate their health concerns (Boyer & Lutfey, 2010). Many patients struggle with complex sets of problems and symptoms and are not able to communicate effectively due to their condition. This inability to communicate not only affects their everyday lives but also extends to their treatment/therapy process. Practitioners expect patients and their families to share information with them that forms the basis of the treatment/care provided to them. This absence of effective information sharing and communication may affect the quality of care the patient receives. In order to address this issue, practitioners need to be more sensitive to the special needs of the patients. They should try to create more scope for effective communication and understanding of patients' problems and needs by seeking information in a more understanding and patient manner and allowing additional time for consultation.

From the systems perspective, the special needs of the patients should be acknowledged and should be incorporated while deciding on the nature of coverage they receive. Patients with DD have more complex health problems than general populations and may need more access to medical resources indicated by higher number of healthcare visits among DD population. Medicaid coverage for individuals with DD is same as the Medicaid coverage for general population, even though individuals with DD may have different types of issues at different rates that may experience differently than general population. This issue can be addressed by developing deeper understanding of the need of population with DD

and developing solutions at systems level that are sensitive to these needs (Boyer & Lutfey,2010).

(ii) Patient informal/paid caregiver relationship:

Besides healthcare practitioners such as physicians, nurses, pharmacists, physiotherapists, and occupational therapists, many other people may help provide care to individuals with DD. These people, considered caregivers, may not necessarily have professional training in providing care and may involve informal caregivers such as family members, friends, and formal paid caregivers. Caregivers generally help manage medications and treatment, and help with activities involved with daily living, household chores and responsibilities, and communicate with healthcare practitioners. Caregivers may bring in advantages like life experience and understanding of patient's needs and personalities that may enable them to have effective interpersonal relationship and communication with the patients (Lau 2010).

Understanding of patient's expectation and environments may also enable them to take decisive action and overcome fear of making medication errors. On the other hand, many factors may also form barriers in effective functioning of caregivers. These factors may involve cognitive and physical limitations, negative influences of close relationships with patients, negative emotional states, and competing responsibilities. Cognitive and physical limitations may involve conditions due to old age and various other factors like lack of literacy and lack of linguistic skills that may impede effective medication management and communication with practitioners. Close relationship with patients may also cloud the judgment of the

caregivers and may lead to them resisting treatment plans and focusing on their own conveniences rather than on patients' comfort and needs. Negative emotional states like grief, frustration, or fatigue may also influence caregiver's decision-making. Also, many caregivers, especially family members, may have other competing responsibilities such as managing their employment responsibilities, and running the household involving other dependents, that may influence their performance and decision making as caregivers. The burden on the primary caregiver can be reduced due to support from multiple caregivers that may also include hired caregiver. However, having multiple caregivers may also have drawbacks as bad interpersonal relationships and lack of communication and understanding between caregivers may negatively influence the medication management process (Lau 2010).

(iii) Physician informal/paid caregiver relationship:

Physicians should effectively communicate the patient's condition and progress to the caregivers and family members and inform them about the patient's wishes and values about advance care planning. Physicians should acknowledge the role of caregivers in providing intellectual and emotional transition for chronic disease patients on death bed, consider the challenges that caregivers who are geographically distant face, be able to detect distress among caregivers and provide them referrals accordingly, appreciate the role of caregivers as part of patient's medical and psychosocial history, and make provisions for the wellbeing of the patients as well as their caregivers via a palliative care plan or a caregiver specific care plan. They should also set boundaries between themselves and

professional caregivers with regards to the specific services provided to prevent conflict, validate the caregiver's role on a regular basis, and respect the caregiver's commitment to provide patient care (MDNEWS website).

(iv)Observation skills:

Healthcare provider's keen sense of observation can play an important role in proactively identifying and managing conditions that affect the health of the patients with DD. Observing DD patients' behavior, developing the ability in differentiating the subtle changes in the patient behavior and paying attention to the caregiver reports about patient behavioral changes, even though time consuming and demanding openness on part of the healthcare provider, can aid in providing medical attention to the DD patients.

(v) Ability to recognize that a person with developmental disabilities may not be able to be served in a typical medical setting:

Adults with DD might have difficulty in accessing care in typical health settings and settings such as patient homes and board and care facilities might be preferred. For instance, special diagnostic equipment suitable for screening or examining adults with DD might have to be arranged. Also, convincing the patients to undergo physical exams and assisting patients with physical positioning while examining them may require careful preplanning and investment of extra time and patience on healthcare provider's behalf. Healthcare providers should have the ability to recognize these special needs of the patients with DD, acknowledge them, and assist the patients.

(vi) Ability to identify, coordinate, and communicate with members of the patient's

interdisciplinary team:

Healthcare providers' ability to identify, coordinate and communicate with the multi-disciplinary team comprising of caregivers, specialty physicians, case coordinators and service providers can ensure that adults with DD receive comprehensive care and their treatment plan is assessed by a variety of experts. Communicating with community partners and agencies can also prove to be a useful resource to direct the patients with DD towards the much-needed services.

III)Attitudes:

(i) Cultural insensitivity:

Another issue that needs attention in the context of patients with DD is cultural insensitivity. Though such patients may be affected by the insensitivity on the basis of factors like race and gender, which also affect general patient population, they may also face problems due to insensitivity to their disabilities and the negative social attitudes associated with them (Reichard 2004). Training providers and caregivers about culturally appropriate behavior that also takes into account the disability culture may help attain cultural sensitivity. Some example of culturally sensitive behavior may include respectful language and terminologies related to patient's condition, and providing language assistance when needed to communicate with the patient (University of California at San Francisco website). Harboring a patient and family centered attitude can foster trust and confidence about the healthcare provider among the patients with DD and their families. Healthcare providers should show respect for the needs of the patient, make

patients and their families part of the healthcare decision making process, use the right terminology while addressing the patients, and converse with them directly.

(ii) Physician Conscientiousness:

Inability of the patients with DD to communicate their symptoms or have a regular follow up with their healthcare providers can make the diagnosis challenging and can result in medical decision making with incomplete information and failure of the planned therapy. Healthcare providers should be flexible, compassionate, possess good listening skills, be understanding towards the day to day challenges contributing to therapy non-compliance in DD patients, and be sensitive to their needs including their living conditions and the special accommodations that they need. In situations where patients with DD might not be able to vocalize their health concerns or symptoms, healthcare providers should be receptive to the concerns comprehended by the families of the patients or formal caregivers or health advocates.

d) Physician services during visits:

(I)Specialist services:

Specialist services are an important part of treatment regimen for adults with DD. A study conducted in adults aged 20-50 years with DD living in Sydney, Australia found that these adults had a greater need of visiting hospitals, by as much as two times more, compared to adults without DD (Beange 1995, Wallace 2008). Adults with DD often require many specialist services, which involves their primary healthcare physician partnering with several healthcare specialists such as

physiotherapists, occupational and language therapists, and mental healthcare providers to assist with motor and communication skills, coordination, speech, morale, and better bonding with the society. Disparities in access to specialized services occur among adults with DD due to lack of formal training among physicians to provide care to patients with DD and help them transition through different stages of adult life (Linsey 2002).

(II)Outpatient services:

There is a need for establishing local outpatient healthcare facilities that can

specifically fulfill mental and physical health needs in adults with DD. Adults with DD visit the ED department to a far larger extent compared to adults without DD; this can be attributed to the lack of sufficient centers providing specialized outpatient services to this unique group of patients and lack of continuity of primary and specialist care (Lunsky 2012).

(III)Family training:

Many adults with DD live with their families and at times it is possible that the family members who are also their informal caregivers are unaware about the needs for regular physician visits and screenings that have to be conducted from time to time. In a survey study administered to adults with DD aged 18 years and older and their informal caregivers/family members residing in Victoria, Australia, researchers found that compared to adults with DD living with their family members, adults with DD living in communities visited their primary care

physician about two to five times more and also underwent more health
screenings for metabolic and cardiovascular disorders. (Iacono 2006)

(IV)Cooperation with service providers:

Lack of physician training is one of the major barriers that impedes them from
providing the appropriate therapy and reaching out to the patients with DD.
Collaboration among different healthcare professionals at the local and national
level is essential to develop standards of care for patients with DD. Dissemination
of information and better understanding and training to cater to the emotional and
specialized physical needs of the adults with DD on a continuous basis may also
help improve the quality of care (Meuwese-Jongejeugd 2005).

D) Appropriateness:

a) Healthcare needs met:

Inability to take into consideration the wishes of patients and their caregivers, lack
of sufficient counseling, communication barriers, lack of structural
accommodations, and inability to properly screen patients or schedule them for
visits pose hurdles to access of care among minority patients with DD residing in
segregated neighborhoods; these factors may also contribute to increase in disease
severity (Hughes 1996, Bolden 1993, Kopac 1998, Palfrey 1994).

b) Quality of care:

Healthcare professionals who are respectful, honest and considerate towards the
needs of individuals with DD tend to provide better quality of care (Darling 1994,

Simons 1987, Wilson 1994). Practices such as providing incorrect treatment, withholding information concerning the health of the minority patients with DD, delaying the necessary treatment, or having insufficient time to provide care are regarded inappropriate by the caregivers of the minority patients with DD (Ebert 1995, McEwen 1988, Welner, 1998, Brooks 1997, Barnett 1988, Grabois 1999, Reichard 2001, Nosek 1995, Ralston 1996).

2.2.7 Chronic disease management in patients with developmental disabilities

Patients with DD have a higher risk of developing type 2 diabetes as well as a higher prevalence of the same. Sedentary lifestyle, poor nutrition and high rates of obesity can lead to an increased risk of type 2 diabetes in patients with DD. (Yamaki 2005, Rimmer 2006). Also, compared to DD patients living in supported housing and residential facilities, the BMI and the risk of developing type 2 diabetes are higher in DD patients living with their families or living on their own. When DD patients live independently, there is a higher likelihood of leading an unhealthy lifestyle with less dietary restrictions (Taggart 2012).

Patients with type 2 diabetes have the following symptoms: fatigue, increased thirst, headaches, blurred vision, increase in frequency of urination, difficulty in concentrating, loss of weight, changes in mood, withdrawal, agitation and verbal and physical aggression. (UKPDS 1998) The onset of type 2 diabetes is generally slower and there is a possibility that the disease condition remains undiagnosed for a long duration in patients with DD. Symptoms of type 2 diabetes in DD patients can be difficult to detect due to challenges faced by this population in communication, or the medication that is being prescribed for pre-existing conditions or the health behavior displayed. This masking of the symptoms due to various reasons is also known

as 'diagnostic overshadowing'. Diagnostic overshadowing might make it difficult for the staff to provide the patients with the necessary care that they need to delay or prevent type 2 diabetes (UKPDS 1998, Taggart 2012).

In North America, the prevalence of type 2 diabetes in the DD population can vary from 7.1% to 14% (Havercamp 2004, Shiremen 2010, McDermott 2006, Lunsky 2011). Besides type 2 diabetes, the prevalence of cardiovascular complications and healthcare utilization is also higher in the DD population. A study in Northern Sydney showed that among people with DD, prevalence of type 2 diabetes complications, medical consultations, inpatient visits and mortality were higher compared to the people without DD. The study population also had many undetected conditions. Out of the 5.4 medical conditions that each patient had on an average, half the conditions were undetected during previous physician visits (Beange 1995). Another similar study conducted by Lennox et al (2007) also showed that the large number of people with DD who were diabetic and obese, went undiagnosed or without any management. When patients are diagnosed with diabetes, as part of their annual regimen, they are subjected to a screening whereby their primary care physician can diagnose other chronic comorbidities associated with diabetes. Many type 2 diabetes patients have hypertension and CVD, which can cause mortality in type 2 diabetes patients. As a result, proper statin therapy and anti-hypertensive medication therapy are needed to control CVD and BP to control disease severity in type 2 diabetes patients (UKPDS 1998). However, there is a high likelihood that diabetic patients with DD get screened less compared to diabetics without DD due to fewer opportunities to actively engage in educational sessions pertaining to disease screening. Also, diabetes management can become quite difficult in case of patients with DD who live in shared housing away from their homes, with people who have similar conditions. The paid caregivers who aid these patients in managing

their diabetes may be apprehensive and may perceive that they are unable to provide the necessary care. In many cases, the turnover of the caregivers is quite high which might interfere with the continuity of diabetes care provided to the DD patients (Rey-Conde 2007). This indicates that diabetics with DD are at a greater disadvantage, in spite of being at a higher risk to developing diabetes related complications due to under diagnosis. This can be avoided if DD patients are screened annually given the increased proclivity to a sedentary lifestyle. ADA has several guidelines and supporting research studies for preventing or delaying type 2 diabetes in pre diabetic patients at a higher risk of developing type 2 diabetes through appropriate lifestyle interventions and proper diet intake (ADA 2002).

2.2.8 Racial health disparities in patients with developmental disabilities

Adults with DD have high health risk behaviors, inadequate emotional support and poor healthcare utilization compared to disabled adults without DD. A study conducted using the 2001 North Carolina Behavioral Risk Factor Surveillance System and the North Carolina National Core Indicators survey showed that compared to disabled adults with DD, adults with DD had a significantly higher prevalence of chronic disease conditions such as diabetes, obesity, high blood pressure, arthritis, CVD and chronic pain. They were also more likely to be sedentary, performed less amount of physical activity, received seven times less emotional support and had low breast cancer and cervical cancer screenings (Havercamp 2004, Ouellette-Kuntz 2005). Studies conducted in Ontario among adults with DD showed that they had significantly higher rates of undiagnosed disease conditions and higher rates of inpatient visits for ambulatory care sensitive conditions (Ouellette-Kuntz 2005). The comorbid conditions associated with DD are more prevalent among adults with low income who also face socioeconomic disparities in seeking healthcare. Minority patients with DD face cultural and language barriers in accessing

healthcare and therefore have poor health outcomes (Surgeon General Report 2002). In studies conducted in US and Australia, mortality rate was higher among African Americans adults with Down syndrome compared to Caucasians and among aboriginal adults with DD (Ouellette-Kuntz 2005). Among racial minority adults with an emotional or physical or mental disability, who require special equipment for performing day to day functions, disparity seems to exist while reporting health status. The percentage of African Americans, Hispanics, Asians and Native Americans with disabilities reporting fair or poor health are 50%, 50%, 38% and 52% compared to 11%, 19%, 6% and 9% of African Americans, Hispanics, Asians and Native Americans without disabilities (Drum 2011). There seems to be a necessity to design culturally appropriate health prevention and health promotion interventions for minorities.

2.2.9 Quality of care in diabetic adults with developmental disabilities

It is important to study quality of care in patients with DD since it is an important contributing factor to better healthcare service utilization and healthcare outcomes in patients with DD. Racial and ethnic disparities in quality of care persist due to a variety of barriers such as socioeconomic status, segregation, language barriers, and discrimination (LaVesit 2008, Yu 2009, Rust 2007). Comprehensive diabetes management includes monitoring HbA1c and serum lipids and getting eye examinations on an annual or semiannual basis to prevent diabetes severity, less utilization of health resources and improved quality of life. The quality of diabetes management or in other words, the quality of the care provided to the diabetic patients can be determined by the extent to which the healthcare providers adhere to the quality indicators and evidence based guidelines provided by accreditation organizations such as the National Committee for Quality Assurance (NCQA). The Healthcare Effectiveness Data and Information Set (HEDIS) is a quality of care performance assessment tool developed by the NCQA (QEHO website). NCQA is an US based

non-profit organization that provides accreditation and HEDIS measures to the healthcare plans who in turn report those measures, indicating the quality of care provided to their employers. The HEDIS also assesses quality of diabetes care for health plan enrollees aged 18-75 years through a variety of measures that indicate management of diabetes and its related complications. These measures look at the number of people who get tested for HbA1c level, have a poorly controlled HbA1c of more than 9%, have a HbA1c level of less than 8% during the first year of diabetes diagnosis, are screened for serum cholesterol level (LDL-C), have LDL-C level less than 100 mg/dl, have an eye exam done and have blood pressure of 130/80 mmHg (NCQA 2006). HEDIS measures used to compare quality of diabetes care in different patient groups are reliable, consistent, defined in a detailed manner and are updated on a regular basis (HEDIS website).

The 2008 National Committee for Quality Assurance (NCQA) report about the state of healthcare quality states that the quality of comprehensive diabetes care is high in patients enrolled in both the Medicare and the private health plans. Compared to 77% diabetics enrolled in Medicaid who get their annual HbA1c monitored, 88% of the Medicare and private insurance enrollees get their annual HbA1c monitored. Similar statistics were reported for LDL-C screening and eye examinations. Compared to 71% and 50% Medicaid enrollees undergoing LDL-C screening and eye examinations respectively, about 83% and 55% Medicare and private insurance enrollees had their LDL-C screening and eye examinations respectively (NCQA 2008). These results were similar to a study conducted within the Kansas Medicaid population in 2006-2007. This study showed that although 93.5% Medicaid enrollees had at least one annual primary care visit, only 51.7%, 44.3%, 29.3% and 18.5% Medicaid enrollees got their annual HbA1c monitored, cholesterol screened, eye examined and micro albuminaria screened respectively (Shireman 2010). The Medicare and private insurance enrollees receive better quality of care

compared to the Medicaid enrollees. However, there is a disparity in the delivery of quality diabetes care even among the Medicaid enrollees, and managed care Medicaid enrollees tend to receive enhanced diabetes care compared to the fee for service Medicaid enrollees (Landon 2007, Roohan 2006).

Research about treatment of comorbid conditions using evidence based guidelines in hypothetical patients has shown that it yields marginal benefits and is an expensive process (Boyd 2005, Tinetti 2004). Evidence based guidelines about a target condition might not consider the related complicated comorbid conditions and patient preferences, thus causing unintended consequences or harm. Also, at times applying evidence based care for two existing conditions might interact negatively or clinicians might perceive that aggressively providing evidence based care might bring little change to the diabetes management of the patients due to their DD. The neurologic, psychiatric and physical impairment in DD patients might discourage the physicians from providing diabetes care similar to that being provided to diabetes patients without DD (Nuyen 2005, Doescher 2000, Reschovsky 2008, Betancourt 2004, Reichard 2004).

Even though previous research indicates that providing evidence based care in patients with multiple comorbidities impacts quality of care due to risk of adverse events and, probability of overlapping guidelines and clinicians divesting time focusing on several aspects of patient care, the research does not focus on patients with DD (Rost 2000, Field 2004, Tinetti 2004). Management of diabetes reduces mortality and improves quality of life. There are very few evidence based guidelines for patients with comorbid conditions since such patients are not included in randomized controlled trials conducted to generate evidence for framing evidence based guidelines for disease conditions. Evidence based guidelines for diabetes management focus only on diabetes and not on the comorbid conditions related to diabetes. Improving

diabetes care in DD patients requires a team based patient centered approach, and not a disease oriented approach since integrating individual patient needs with the disease perspective is a characteristic of effective care (Starfield 2003).

2.3 Theoretical model

This study examines the predictors of type 2 diabetes medication adherence in DD Medicaid enrollees. It also further explores the impact of medication adherence on patients' healthcare utilization and costs. The theoretical framework for this study is based on two health behavior models. One model is the modification of health belief model by Becker and Maiman that describes the association of sociobehavioral determinants of adherence with health and medical recommendations. The other model is the Aday-Andersen's model for healthcare utilization. According to this model, healthcare utilization is a function of three sets of determinants: predisposing factors, enabling factors, and need-related factors. The detailed explanation of both the models is provided below in the following sections:

2.3.1 Health Belief model:

The health belief model (HBM) is a psychological model based on value expectancy theory. HBM posits to explain individual behavior under uncertain circumstances. According to the model, individuals desire to avoid illness or become healthy by believing in the performance of certain actions. HBM, which was initially used to explain screening behaviors by Rosenstock was further adapted to explain preventive care, illness behavior and sick-role behavior. HBM proposes that the action taken by individuals to prevent illness occurs only under certain possibilities are met such as a) in the presence of the risk of developing a condition and provided this risk is higher in propensity compared to the predisposed high risk already associated with the

disease condition or b) the feeling that undertaking appropriate actions will have serious implications or c) the feeling that the undertaking actions will decrease the susceptibility to disease or severity of the disease condition or d) if more benefit is perceived compared to more harm given the performance of the intended action.

The HBM consists of six components:

(1) **Perceived threat**: This indicates an individual's perceived susceptibility to contract a disease condition.

(2) **Perceived severity**: This indicates the importance that is placed on a disease condition and the consequences of non-treatment of the same.

(3) **Perceived benefit**: This indicates the patient's perception about the effectiveness of the action to mitigate the perceived severity of the disease. The rationale behind this is that an appropriate action will be performed to alleviate the perceived threat, and the action chosen will be beneficial to the person taking it.

(4) **Perceived barriers**: These are the barriers that prevent an individual from taking the required action that prevents illness. Before executing the actual action, the individual tries to contemplate if the benefits of the intended action outweigh its risks

(5) **Cues to action**: The factors that determine an individual's readiness to take action, act as cues for initiating that particular action. These factors could be internal such as physical sensation or external such as stimulus triggered by mass media to encourage beneficial health behavior.

(6) **Self efficacy**: This indicates the patient's belief in successfully executing the health behavior in order to experience the desired outcomes (Becker 1967, Kogan 1964, Becker 1974, Rosenstock 1990, Fishbein 2001, Strecher 2008, Rosenstock 1966, Feather 1959, Rosenstock

1975, Janz 1984).

Individual perceptions	Modifying factors	Likelihood of action

Modifying factors
Demographic variables (age, sex etc),
Sociopsychological variables (personality, social class etc.)

Perceived benefits (avoiding hospitalization) minus perceived barriers (cost of medications, insurance) to behavior change

Perceived susceptibility to severity of disease : Diagnosis of diabetes, severity of diabetes

Perceived threat of disease

Likelihood of behavior change: Increased medication use

Cues to action Education, counseling, disease management, symptoms

Figure 2.2 Original Health Belief Model developed by Rosenstock

2.3.2 The modified Health Belief Model by Backer and Maiman

Health Belief Model (HBM) was originally proposed to explain general preventive health behavior and since has been modified to explain behavior in a wide range of health behavior

contexts. The Becker and Maiman model (1975), derived from the Health Belief Model, was specific to adherence and persistence as target behaviors. This modified model by Becker and Maiman conceptualizes three dimensions as primary contributors to adherence behavior. These are:

1. **Readiness to undertake recommended adherence behavior**: The key contributors to this dimension are the perceptions of 'susceptibility' and 'severity'; here 'susceptibility' refers to the perceived likelihood of getting affected by an illness and 'severity' refers to the extent of perceived consequences of the illness. This component is influenced by a range of factors like patients' motivations (concern about health issues, willingness to seek and implement medical advice,), value of illness threat reduction (perceived vulnerability, presence of symptoms etc) and patients' perceptions about the efficaciousness of the recommended behavior.

2. **Modifying and enabling factors**: These factors modify the patient readiness towards the recommended behavior. They involve the individual's evaluation of the behavior in terms of its feasibility and effectiveness, and potential barriers to performance of the behavior. These may include a wide range of factors such as demographic, structural, interaction based, attitudinal, and enabling factors. This study included demographic, clinical and medication related variables as part of predisposing, modifying and enabling factors to measure medication adherence in the study population.

3. **Compliant behavior:** This is the likelihood of the patients' adherence with recommended health behavior. The modified model proposed in this study examined patient outcomes such as healthcare costs and healthcare utilization as a consequence of medication adherence in type 2 diabetes Medicaid patients aged 18- 65 years (Becker 1975).

Readiness to undertake compliant behavior	Enabling and Modifying factors	Adherent behavior

Motivations

Concerns about health matters in general
Willingness to seek and accept medical directions
Intention to comply

Value of illness threat reduction
Subjective estimate of:
Susceptibility
Vulnerability to illness
Extent of possible bodily harm
Extent of possible interference with social roles
Presence of symptoms

Probability that compliant behavior will reduce the threat

Subjective estimate of:
Proposed regimen's safety
Proposed regimen's efficacy to prevent, delay or cure (incl. "faith in doctors and medical care" and "chance of recovery")

Demographic (very young or old)

Structural (cost, duration, complexity, side effects, accessibility of regimen; need for new patterns of behavior)

Attitudes (satisfaction with physician, other staff, clinic procedures and facilities)

Interaction (length, depth, continuity, quality and type of patient-provider relationship, mutuality of expectation, physician agreement with patient; feedback to patient etc)

Enabling (prior experience with action, illness or regimen, source of advice and referral, social pressure)

Likelihood of adherence with preventive health recommendations and prescribed regimen: e.g., screening, immunizations, prophylactic exams, drugs, diet, exercise, personal and work habits, follow-up tests, referrals and follow-up appointments, entering or continuing a treatment

2.3.2 Modification of Health Belief Model by Becker and Maiman

2.3.3 Application of Health Belief Model to type 2 diabetes

(A) Patient beliefs:

According to Gentili et al (2001), Health Belief Model is an appropriate framework to plan diabetes management programs and develop approaches for counseling diabetic patients (Gentili 2001). The four key predictors of health behavior according to HBM are perceived susceptibility, perceived severity, perceived benefit, and perceived barriers. In the context of diabetes, variations in perceived susceptibility may alter patients' estimation of their chance of contracting diabetes; patients with higher perceived susceptibility may be more likely to follow the recommended health behavior. For example, someone whose parents are diabetic may consider oneself more susceptible and therefore is more likely to perform the recommended health behavior. Perceived severity refers to the extent/degree of negative consequences associated with the illness. Perceived severity in diabetes patients may include evaluation of consequences such as inpatient visits and co morbidities, or consequences related to cost and life style changes. The perceived benefits associated with diabetes patients' adherence to recommended behaviors are improved glycemic control, reduction in healthcare costs, and overall, a better quality of life. Patients may face different barriers like unwanted side-effects, difficult dosing regimen, and medication costs and be unwilling to make lifestyle and dietary modifications.

(B) Caregiver Beliefs:

In case of patients who are severely cognitively impaired, symptom management can be largely driven by caregiver knowledge and beliefs. In case of patients who are entirely dependent on caregivers for self-care, feelings of isolation, depression, loneliness, fear and anxiety can be seen

in caregivers. At times, caregivers who also work can have limited time for themselves due to the care giving demands. Increase in work responsibility can result in frustration among caregivers which can manifest in the form of neglect for the patients. Caregivers may also engage in behaviors such as yelling, withholding food and hitting or neglect patient's nutrition and pain management. Caregivers might believe that they are unable to care for the patients due to patient's cognitive impairment, when care giving is criticized or when care givers take wrong care decisions (Reinhard 2008). One of the issues that caregivers grapple with is pain management in DD patients. Caregivers provide care, medications, social support, comfort, measuring blood sugar, interpreting symptoms and making care decisions for the DD patients. For performing their duties appropriately, caregivers need training for monitoring and differentiating patient symptoms, reporting those symptoms to physicians and procuring services from community agencies. Caregivers also have to gain knowledge about disease management. Caregiver beliefs about providing relief to the patients from their pain depend essentially on their understanding of the patient symptoms. Caregivers, who believe that the patient is in pain, might make an inaccurate assessment while caring for patients with communication difficulties. (Reinhard 2008) In a study conducted by Allen et al (2002), researchers found that the perception of pain in caregivers of cognitively impaired patients was the same as caregivers of patients without cognitive impairment. The study also found that 3.4% caregivers were unable to precieve the patient's pain when the patient was actually in pain. On the other hand, almost 29% of patients were not in pain but their caregivers perceived that they were in pain. Family caregivers tend to rely more on non verbal cues of pain in patients with cognitive impairment. Female patients tend to respond more to pain and possess more knowledge about pain management (Allen 2002). Focusing on interventions based on educating caregivers about

chronic disease management including pain can help them in better assessment of the patient symptoms, improve their attitudes and knowledge, make them more confident and can reduce their depression, fatigue and anxiety (Ferell 1995).

2.3.4 The Aday Andersen model for healthcare utilization

The Aday Anderson's model of healthcare utilization has been used extensively to study healthcare seeking behaving and predicting healthcare utilization. According to the model several factors are responsible for determining healthcare utilization and these factors have been clubbed under three main factors: predisposing factors, enabling factors, and need-related factors. The model posits how different factors influence an individual's propensity, ability and need to access the available resources that result in medication usage and healthcare service utilization (Aday 1974, Andersen 1995). The model provides an understanding of the characteristics of the vulnerable population at risk. The three factors are described as follows:

Predisposing factors: These factors exist in individuals or group of individuals prior to them having the disease condition. These factors indicate the tendency of the individuals towards utilization of healthcare services and they include socio-demographic characteristics like patient age, gender, race, education level etc. (Aday 1974, Andersen 1995).

Enabling factors: These factors consist of the means that affect an individual's predisposition to utilize healthcare services i.e. they influence the accessibility to services and insurance status, access to care, source of care and income level (Aday 1974, Andersen 1995).

Need factors: These include self-perception of individuals about their health status and the evaluation of the individual's healthcare provider. They comprise of perceived health status, severity of disease, number of physician visits, presence of comorbidities and quality of life (Aday 1974, Andersen 1995).
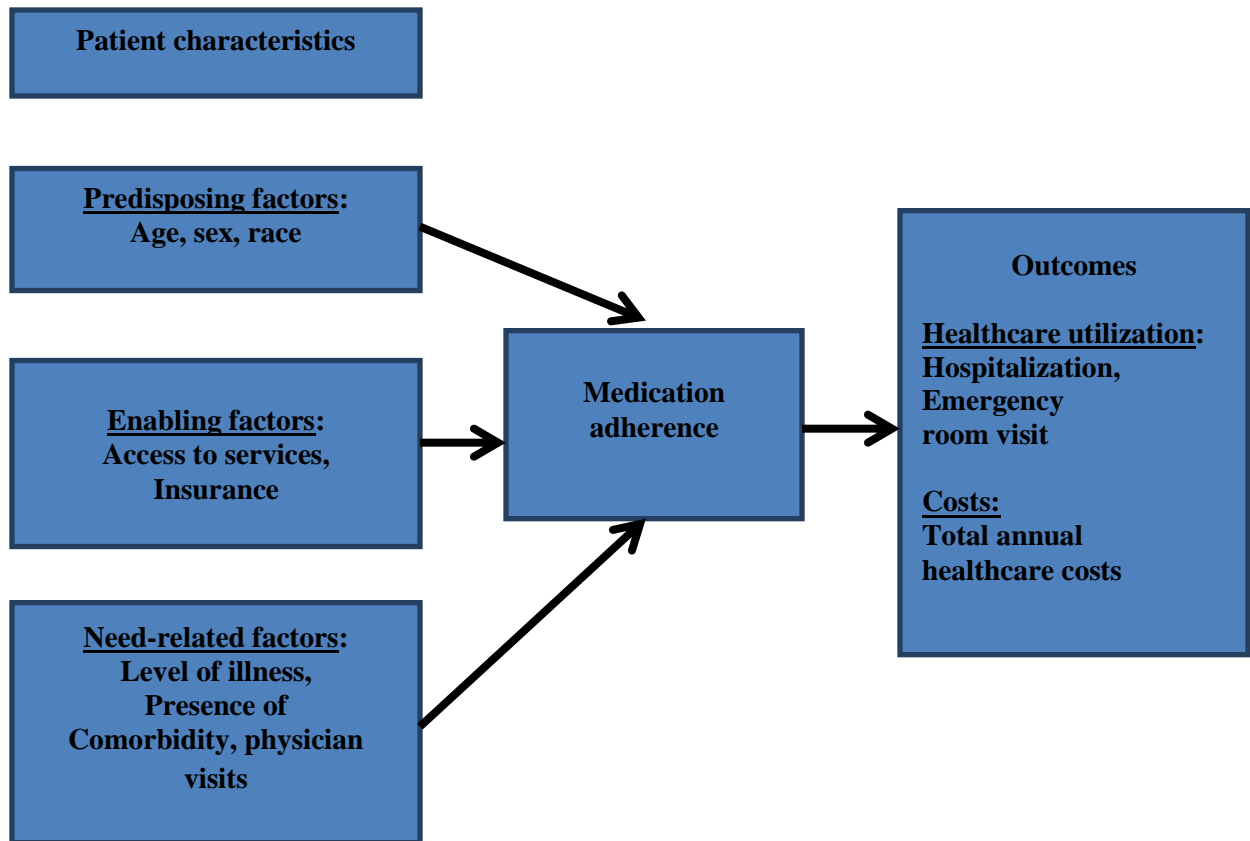
Figure 2.4. The Aday-Andersen Model for determinants of healthcare utilization

2.3.5 Theoretical model proposed for the study

The proposed model for this study was based on the Health belief model and the Aday Andersen's model of healthcare utilization (Figure 2.3.5) (Aday 1997, Andersen 1973, Andersen 1995, Becker 1975). The Aday Andersen's model is based on the premise that healthcare outcomes are a result of a) factors that predispose individuals to seek care, b) factors that might enhance or pose barriers to access care and c) factors that can aid the healthcare professionals or patients to make an assessment about their health status. Together the predisposing, enabling and need factors determine the patient's health behavior and outcomes.

In the proposed model, the predisposing factors were race, gender, age and patient/caregiver health beliefs. The enabling factors that could improve or impede access to care were availability

of care, affordability of care, accessibility to healthcare services and appropriateness of healthcare services. Factors such as access to physician services and clinical logistics (accessibility to healthcare services) or information and referral systems (availability of care) were included as part of enabling factors since the study looks at Medicaid enrollees with DD, a highly vulnerable population. The need factors in the model that determined the need to seek care were level of illness, presence of comorbidities and number of prescription refills. In addition to type 2 diabetes, presence of other chronic disease conditions were accounted for, by including them in the Charlson comorbidity index.

The proposed model shows an interaction between race and medication adherence. The interaction allows for determining the influence of race and medication adherence on healthcare utilization and healthcare costs at many different levels. These levels can be classified as Caucasians with high medication adherence, Caucasians with low medication adherence, African Americans with high medication adherence and African Americans with low medication adherence. The influence of these levels on the health outcomes were measured after controlling other covariates (Mobley 2009).

Health behavior, according to the proposed model, was determined by the predisposing, enabling and the need factors. In turn, health behavior influenced health outcomes. The health behavior variables in this study were anti diabetic medication adherence and medication persistence that influenced healthcare utilization (inpatient visits, outpatient visits and ER visits) and healthcare costs (medication costs, inpatient and outpatient costs and overall costs). The model has many covariates that are part of enabling factors such as availability of care, accessibility to healthcare services and appropriateness of healthcare services. There is evidence that supports that these variables impact health outcomes but due to their unavailability in the dataset, they could not be

measured. The stronger influence of predisposing factors (race) and enabling factors (health insurance, income) on healthcare utilization compared to need factors can indicate disparity in access to care whereas the stronger influence of need factors on healthcare utilization compared to predisposing and enabling factors can indicate equitable access to care (Aday 1997).

Predisposing factors:

A) Age
B) Sex
C) Race
D) Patient/caregiver health beliefs

The Combined Effects
A) Diabetic Caucasian patients with DD and lower medication adherence
B) Diabetic Caucasian patients with DD and higher medication adherence
C) Diabetic African-American patients with DD and lower medication adherence
D) Diabetic African-American patients with DD and higher medication adherence

Medication adherence
Medication persistence

Outcomes
A)Healthcare utilization:
(i) *Inpatient visits*
(ii) *Outpatient visits*
(iii) *ER visits*
B)Costs:
(i)*Medication healthcare cost*
(ii)*Medical healthcare costs*
(ii)*Overall medication costs*

Enabling factors:
A)Availability

a)Provider availability
b)Coordination of healthcare
c)Information and referral systems
d)Distance and transportation
e)Continuity of care

B) Affordability

Insurance [type of health plan (FFS/capitation)]

C) Accessibility to services

(a)Clinical logistics
(b)Emotional support
(c)Competency of healthcare provider

(i)Knowledge

(ii) Skills
    *Patient healthcare practitioner relationship/communication
    *Patient informal/paid caregiver relationship
    *Physician informal/paid caregiver relationship
    *Observation skills
    *Ability to recognize that a person with developmental disabilities may not be able to be served in a typical medical setting
    *Ability to identify, coordinate, and communicate with members of the patient's interdisciplinary team

(iii) Attitudes
    *Cultural insensitivity
    *Physician Conscientiousness

(d)Physician services during visits

(i)Specialist services
(ii)Outpatient services
(iii)Family training
(iv)Cooperation with service providers

D) Appropriateness

(i) Healthcare needs met
(ii) Quality of care

Need-related factors:
A) Level of illness
B) Presence of Comorbidities
C) Number of prescription refills

Figure 2.3.5. Theoretical   model proposed for the study

Chapter 3 Methodology

The methodology used in the study will be discussed in the sections below. The sections discussed will be: data source, study design, study perspective, database elements, descriptive variables, statistical analyses, hypothesis and different types of analytical methods to be used in the study.

3.1 Database and Management

This section describes in details the contents of the dataset to be employed for the study as well as the process of derivation of the final sample size.

3.1.1 Marketscan Multi-State Medicaid Database

The database used for this study was the MarketScan® Multi-State Medicaid Database. The licensure for using this data was obtained from Thomson Reuters®. The database consists of enrollee information residing in eight states of the US covered by Medicaid insurance and amounts to about 22 million people. For purposes of privacy, the names of the states are not disclosed. However, the eight states are dispersed across each of the six regions of the US.

The MarketScan® Multi-State Medicaid Database contains a variety of disease conditions that patients have. The disease conditions include diabetes, hypertension, hyperlipidemia, breast cancer, and major depression. It includes records of inpatient services, inpatient admissions,

outpatient services, prescription drug claims, as well as information on long-term care and other medical care. Data on eligibility (by month) and service and provider type are also included. In addition to standard demographic variables such as age and gender, the database includes variables of particular value to researchers investigating Medicaid populations, such as aid category (blind/disabled, Medicare eligible) and race. The time period of the MarketScan® Multi-State Medicaid Database is from January 1st, 2003 to December 31, 2007.

To protect the privacy of patient data, the MarketScan™ research databases fully comply with the Health Insurance Portability and Accountability Act (HIPAA) of 1996. The MarketScan™ data features encrypted member and service provider identification numbers. All patient-level and provider-level data within the MarketScan™ research databases contains synthetic identifiers to protect the privacy of individuals and data contributors.

3.1.2 Characteristics of the database

The MarketScan® Multi-State Medicaid Database contains a unique enrollee identifier (ENROLID) which is a personal level identifier and is assigned to each enrollee, thereby making it easy to longitudinally track patients and families. The ENROLID is created by encoding personal information provided by employers. Thus the ENROLID cannot be linked to recipient ID, social security number, or any other external identifier, thereby protecting patient confidentiality. ENROLID consists of information such as the employee identification, the relationship of the enrollee to the contract holder, the gender of the enrollee, and the enrollee's date of birth. The standardized fields in each of the individual 8 databases are combined and are linked across data types and through the different years (Marketscan 2007, Adamson 2008). The clinical variables in the MarketScan® Multi-State Medicaid Database are categorized in two

ways: by diagnosis and by procedure. The diagnosis codes in the dataset are based on the International Classification of Disease, 9th Division, Clinical Modifications (ICD-9-CM). These codes are 3 to 5 digit long and upto 2 diagnoses (DX1 and DX2) are recorded for inpatient services. In case of hospital claims, inpatient admissions are identified as discharge diagnosis. Each inpatient admission record has 14 secondary diagnosis codes taken from inpatient service records and are numbered from DX2 to DX15 whereas each outpatient service record has up to 2 diagnosis codes (DX1 and DX2). Each facility head has nine diagnosis codes numbered from DX1 to DX9 (Marketscan 2007, Adamson 2008).

For diagnosing procedures, Marketscan dataset uses 3 classification systems: the Current Procedural Terminology- the 4th Edition (CPT-4) procedure codes, the ICD-9-CM procedure codes, and the HCFA Common Procedural Coding System (HCPCS) procedure codes. The CPT-4 and ICD-9-CM codes are used more frequently in the dataset. The CPT-4 codes are 5 digit numbers and are used for identifying physician claims and outpatient facility claims. The ICD-9-CM codes are 3 to 4 digit numbers and are used primarily for identifying hospital claims. Each inpatient service record has one procedure code (PROC1), which represents one inpatient admission. Each PROC1 is named as the principal procedure (PPROC). Each inpatient service record has upto 14 secondary procedure codes numbered from PROC2 to PROC15 whereas each outpatient service record has only 1 procedure code (PROC1). Each facility header has upto 6 procedure codes. Certain diagnosis and procedure codes provided by payers or administrators are edited by Thomson Reuters® to maintain data quality (Marketscan 2007, Adamson 2008).

3.1.3 Advantages of the database

Marketscan dataset has several advantages. It has a large sample size with 69 million patients.

Marketscan is one of the largest proprietary databases available in the market since 1996 with a good representation of Americans covered under commercial insurance and Medicaid. During the recent five years, the MarketScan™ Commercial and Medicare Supplemental dataset has 29 million patients with at least 12 month continuous enrollment in either a government or private insurance plan. The Marketscan data is coded comprehensively with diagnosis codes for 99% claims, procedure codes for 85% of physician claims, complete payment information including amount paid by the patient, complete outpatient prescription drug claims including copayments, mail order pharmacy claims, injectable claims, specialty pharmacy claims, carve out care claims, electronically submitted claims, plan/formulary summaries and fully paid and adjudicated claims. The Marketscan data contains claims for patient's inpatient and outpatient visits, mainly for different services and drug therapy obtained through physician office visits, hospital stays, retail pharmacy, mail order pharmacy, specialty pharmacy and carve out care. Capturing claims for both the inpatient and outpatient care procured by patients can help in measuring if the patients get continuous care or not. The Marketscan Hospital Drug dataset has hospital discharge records with claims for inpatient drug utilization. A proprietary projection method can provide insight about drug usage in the hospitals, switching drugs, combination drug therapy and impact of drug introduction at an earlier stage on clinical and economic outcomes of the patients. The claims for the outpatient drug utilization in the Marketscan database helps researchers to study the actual drugs usage patterns unlike other claims databases, by identifying the type of disease that the patient has, the drugs prescribed in combination and the impact of the clinical, demographic and provider characteristics on drug prescribing.

The Marketscan dataset is also useful for designing studies with different methodologies such as cost-effectiveness and cost-offset studies, pharmacoeconomic outcomes studies, burden of illness

studies, surgical and pharmaceutical treatment studies, forecasting and modeling studies, studies assessing evidence based practices and guidelines and clinical trials. Marketscan dataset follows patients over many years, thereby monitoring care received by patients on a continuous basis. The duration of tracking patients in the Marketscan database is much longer compared to other claims datasets since the data is generally obtained from employers running large firms and these employers have the ability to track patients across multiple health plans. The tracking of patients across different health plans also helps to capture patients who change health plans when they change jobs and thus prevents the loss of information by almost 17% as seen with other claims datasets. (Marketscan 2007, Adamson 2008)

3.1.4 Limitations of the database

The Marketscan database has certain disadvantages mainly due to the nature of its sample and the claims that it contains. The data in the Marketscan dataset is generally provided by employers representating large firms. Marketscan dataset does not contain claims of people employed by small and medium firms. Also the sample of the Marketscan dataset is a large convenience sample with many biases and little generalizability to other populations (Marketscan 2007, Adamson 2008).

3.1.5 Construction of the MarketScan® Multi-State Medicaid Database

The MarketScan® Multi-State Medicaid Database consists of inpatient and outpatient service claims and prescription drug claim records which are collected from employers, health plans, and state Medicaid agencies. After the data is obtained, Thomson Reuters® performs the case construction process that involves assembling the inpatient paid services into a single record per inpatient admission. The Outpatient Pharmaceutical Claims Table consists of clinical

information in the form of therapeutic class, therapeutic group, manufacturers' average, wholesale price, and generic product identifier. The financial, clinical, and demographic data are also standardized as per the commonly established definitions. The construction of the Marketscan dataset involves several quality checks such as checking diagnosis against age, diagnosis against gender and checking charge against payment to improve data validity and prevent incorrect coding during data construction process. The process of Marketscan dataset creation is detailed in figure 3.1. The complete Marketscan dataset provides one of the largest collections of patient data procured from 77 employers, 126 unique carriers and 12 health plans, featuring over four billion patient records of 69 million covered lives. The entire MarketScan™ database comprises of a total of 8 claims databases: Commercial Claims and Encounters, Medicare Supplemental and Coordination of benefits (COB), Health and Productivity Management (HPM), Benefit Plan Design, Health Plan and Medicaid. The present study makes use of the Marketscan Medicaid dataset only (Marketscan 2007, Adamson 2008).
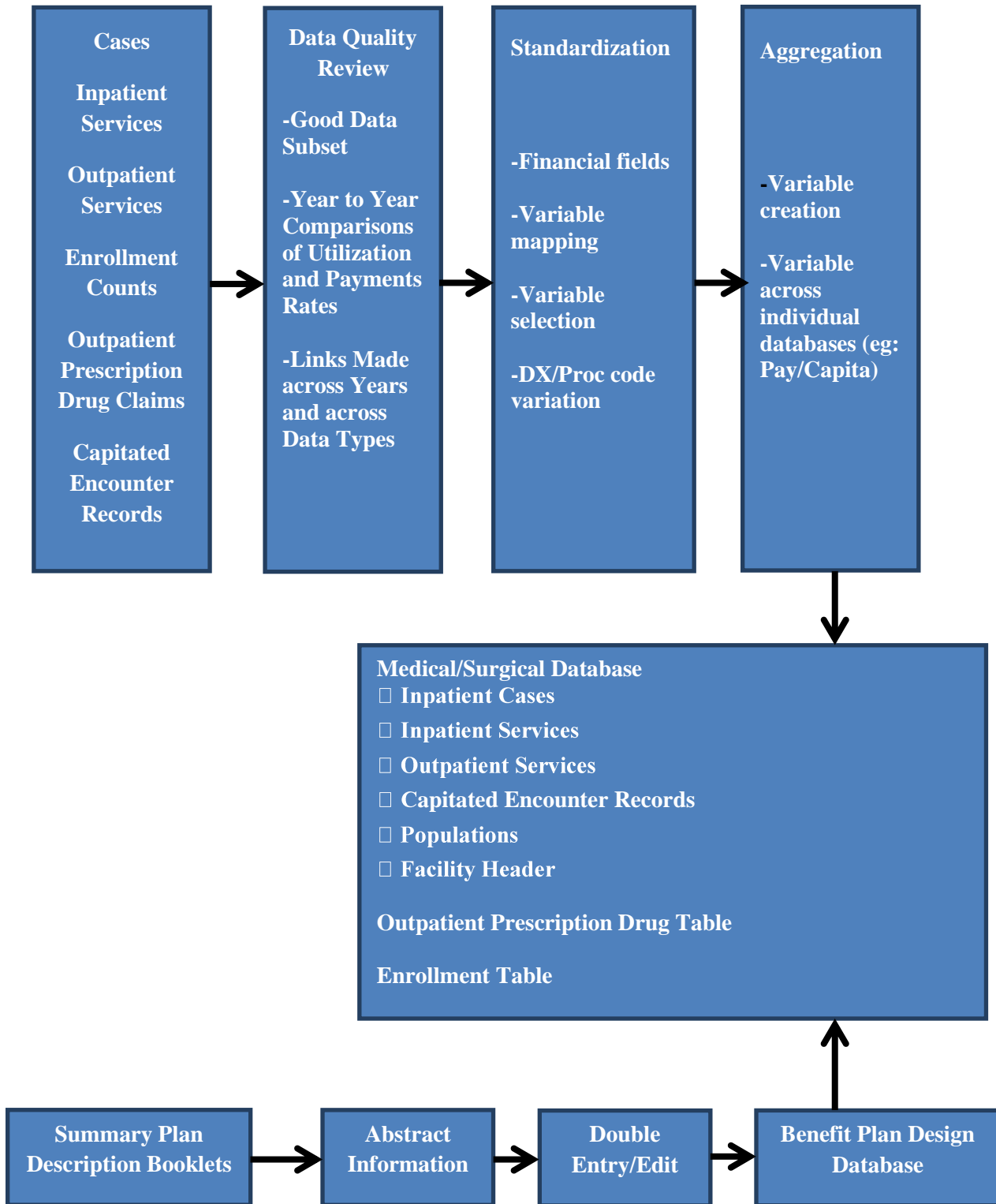
Figure 3.1: Marketscan dataflow

3.2 Study Design

This study was a retrospective cohort study. The MarketScan® Multi-State Medicaid Database was used to identify the study population.

3.2.1 Study population

The study population comprised of DD patients aged between 18 to 64 years who were diagnosed with type 2 diabetes and were prescribed at least one new oral hypoglycemic drug during the index period. The diagnosis of the study population was identified using the International Classification for Disease Code 9th revision Clinical Modification (ICD-9) codes: 250.0x, where x=0 or 2, 343.0-343.4, 343.8,343.9, 299.00,299.01, 758.0, 317, 318.0, 318.1, 318.2 and 319. The data from January 1st, 2003 to December 31st, 2007 was collected for conducting the study. Approval from the Institutional Review Board (IRB) at the University of Michigan was sought prior to the approval of the study.

3.2.2 Definitions of the terms used

Monotherapy: an OHA medication with a single drug regimen

Dual therapy: drug regimen with 2 anti diabetic medications taken separately (2 pills)

Fixed-dose combination therapy: drug regimen with 2 anti diabetic medications combined together in fixed doses (1 pill containing both medications)

Study period: from January 1, 2003 to December 31, 2007. Entire study period was further classified into three specific periods:

Follow up periods:

(1) Preindex period: 12 months prior to the index date. This was used to verify continuous

Medicaid eligibility of patients for baseline characteristics before starting any therapy, such as predisposing, need and enabling variables as specified in the theoretical model. Also, this helped to determine patients who did not have any OHA claims in this period and confirm a new start of the OHA medications in the index date.

(2) Identification period: the period from January 1, 2004 to December 31, 2006 was used to identify patients who newly started the OHA medication/s.

(3) Postindex period: this period began after the patient's index date and extended until the end of the study duration. It was used to ensure that the patients had at least 12 months of follow-up period, such as continuous medication prescription. Health-related behaviors (e.g., medication taking behavior) and outcomes (e.g., costs) were examined in this period.

Index date: date of first prescription claim in the identification period of patients who remain on the same medication therapy throughout the study period

Index prescription: first anti diabetic prescription for patients remaining on the same medication therapy throughout the study duration

Drug naïve patients: These patients had no anti-diabetic prescriptions in the pre-index period. Patients who were already on anti-diabetic medications (established patients) were excluded from the study on account of the differences in medication use behavior. Apparently, newly treated patients beginning their first course of medication (first-line patients) are likely to have significantly different medication use behavior and responses to medications compared to those who are on a particular therapy. The study included only newly started cases to understand the medication use behavior of patients who were naïve to the anti-diabetic medications therapy.

Continuous Medication Therapy: was defined by the following criteria:

a) therapy without a lapse of >120 days between the date of days' supply expiration of any prescription fill and the subsequent claim date (days between end date of first fill and first date of next fill) and b) at least 2 prescriptions of the index medication

3.2.3 Inclusion criteria

1. Patients with continuous Medicaid eligibility in the pre and postindex periods (12 months before and after the index date). The continuous enrollment criteria ensured that all patients had the same follow-up period and reduced bias due to failure to follow-up. We included patients who had continuous enrollment in each year for ≥10 months.

2. **Patients with type 2 diabetes and DD diagnosis.** Patients were identified using the *International Classification for Disease Code 9th revision Clinical Modification* (ICD-9-CM) for at least one primary or secondary diagnosis of type 2 diabetes (250.0x, where x=0 or 2) and DD (Cerebral palsy: 343.0-343.4, 343.8,343.9, Autism: 299.00,299.01, Down syndrome: 758.0, Mental retardation: 317, 318.0, 318.1, 318.2, 319) from outpatient or inpatient claims during January 1, 2003 to December 31, 2007.

3. **Patients aged 18 to 64 years old at the index date.** The reason for excluding patients aged 65 years and above was that these patients may be dual beneficiaries (Medicare and Medicaid enrollees) and therefore obtaining complete data on these patients may not be possible.

4. Drug naïve patients in the preindex period. This criteria concerns that newly treated patients beginning their first course of medication (first-line patients) are likely to have significantly different medication use behaviors and responses to medication than those who are already on a particular therapy. The current study included only newly started cases to understand the medication use behavior of patients who are naïve to OHA/s.

5. **Patients starting OHA medication therapy during the index period window** (January 1, 2004 to December 31, 2006)**.** An index prescription date was assigned to each patient. Evidence of OHA use was identified using therapeutic class in the MarketScan® Multi-State Medicaid Database. Therapeutic Class refers to a 3-digit code that indicates the therapeutic/pharmacologic category of the drug product. For example, the Therapeutic Class value equal to 173 and 174 refers to patients who had an administrative claim for taking OHA. The Therapeutic Class was used to identify patient's OHA use status.

3.2.4 Exclusion criteria

The following criteria were used to filter out the final cohort:

1. **Patients with dual eligibility** (Medicaid and Medicare coverage). These patients also get reimbursed by Medicare hence it is difficult to get complete healthcare utilization data for them. These dual eligible patients mainly include elderly patients aged 65 years and above. Hence, the subjects of this research were limited to only Medicaid recipients younger than 65 years. Also, patients 18 years and younger were excluded because the present study was intended to focus on adults and also those patients are more likely to be type 1 diabetes.

2. **Patients diagnosed with type 1 diabetes** (ICD-9-CM=250.0x-250.9x, where x=1 or 3) or **gestational diabetes** (ICD-9-CM=648.8x, where x=0-9). These patients were excluded from the study as they mainly use insulin therapy and the primary objective of this study was to measure OHA medication adherence.

3. **Patients who were already on OHA medication therapy (established patients) in preindex period**.

4. **Patients were prescribed insulin therapy**. The reason for excluding these patients is that these are high risk patients whose level of severity is high compared to those on oral therapy. Additionally, medication use behavior for patients on insulin therapy is substantially different from those taking oral medications due to complexity of dosing regimen.

5. **Patients taking OHA medications other than sulfonylurea, metformin and TZDs**. Research has shown that there are very few patients on meglitinides and α-glucosidase inhibitors; so these patients were not included in the study cohort.

MarketScan® Multi-State Medicaid Database
The study duration:
January 1st, 2003 to December 31st, 2007

Initial Study Cohort

1. Patients newly diagnosed with ICD-9-CM codes: 250.0x-250.9x, where x=0 or 2, 343.0-343.4, 343.8,343.9, 299.00,299.01, 758.0, 317, 318.0, 318.1, 318.2, 319; during the index period: January 1st, 2004 and December 31st, 2006. An index diagnosis date was assigned for each patient.

2. Patients newly prescribed at least OHA during the study period: one year follow up after the index diagnosis date

3. Patients with maintained continuous Medicaid eligibility one year before and one year after the index diagnosis date

Final study cohort

1. Patients aged between 18 to 64 years during the study period.
2. Drug naïve patients.
3. DD patients with type 2 diabetes during the study period

Figure 3.2 Patient selection in the study

Table 3.1 Selected variables in the main dataset

1)Eligibility/enrollment file:

  Enrollee ID (ENROLID)
  BOE category (BOE)
  Date enrollment start (DTSTART)
  Day enrollment end (DTEND)
  Patient birth year (DOBYR)
  Gender of patient (SEX)
  Race (STDRACE)
  Medicaid case number (MCASENUM)
  Medicare eligibility (MEDICARE)
  Member days (MEMDAYS)
  Medicaid Capitation flag (CAP)

2. Inpatient admission:

  Enrollee ID (ENROLID)
  Date of admission (ADMDATE)
  Date of discharge (DISDATE)
  Diagnosis related group (DRG)
  Major diagnostic category (MDC)
  Diagnosis principal (PDX)
  Diagnosis 1 (DX 1)
  Diagnosis 2 (DX 2)
  Discharge status (DSTATUS)
  Date claim paid (PDDATE)
  Procedure principal (PPROC)
  Procedure 1 (PROC 1)
  Length of stay (DAYS)
  COB and other savings total case (TOTCOB)
  Coinsurance total case (TOTCOINS)
  Copayment total case (TOTCOPAYS)
  Deductible total case (TOTDED)
  Payments net case (TOTNET)
  Payments total case (TOTPAY)

3. Inpatient services:
  Enrolled ID (ENROLID)
  Case and services link (CASEID)
  COB and other savings (COB)
  Coinsurance (COINS)
  Copayment (COPAY)
  Diagnosis primary (PDX)
  Quantity of services (QTY)

Revenue code (REVCODE)
Sequence number (SEQNUM)
Place of service (STDPLAC)
Service type (STDSVC)
Type of provider (STDPROV)
Date service incurred (SVCDATE)
Date of service ending (TSVCDAT)

4. Outpatient claims:

Enrollee ID (ENROLID)
Date service incurred (SVCDATE)
Date of service ending (TSVCDAT)
Date year incurred (YEAR)
Diagnosis 1 (DX1)
Diagnosis 2 (DX2)
Procedure 1 (PROC 1)
Procedure group (PROCGRP)
Procedure code type (PROCTYPE)
Place of service (STDPLAC)
Provider type (STDPROV)
Quantity of services (QTY)
Major diagnostic category (MDC)
Payment (PAY)
Payment net (NETPAY)
Date claim paid (PDDATE)
COB and other savings (COB)
Coinsurance (COINS)
Copayment (COPAY)
Coverage indicator drug (DRUGCOVG)

5. Prescription drugs:

Enrollee ID (ENROLID)
Date service incurred (SVCDATE)
Coverage indicator drug (DRUGCOVG)
Date claim paid (PDDATE)
National Drug Code (NDCNUM)
Day supplied (DAYSUPP)
Quantity of services (QTY)
Average wholesale price (AWP)
Ingredient cost (INGCOST)
COB and other savings (COB)
Coinsurance (COINS)
Copayment (COPAY)
Payment (PAY)

Generic indicator (GENIND)
Generic product ID (GENERID)
Dispensing fee (DISPFEE)
Metric quantity (METQTY)
Refill Number (REFILL)
Therapeutic class (THERCLS)
Therapeutic group (THERGRP)

Step 1:

There were 213,644 DD patients in the MarketScan® Multi-State Medicaid Database from January 1st, 2003 to December 31st, 2007 (the study duration).

↓

Step 2:

22,093 DD patients (intellectual disability, cerebral palsy, autism) aged 18 to 64 years had a diagnosis of type 2 diabetes from January 1st, 2004 to December 31st, 2006 (the index period) were included. Each patient was assigned to have an index diagnosis date. There were 21,617 patients who had medication information. Patients with dual Medicare and Medicaid eligibility were excluded. There were 8772 patients meeting these exclusion criteria.

↓

Step 3:

Patients who were diagnosed with DD and were prescribed with an OHA during the index period were included in the study. The Medicaid IDs (ENROLID) were used to link the prescription drug claim to the detailed enrollment claim. 4,641 patients met these criteria.

↓

Step 4:

Patients having using any OHA during the pre-index period (12 months before the index diagnosis date) were also excluded. There were 2505 patients excluded in this step. Patients were required to be continuously enrolled from 12 months (the pre-index period) before and 12 months (the study period) after the index diagnosis date. There were 1529 patients who met the criteria and constituted towards the final sample of this study.

Figure 3.3 Steps involved in creation of the analytical dataset for the study

3.3 Study Perspective

A) Patient's perspective:

The burden of chronic disease conditions in adults with DD is high. In addition to their disability, the intake of numerous medications can increase their risk of side effects and drug interactions (Horwitz 2000). High prevalence of chronic disease conditions, deinstitutionalization, lack of adequate number of trained PCPs, providers showing reluctance to treat DD patients, availability of few education materials for physicians, inadequate preventive care and unavailability of care in rural areas are some of the issues that impede DD patients' access to care (Lewis 2002, Messinger-Rapport 1997). Adults with DD are subjected to prejudice and their encounters with primary care physicians might be painful and stressful at times. Some providers tend to exclude women with DD from preventive screenings due to their assumption that they are asexual. Lower rates of PAP smears and mammograms in women with DD increase their risk of breast cancer compared to women without DD (Brown 2002, Havercamp 2004). Also higher rates of dental problems in this population can lead to a higher prevalence of chronic diseases such as diabetes, respiratory disease, osteoporosis and CVD (Horowitz 2000). Interventions such as a)providing health advocacy training for family members and unpaid caregivers, reimbursing them for regularly monitoring the health of the DD patients and ensuring that they receive the necessary screenings (Moss 2008) b) building patient centered planning teams involving health advocates and case managers, c) expanding dental coverage for Medicaid enrollees (U.S. General Accounting Office 2000) and d)training PCPs and specialty care providers (Fenton 2003) can improve continuity of care in DD patients. Interventions should focus on delivering the needed care quickly in DD patients. Depending on the disability, patients might not be able to make health related decisions or express themselves in which case, their case managers or non

guardian caregivers can provide valuable insight about the DD patient's condition. Both the physicians and the case managers should chalk out the best treatment options for the DD patients based on the patient's quality of life and the benefits/risks associated with the treatment (Ellison 2007).

B) Physician's perspective:

There is disproportionate distribution of PCPs that serve the Medicaid population and with the increase in number of Medicaid patients from 2014; this need will become more pressing. The PCPs that are supposed to get moderate share of the Medicaid patients but end up serving more Medicaid population, practice in small groups whereas PCPs that are supposed to get high share of Medicaid patients but serve less Medicaid patients practice in hospitals and community centers and offer resources that are difficult to procure somewhere else. One of the reasons for this discrepancy in delivering care is that high share PCPs practice in high income areas that are more accessible to Medicare population rather than the Medicaid population (Sommers 2011). Larger hospitals acquiring or collaborating with small private practices can help in expanding access to Medicaid services, provided such a change takes place at the national level and not just locally. Physicians also tend to deny Medicaid patients due to lower reimbursements but besides that, there are several other reasons that impede the access to care in Medicaid patients such as lack of infrastructure, longer working hours, paperwork, difficulty in referring to specialists, burden of illness and hassle of attending to the non-medical needs of the Medicaid population. From physician's perspective, with the enactment of the Affordable Care Act, the coverage for Medicaid has increased and physicians might see more of slightly healthier Medicaid patients than their current or past patients, thereby increasing access to services for those patients (Sommers 2011).

C) Payer's perspective:

This study is conducted from payer's perspective .i.e. from Medicaid program's perspective. The study looks at the combined effect of race and medication adherence on healthcare utilization in diabetic adults with DD. These adults and their families who are being provided health assistance by Medicaid have a low SES and might have dependent children. Medicaid programs get their funding from the state and the federal government and the present study can help policy makers frame coverage policies which can in turn benefit this vulnerable group of individuals. Medicaid reimbursements are made on a retrospective, fee-for-service basis and payments made for filling prescriptions comprise either the lower end of the usual payment rates or a pre-established rate of $1-$4. Some Medicaid programs reimburse for inpatient visits, emergency room visits, and physician visits for eligible patients. The payer's perspective is chosen since better medication usage could potentially reduce Medicaid reimbursements alongwith reduced healthcare costs and resource utilization. The findings of the current study can pave the way for designing interventions for reducing medication non adherence, improving overall healthcare utilization and allocating limited healthcare resources among type 2 diabetes patients.

3.4 Database Elements

The dataset in this study was retrieved from the MarketScan® Multi-State Medicaid Database. Variables were further categorized into five groups: eligibility/enrollment, inpatient admissions, inpatient services, outpatient claims, and prescription drugs. Social demographic variables such as age, gender and race were also retrieved. Variables associated with health service utilization such as inpatient visits and emergency room visits were also included in the study.

3.5 Study Variables and Measurement

The operational definitions of the study variables and their measurements are described in this section. The dependent variables in this study included medication adherence, medication persistence, inpatient visits, outpatient visits, emergency room (ER) visits and healthcare costs. The key tested hypothesized independent variables were race, comorbidity, and the interaction effect of race and comorbidity. Other independent variables (covariates) included age, gender, access to healthcare, and the disease severity. A detailed operational definition of each variable is described in the following sections.

3.5.1   Dependent variables

(A)Medication Adherence:

Medication adherence was the first dependent variable in this study.   Medication adherence indicates medication usage by patients. It is act of conforming to physician's recommendations with regards to the timing, dosage, and frequency of medication intake.The International Society of Pharmacoeconomics and Outcomes research defines medication adherence as the compliance of the patients with the recommended medication dosage (Hess 2006). MPR is an indirect measurement of patients' medication adherence, especially when using administrative claim data. MPR is defined as administered doses per defined period of time, reported as a proportion (%) of prescribed doses (D) taken at the prescribed time interval (T) as measured by the period of time. In order to take the last days supply into consideration, MPR was further modified (MPRm), by dividing the total days" supply of medications by the period between the last claim date and the first claim date plus the last day's supply of medications.

MPRm = *[Number of days supply obtained/(Date of the last claim—Date of the first claim┼Days' supply of the last claim)] * 100*

Medication adherence can be measured in an inexpensive and efficient way using the administrative claims data. There are many ways of measuring medication adherence. It can be measured either directly through biological markers, blood and urine assays or indirectly through patient interviews, pill counts, prescription refills, and electronic monitoring (Claxton 2001, Hess 2006).

Knowledge of medication adherence can provide information about the frequency and timeliness of refills of prescribed medication and the patients are unaware if they have been measured which eliminates the Hawthorne effect. Karve et al (2008) reviewed eight different measurements of medication adherence using administrative claims data and found that MPR had the highest predictive validity for measuring medication adherence. Pharmacy records have good predictive validity for measuring medication gaps and fills (Steiner 1998).

Recording MPRs can be challenging in presence of unusual refill patterns, multiple conflicting drugs and in case of patients visiting multiple pharmacies. Also, since this study will assume that a prescription filled is a prescription taken, it will not be possible to measure actual medication consumption (Balkrishnan 2005, Hess 2006). In this study, medication adherence was coded as a dichotomous variable. The cut off for MPR was set to 0.8 based on the evidence presented by Karve et al (2008). This cut off could accurately predict inpatient visits caused by medication non adherence especially in type 2 diabetes patients.

Working Definition of Medication adherence:

Medication adherence in this study was defined as patient's adherence to the newly started

OHAs. Since the current study uses a claims dataset, claims for prescription refills were used to measure medication adherence. In the current study, the observation period begins with the first date of dispensing within each year and ends with the last dispensing date of the last prescription. Information about filled prescriptions was extracted from the Medicaid claims. Each prescription record had the following information: dosage, quantity dispensed, date of the drug supplied, and number of days supplied. Specific formulae for computing the MPR was as follows:

For monotherapy or fixed dose regimen: *MPR= Total days' supply obtained/ (Date of the last claim—Date of the first claim ╅ Days' supply of the last claim)*

For dual therapy or fixed dose regimen: *MPR= (Total days' supply obtained/2)/(Date of the last claim—Date of the first claim ╅ Days' supply of the last claim)*

The Marketscan Medicaid database has claims for a 30 days supply of OHAs. The days supply was calculated by dividing the total amount of dispensed OHAs by the maximum amount of OHAs used in aday. The observation period for the current study included the post-index period or at least a 12 month follow up period. The number of hospital days were subtracted from the denominator since any OHA intake during this period was supplied by the hospital and could be captured in pharmacy records (Cramer 2008, Vanderpoel 2004, Karve 2009, Karve 2008, Hess 2006, Farmer 1999, Balkrishnan 2005).

 (B)Medication persistence: Medication persistence measures the duration from the initiation to the discontinuation of a medication. It measures the accordance of the patient with the drug therapy for the intended duration. It was possible to measure medication persistence in the Marketscan dataset since it comprises of detailed prescription refill record. For the purposes of

this study, medication persistence was be defined as the duration of an OHA intake i.e. the number of days during which an OHA is started and discontinued. Studying gap between medication refills can help understand medication persistence. Delay in medication refill can be an indicator of poor medication adherence but not necessarily an indicator of poor medication persistence. Delay in medication refill can be attributed to reasons such as improvement in clinical outcomes or occurrence of adverse events. Hence, studying medication persistence to OHAs is important. Patients were defined as non-persistent if they had a refill gap greater than 120 days in the current study (Cramer 2008, Linden 2000, Mullins 2005, Mullins 2006, Farmer 1999).

(C) Outpatient visits: The number of outpatient visits was a count variable identified from the MarketScan® Multi-State Medicaid Database. Outpatient visits were also coded dichotomously. In the data, each procedure was assigned to have a procedure code. Patients who had the procedure code equal to 101 (office visits for new patients) or 104 (office visit for existing patients) were determined as having an outpatient visit during the study period.

(D)Inpatient visits: Inpatient visit was a dichotomous and a count dependent variable in this study. Patients were identified as having an inpatient visit if they had an event of any inpatient visit in the claims. Variables such as date of admission and date of discharge in the MarketScan® Multi-State Medicaid Database were used to identify patients' inpatient visits.

(E)Emergency Room (ER) visit: Patients were identified as having an ER visit if they had any of the following events reported in the MarketScan® Multi-State Medicaid Database. Based on the procedure codes, the MarketScan® Multi-State Medicaid Database provided an indicator variable for the type of related outpatient procedures. Patients who had the procedure group (PROCGRP) value equal to 110 (emergency room visit for new patients) or 114 (emergency

room visits) were determined as having an ER visit during the study period. The ER visit variable was coded as a dichotomous (yes/no) variable and as a count variable.

Type 2 diabetes has the ICD-9-CM code of 250.0x, where x=0 or 2. Any patient utilization related to the above ICD-9-CM code was defined as type 2 diabetes related healthcare utilization. For example, a type 2 diabetes-related office visit, coded as dichotomous (yes/no), was determined by whether patients had an office visit related to type 2 diabetes during the study period.

(F)Healthcare costs: Patients healthcare costs were directly identified from the MarketScan® Multi-State Medicaid Database. The overall healthcare costs included patient's inpatient, outpatient, and prescription expenditures during the study period. Type 2 diabetes healthcare costs were the expenditures that were relevant to the DDs identified using the ICD-9-CM codes.

3.5.2 Independent variables

(A)Race: Race was self-reported information obtained from patients when they were first enrolled in the Medicaid program. The variable was directly derived from the MarketScan® Multi-State Medicaid Database. It was categorized as Caucasians, African Americans and other races.

(B) Medication Adherence: Medication adherence during the 12 month study period was calculated using MPRm. Medication adherence with a MPRm>0.8 was classified as high medication adherence and MPRm<0.8 was classified as low medication adherence. DD patients with a diagnosis of type 2 diabetes were classified as having low or high medication adherence for anti-diabetic medications. MPRm was coded as dichotomous (>0.8/<0.8) variable.

(C)The combined effect: The combined effect of race and medication adherence was the

interaction term between race and medication adherence.

3.5.3 Other independent variables (covariates)

The selection of covariates was based on the proposed theoretical framework in Figure 2.5. Variables were categorized into three groups: predisposing factors, enabling factors, and need factors. Predisposing factors included sociodemographic variables, such as age and gender. Enabling factors included variables related to access to healthcare and economic variables. Need factors were variables related to the severity of the disease.

Each group of covariates is described in the following sections.

(A)Predisposing factors:

Sociodemographic variables: Sociodemographic variables in this study included patients age and gender. Patient's age was calculated as the year of index date minus the year of birth. All sociodemographic variables were identified from the MarketScan® Multi-State Medicaid Database.

(B)Enabling factors:

Economic variables: The economic variables in the current study were determined by the type of health plan (FFS vs. capitation vs dual). The type of health plan was directly identified from the MarketScan® Multi-State Medicaid Database.

(C)Need factors:

Need factors: Need factors in the Andersen model were referred as the severity of the disease. Need factors in this study included number of prescription refills, variables of the pre-index period and comorbidities measured by the Charlson comorbidity index.

(D)Variables of the pre-index period resource utilization:

Several variables in the pre-index period considered to have an influence on medication-related outcomes in the index period were included and adjusted when performing data analyses. Patients having high health resource utilization in the pre-index period could also have high health resource utilization in the index period. Therefore, variables in the pre-index period related to health resource utilization were controlled. Variables related to health resource utilization in the pre-index period included the outpatient visits in the pre-index period (yes/no), inpatient visits in the pre-index period (yes/no) and Charlson comorbidity index in the pre-study period (yes/no). A comorbidity index was used to adjust the influence of comorbid conditions other than DD on health outcomes. The Charlsonr index used to adjust the comorbid conditions in this study, will be discussed in the following sections.

(E)The Charlson comorbidity index: Comorbidity indices identify the comorbid conditions in patients and apply weights to those conditions depending on the disease severity. The weight that is assigned to a comorbid condition depends on its impact on the main disease condition. In 1987, Charlson developed a comorbidity index based on 17 comorbidities (Charlson 1987). The comorbid conditions included in the Charlson's index are myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, rheumatologic disease, ulcer, mild liver disease, hemiplegia, moderate or severe renal disease, any tumor, leukemia, lymphoma, moderate or severe liver disease, metastatic solid tumor, and AIDS. ICD-9-CM codes used to identify these conditions are given in table 3.2. The Charlson index assigns weights of 1, 2, 3 or 6 to the 17 comorbid conditions based on their severity. The diseases that have a higher impact on mortality such as cancer or AIDS have a weight of 6 as opposed to conditions such as myocardial infarction and congestive heart failure that are assigned a weight of 1. All the weights

for all the 19 comorbidities are totaled for each patient to calculate the index severity score. The index has been used to measure in hospital mortality (Poses 1996, Sundararajan 2007) and post discharge mortality (Charlson 1994). To assess the risk of mortality, occurrence of disease in patients can be accessed through medical charts, medical examinations, interviews and recollection of events. The Charlson index, though mainly developed for measuring mortality as an outcome, is now being used to measure outcomes such as healthcare utilization and healthcare costs (Charlson 2008). The Charlson index has been adapted for its use in administrative claims databases (Deyo 1992, D'Hoore 1993, Romano 1993). This study uses the Deyo's modification of the Charlson index. The Deyo version can be used to measure the risk of mortality associated with comorbid conditions.

Table 3.2 ICD-9-CM codes of conditions included in Charlson Index

Comorbidity	ICD-9-CM Codes
1. Myocardial infarction	410.x, 412.x
2. Congestive heart failure	428.x
3. Peripheral vascular disease	443.9, 441.x, 785.4, V43.4 Procedure 38.48
4. Cerebrovascular disease	430.x–438.x
5. Dementia	290.x
6. Chronic pulmonary Disease	490.x–505.x, 506.4
7. Rheumatic disease	710.0, 710.1, 710.4, 714.0–714.2, 714.81, 725.x
8. Peptic ulcer disease	531.x–534.x
9. Mild liver disease	571.2, 571.4–571.6
10. Diabetes without chronic Complication	250.0–250.3, 250.7
11. Diabetes with chronic Complication	250.4–250.6
12. Hemiplegia or paraplegia	344.1, 342.x
13. Renal disease	582.x, 583–583.7, 585.x, 586.x, 588.x
14. Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin	140.x–172.x, 174.x.–195.8, 200.x–208.x
15. Moderate or severe liver disease	456.0–456.21, 572.2–572.8
16. Metastatic solid tumor	196.x–199.1
17. AIDS/HIV	042.x–044.x

3.6 Statistical Analyses and Hypothesis Testing

The objective of the current study was to examine the association of race and medication-related outcomes (medication utilization, medication persistence, medication adherence, and medication expenditures) in Medicaid-enrolled DD patients with type 2 diabetes. The required statistical analyses employed in examining the study objectives and hypothesis testing are described in the following sections:

3.6.1 Study objectives

Objective 1: To describe select patient characteristics (sociodemographic factors and medication-related factors) of Medicaid-enrolled DD patients with a diagnosis of type 2 diabetes and examine the predictors of medication adherence in Medicaid-enrolled DD patients with a diagnosis of type 2 diabetes, after adjusting for select confounders.

Descriptive statistics were used to describe patient characteristics, which included sociodemographic factors and medication-related factors such as healthcare costs, prescription utilization, and health service utilization of DD patients with diagnosis of type 2 diabetes. The average value (mean) was used to describe the continuous variables and a proportion (%) was used to describe the categorical variables. The Student"s t-test was used to differentiate the mean difference of the continuous variables between DD patients with a diagnosis of type 2 diabetes. Chi-square tests were used to assess the difference of the categorical variables between DD patients with a diagnosis of type 2 diabetes.

Medication adherence was assessed by MPRm, which was the dependent variable in the regression model. An Ordinary Least Squares (OLS) regression model was used to assess the association between MPRm and key tested variables as well as other covariates. When the dependent variable is skewed and heteroskedastic, a log-transformation for the dependent variable is needed. Shapiro-Wilk test and White test were used to test the normality and heteroskedasticity (D'Agostino 1971). A log-transformed MPRm is not necessary if the distribution of MPRm values is normal. The OLS regression model was used to examine the association between medication adherence and race. The key tested variable was race. The selection of covariates was based on the proposed theoretical framework shown in Figure 2.5. Covariates were categorized into predisposing, enabling, and need factors. Predisposing factors

included age and gender. Enabling factors in this study were determined by the type of health plan (FFS vs. Capitation). Need factors in the study referred to the number of prescription refills and severity of the disease. The factors determined were if patients had inpatient visits in the pre-study period (yes/no), if patients had outpatient visits in the pre-study period (yes/no), if patients had ER visits in the pre-study period (yes/no), the Charlson comorbidity index during the study period and the Charlson comorbidity index during the pre-study period. The following equations show the OLS regression model that includes key tested variables, predisposing factors, enabling factors, and needed factors as well as their relationship with MPRm.

$Y: MPRm = \beta_0 + \beta_1 \ (race) + \beta_2 \ (predisposing \ factors) + \beta_3 \ (enabling \ factors) + \beta_4 \ (need \ factors) + error$

The interpretation of the association between MPRm and covariates is that for every unit increase in a particular covariate, the value of MPRm will be assumed to change with a parameter unit of the particular covariate, holding all other variables in the model constant. In addition to evaluating medication adherence as a continuous variable, medication adherence was further categorized into a dichotomous variable. A value of MPRm smaller than 80% (MPRm< 80%) was defined as lower adherence (Karve 2009). Logistic regression was used to examine the association between the likelihood of being adherent to the medications and race, after adjusting for other covariates. The following logistic regression model describes the association.

$Y: Medication \ adherence \ (yes/no) = \beta_0 + \beta_1 \ (race) + \beta_2 \ (predisposing \ factors) + \beta_3 \ (enabling \ factors) + \beta_4 \ (need \ factors) + error$

Objective 2: To examine the predictors of medication persistence in Medicaid-enrolled DD

patients with a diagnosis of type 2 diabetes, after adjusting for select confounders.

Medication persistence in this study was operationally defined as the duration for which prescriptions were taken. It was the number of days determined by the initiation of taking the medicine to the end of taking the medicine. Medication persistence is a time-dependent variable. The censored time was referred as the time of persistently taking anti-diabetics during the study period. Unadjusted Kaplan-Meier survival curves were used to compare the differences of censored time between Caucasian and African American DD patients with a diagnosis of type 2 diabetes. A Cox proportional hazard model was used to estimate the different hazard ratios in patients from different races who were the first to stop taking OHAs, after adjusting for other covariates. The following equation describes the Cox proportional hazard model.

Y:Medication persistence (time) $= \beta_0 + \beta_1$ *(race)* $+ \beta_3$ *(predisposing factors)* $+ \beta_4$ *(enabling factors)* $+ \beta_5$ *(need factors)* $+$ *error*

Objective 3: To examine the effect of race, medication adherence, and the combined effects of race and medication adherence on type 2 diabetes related health resource utilization (outpatient visits, inpatient visits and emergency room (ER) visits) in Medicaid enrolled DD patients with a diagnosis of type 2 diabetes, after adjusting for select confounders.

Type 2 diabetes related health resource utilization in DD patients such as outpatient visits, inpatient visits, and ER visits were considered as count dependent variables in this study. OLS regression was not appropriate to obtain a robust estimate for assessing the association between healthcare utilization and race. Due to the differences between the variance and the mean, the negative-binominal distribution was more appropriate for assessing the association. Since the number of DD related inpatient visits, outpatient and ER visits were highly skewed, a two-part of

regression model was used to model the association of type 2 diabetes related health resource utilization with race, medication adherence, and combined effects, adjusting for other covariates. Multivariate logistic regression analyses constituted the first part of the two-part model. Logistic regression analyses were used to estimate the probability of occurrence of any event of health resource utilization. Then, the second part was the multivariate negative binominal regression analyses. It was used to estimate the level change of health resource utilization among patients having at least one event of health resource utilization.

Logistic regression analyses:

Y: type 2 diabetes related office visits (yes/no) = β_0 + $\beta1$ (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

Y: type 2 diabetes related inpatient visits (yes/no) = β_0 + $\beta1$ (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

Y: type 2 diabetes related ER visits (yes/no) = β_0 + $\beta1$ (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

Negative binominal distribution regression analyses

Y: type 2 diabetes related office visits (a count variable, the number of office vists) = β_0 + $\beta1$ (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5

(enabling factors) + β₆ (need factors) + error

Y: type 2 diabetes related inpatient visits (a count variable, the number of inpatient visits) = β_0 + β_1 (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

Y: type 2 diabetes related ER visits (a count variable, the number of ER vists) = β_0 + $\beta1$ (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

Objective 4: To examine the effect of race, medication adherence , and the combined effects of race and medication adherence on type 2 diabetes related costs including medications, medical and overall costs in Medicaid enrolled DD patients with diagnosis of type 2 diabetes after adjusting for select confounders.

An OLS regression model with log transformation was used to assess the association between type 2 diabetes related healthcare costs and key tested variables as well as covariates in the regression model. Since the healthcare costs were highly skewed, log transformation was needed to obtain normality. The log-transformed OLS model was an exponential model, with non-linear estimated regression coefficients. In order to obtain the incremental effect of a one-unit change of the estimated regression coefficients, retransformation was necessary. A "smearing" term was incorporated in the retransformation process (Manning 1998, Duan 1983). The assumption of the retransformation with a smearing term in the estimated coefficients was that that

homoscedasticity exists among the errors. A Breusch-Pagan test was used to test the heteroskedasticity in this study (Breusch 1979).

Y:Ln (type 2 diabetes related medication costs) = β_0 + β_1 (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

Y:Ln (type 2 diabetes related medical costs) = β_0 + β_1 (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

Y:Ln (type 2 diabetes related overall costs) = β_0 + β_1 (race) + β_2 (medication adherence) + β_3 (combined effect) + β_4 (predisposing factors) + β_5 (enabling factors) + β_6 (need factors) + error

3.7 Regression Diagnostics

An OLS regression model has certain assumptions such as existence, linearity, independence, homoscedasticity and normality that need to be met so that robust estimates can be obtained. The assumption of existence means that the dependent variable Y with a finite mean and variance depends on value of the independent variable X. Linearity assumption means that the mean value of dependent variable Y is a straight-line function of independent variable X. In this study, MPR is a linear function of the independent variables and other covariates. Thus, the current study meets both the assumptions of existence and linearity. The current study also meets the other statistical assumptions such as independence, homoscedasticity and normality by using a variety of regression diagnosis described in the sections below. Overall, the OLS model to be implemented in the study meets all the statistical assumptions. (Kleinbaum 1998)

3.7.1 Autocorrelation

Cross sectional studies generally meet the OLS assumption that each dependent variable is independent of the other dependent variables i.e. each Y is not correlated with others Ys in the study. When this assumption is violated, autocorrelation, a time series problem occurs and errors from one period are correlated with errors from another period. Autocorrelation is generally seen in studies involving medication adherence to chronic disease conditions and therefore OLS regression model should always be checked for autocorrelation. Due to autocorrelation, the estimators become inefficient and biased. Autocorrelation can be detected using the Durbin-Watson test. The null hypothesis of this test states that autocorrelation gets removed over time. The Durbin-Watson test statistic value is between 0 and 4 and a value of 2 indicates no autocorrelation over time. In terms of interpretation, a positive autocorrelation can be detected if the Durbin-Watson test statistic value is close to 0.143 and a negative autocorrelation can be detected if the Durbin-Watson test statistic value is close to 4. The positive and negative nature of autocorrelation can be determined by plotting the graph of residuals against time. Autocorrelation can be removed from the model by using lagged variables in the model or GLS regression (Kleinbaum 1998, Gujarati 2003).

3.7.2 Heteroskedasticity

One of the assumptions of the OLS model employed in this study is that the variance of error term is constant for any value of independent variable. This assumption is called homoskedasticity. If the variance of the error term is correlated with any of the independent variables, the error variance will also be different for each observation. Heteroscedasticity is an OLS violation. Heteroscedasticity occurs in an OLS model in error learning models, upon use of incorrect functional form, omitting variables or wrongly specifying the model, when there are

outliers and when the distribution is skewed. Heteroskedasticity leads to biased standard errors of parameter estimates even though the parameter estimates are not biased, less significant F and t test due to large standard errors, narrow confidence intervals and very large OLS variance estimators. The Busch -Pagan-Godfrey test can detect heteroskedasticity in an OLS model. In the Busch-Pagan-Godfrey test, OLS is estimated followed by obtaining residuals and error variance. The squared residuals are divided by error variance to construct a variable p which is regressed on Z's; some or all of independent variables can serve as Z. The explained sum of squares (ESS) is obtained, θ is defined as ESS/2 and the null θ hypothesis of homoscedasticity states that θ follow the chi-square distribution with (m -1) degrees of freedom, where m is number of Z's. Thus the Breusch-Pagan-Godfrey test looks at the dependence of the estimated variance of the residuals obtained by running an OLS model on the values of the independent variables.

If the null hypothesis is rejected, heteroskedasticity exists. Unlike the Breusch-Pagan-Godfrey test, the Goldfeld-Quandt test works accurately provided a certain number of central observations are omitted the independent variable related to variance is identified. Breusch-Pagan-Godfrey test is a desirable test for identifying heteroskedasticity (Kleinbaum 1998, Gujarati 2003).

3.7.3 Normality

The accuracy and reliability of an OLS regression model depends on the fulfillment of its normality assumptions. Robustness of the point estimates and confidence intervals in an OLS regression model can be obtained by making the distribution of the fixed values of X and Y normal. Normality can be confirmed employing the Shiparo-Wilk test and a plot histogram of residuals. If the distribution is normal, the dependent variable Y can be log transformed. However, in the process it is possible that the model becomes homoscedastic. Hence, after

transforming the log of Y, it is necessary to confirm that non violation of the assumptions of homoscedasticity (Kleinbaum 1998, Gujarati 2003).

3.7.4 Multicollinearity

When an OLS regression model is to be applied, the model should satisfy the basic assumptions. With the basic assumptions satisfied, the model should be checked for multicollinearity. Multicollinearity occurs when one or more independent variables are linearly related with other independent variables. If multicollinearity persists, the beta coefficients of the mutlicollinear variables cannot be measured correctly since there is not enough variation between them which makes estimating their separate effects challenging. Multicollinearity can be attributed to many causes such as true linearity between the independent variables, inadequate data collection, over determined model and addition of too many polynomial variables. Multicollinearity is less than perfect and it can lead to instability of the point estimate and the standard error. The OLS estimate changes are correlated with small changes in data. In case of imperfect multicollinearity, the beta coefficients can still be estimated using OLS which provides the best linear unbiased estimates but also large standard errors, statistically insignificant t and large confidence intervals for parameter estimates. Multicollinearity can be detected using the Variance Inflation Factor (VIF), an index that determines the change in the magnitude of the variance of an estimated coefficient that correlates with multicollinearity. The VIF value is directly proportional to the degree of multicollinearity in the model and a VIF value of 10 indicates severe multicollinearity. Other ways of detecting multicollinearity are observing the correlations between independent variables, checking for high R-squared and presence of several insignificant t tests, wrong signs for coefficients and big changes in estimated coefficients upon addition or deletion of a variable. Multicollinearity can be corrected by respecifying the OLS

model, running auxiliary regressions (obtained by regressing one independent variable over others) and gathering more sample data or expressing variables in deviation terms (Kleinbaum 1998, Pagano 2000).

3.7.5 Model Specification

When one or more applicable variables are not included in the model or when one or more unrelated variables are included in the model, a specification error occurs. If the applicable variables are absent in the model, the common variance may be erroneously shared by the applicable variables and this may lead to inflation of the error terms in the model. On the other hand, if the unrelated variables are present in the model, the common variance may be erroneously shared by the applicable variables and this may lead to deflation of the error terms in the model. The regression coefficients can be affected considerably due to presence of specification errors in the regression model (Vittinghoff 2004).

3.7.6 Model diagnostics

Specification errors can be detected in the linear regression models using the specification error link test. The goodness of fit for the logistic regression models can be determined by using the Hosmer Lemeshow chi square test. The discrimination power of the model can be measured using the Receiver Operating Characteristics (ROC) curve. For the multivariate negative binomial regression models, the likelihood ratio (LR) test and the Vuong test can be performed respectively. Both the LR and the Vuong test are considered significant if their p value is less than 0.05 (Vittinghoff 2004).

3.7 Data Management and Analyses

The data extraction, management and analysis of the Marketscan ® Multi-State Medicaid Database were done using STATA 13 (StataCorp LP, College Station, Texas) and SAS softwares

(StataCorp 2013, SAS Institute 2011). Estimates of means, proportions, and standard errors with

95% confidence intervals (CI) were derived from the statistical estimation. Two-tailed tests and a

0.05 level of significance were used to determine statistical significance. The study protocol was

approved by the Institutional Review Board (IRB) at the University of Michigan (Appendix 1).

Chapter 4 Manuscript One

Title: Predictors of medication adherence and persistence in Medicaid Enrollees with Developmental Disabilities and type 2 diabetes

Abstract

Objectives: The prevalence of diabetes mellitus is high among patients with developmental disabilities (Cerebral Palsy, Autism, Down's syndrome and cognitive disabilities). Developmentally disabled individuals experience delays in detection of chronic comorbidities, poor disease management and low quality of care. This research examines the racial health disparities in medication adherence and medication persistence in developmentally disabled adults with type 2 diabetes enrolled in Medicaid.

Methods: This was a retrospective cohort study based on the Health belief model and Aday Anderson's model of healthcare utilization. The dataset used for this research was the MarketScan® Multi-State Medicaid Database. Adults aged 18-64 years with a prior diagnosis of a developmental disability (cerebral palsy/autism/down's/cognitive disabilities) and a new diagnosis of type 2 diabetes enrolled in Medicaid from January 1, 2004 and December 31, 2006, were included. Adults were included if they had a continuous enrollment for at least 12 months and were excluded if they were dual eligible. Anti-diabetic medication adherence and diabetic medication persistence were measured using multivariate logistic regression and the Cox-proportional hazard regression respectively.

Results: The study population comprised of 1529 patients. After controlling for covariates, African Americans had significantly lower odds (25%) of adhering to anti-diabetic medications compared to Caucasians (OR = 0.75, 95% CI = 0.58-0.97, p<0.05). Also, after controlling for other covariates, the hazard was higher in African Americans compared to Caucasians (Hazard Ratio = 1.03, 95% CI = 0.91-1.18, p<0.629).

Conclusion: The needs of the developmentally disabled individuals are somewhat different than the needs of individuals without disabilities. Policy recommendations should focus on increasing the number of outpatient centers as well as primary caregivers who can understand the disease management needs of the patient and accordingly collaborate with other specialized healthcare professionals to enhance the overall quality of care of the patients.

Introduction

Developmental disabilities (DD) are a group of conditions that begin during the developmental period, and may result in physical, learning, language, or behavioral impairments. These conditions, affecting around one in six children in U.S., may impact everyday functioning, and usually last through a person's lifetime (Boyle 2011). According to recent estimates, about 15%, of children aged 3 through 17 years have one or more DD. These disabilities include ADHD, autism, cerebral palsy, downs syndrome, hearing loss, intellectual disability, learning disability, vision impairment and other developmental delays (Boyle 2011). Research shows that adults with developmental disabilities (DD) tend to have a more sedentary lifestyle, do not exercise often and tend to consume high calorie diet (McGuire 2007, Temple 2003, Ewing 2004). These practices can lead to obesity which is a risk factor for type 2 diabetes. Type 2 diabetes is a leading cause of morbidity, mortality, functional disability, reduced quality of life and several micro and macrovascular complications such as cardiovascular illnesses and blindness (Norris 2011, Gregg 2002).

According to the 2011 Centers for Disease Control and Prevention estimates, 25.8 million children and adults out of 311 million have diabetes and out of these 25.8 million, there are about 7 million people who have undiagnosed diabetes. In 2009, the number of diabetic people was 23.6 million so in just 2 years, this number has increased by 2.2 million (CDC 2011, U.S. Census Bureau). Adults older than 65 years have a seven times higher risk of developing type 2 diabetes compared to adults aged 20-44 years old (Diabetes Report Card 2012). In 2007-2009, the age estimated numbers stated that adults aged 20 years or more who were diagnosed with diabetes constituted 16.1% American Indians and Alaskan Natives, 12.6% non Hispanic African Americans, 11.8% Hispanics, 8.4% Asian Americans and 7.1% non Hispanic Caucasians

respectively (CDC 2011). Medicaid enrollees have twice the prevalence of diabetes compared to the general US population (Cohen 2007, Smith 2006). Debilitating comorbidities in diabetic patients can make the process of medication adherence challenging since more the number of conditions the patient has, more are the medications and more complex is managing several conditions at the same time. About 40% patients with diabetes have as many as three comorbidities (Maddigan 2005). Medication therapy in type 2 diabetes helps in achieving optimum glycemic control (Rozenfeld 2008, Ho 2006, Krapek 2004, Lawrence 2006, Schectman 2002, Pladevell 2004), controlling the related micro and macro vascular complications (UKPDS 33 1998, Stratton 2000) and reducing mortality (Ho 2006). The National Diabetes Statistics estimated by the 2007-2009 National Health Interview Survey show that among US based adults with either type 1 or type 2 diabetes, 58% consume only oral medications, 14% take both insulin and oral medications, 12% take only insulin and the remaining 16% do not take either of the two respectively (National Diabetes Statistics 2011). In a study by Krepek (2004), higher adherence levels were associated with a 10% reduction in HbA1c (Krapek 2004).

According to Adams et al (2005), African –Americans were more likely to display increased HbA1c in a HMO setting after adjusting for baseline Hba1c, Body Mass Index (BMI), age, annual measures of type of diabetes medications, diabetes-related hospitalization, number of HbA1c tests, physician visits, and non-diabetes medications. Minority patients with DD face cultural and language barriers in accessing healthcare and therefore have poor health outcomes. (Surgeon General Report 2002) In studies conducted in US and Australia, mortality rate was higher among African Americans with Down syndrome compared to Caucasians and among aboriginal adults with DD respectively (Ouellette-Kuntz 2005).

Diabetes is seen in 10.4% patients with DD (McDermott 2006). Another study using the 2006

Medical Expenditures Panel Survey (MEPS) showed that the prevalence of diabetes was higher in adults with cognitive disabilities (19.4%) compared to adults without cognitive disabilities (3.8%) (Reichard 2011). Adults with DD experience disparity in receipt of healthcare due to their physical and mental chronic comorbidities (Havercamp 2004, Fisher 2004, Parish 2006, Phillips 2002). Limited information exists about the prevalence and management of type 2 diabetes in adults with DD. The management of diagnosed chronic disease conditions in DD patients is poor (Beange 1995). Adults with cognitive disabilities are more likely to have four or more chronic disease conditions (Reichard 2011).

One study conducted in the Kansas Medicaid population showed that DD patients with diabetes had lower quality of care compared to the national standards (Shiremen 2010). Another study conducted in the same state showed that the screening rates of patients were better than the national standards, provided the diabetic patients had only physical disabilities (Reichard 2012). There is not a single study to date that has looked at the medication usage outcomes in adults with DD and type 2 diabetes. The life expectancy of the adults with DD has increased in recent decades but the additional years brought along by the increase in life expectancy have also brought along the burden of morbidity. There is a national concern about the health of adults with DD. They possess a higher risk for developing type 2 diabetes, need special accommodations for getting the appropriate care and face a number of challenges in accessing healthcare. Hence, this research looks at the fulfillment of type 2 diabetes needs in adults with DD enrolled in Medicaid, with regards to medication adherence and medication persistence.

Methods

Data source:

The study used the MarketScan® Multi-State Medicaid Database. The database comprises of

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data representing eight states in the United States. The Marketscan database also has information about the enrollment history, diseases that patients have, inpatient and outpatient claims, clinical variables, demographics and prescription claims. Patients' chronic disease conditions were diagnosed by using ICD-9-CM codes. Each patient also has a unique enrollee identifier which remains same during the entire period of enrollment in the database (Thomson Reuters 2007).

Sample selection:

The study is a retrospective cohort study with the study population enrolled from January 1st, 2003 to December 31st, 2007. The inclusion criteria comprised of participants aged 18-64 years with a developmental disability (DD) and a new diagnosis of type 2 diabetes. The index period was from January 1st, 2004 and December 31st, 2006. The study measured claims for oral hypoglycemic drugs newly started during the index period. Each subject was assigned an index diagnosis date when they first got a prescription filled for diabetes. The study population had a continuous enrollment of 12 months after the index diagnosis date. Patients with Medicaid and Medicare coverage (dual eligibles) were excluded. Only subjects who did not have claims for oral hypoglycemic medications in the 12 months before the index diagnosis date were included. After employing all the inclusion and exclusion criteria, the final study sample had 1,529 patients. Figure 4.1 presents a flowchart outlining the process of sample selection. ICD-9 codes that were used to identify diagnostic codes in the study table 4.1.

Study variables:

Dependent variables:

Adherence:

The first dependent variable in this study was medication adherence. Medication adherence was measured by using the Medication Possession Ratio (MPR). MPR is a widely accepted measure used in administrative claims dataset for determining medication adherence. MPR is defined as the number of days' supply during the study duration divided by the total number of days in the study duration (Karve 2008). The modified MPR (MPRm) takes into consideration the last day's supply. MPRm is defined as the total days supply of medications divided by the difference between the days supply of medications on the first and the last claim date added to the days supply of medications on the last date (Hess 2006, Vanderpoel 2004). In this study, MPRm was treated as a continuous variable and categorized as a dichotomous variable with a value of greater than or equal to 0.8 (high adherence) and less than 0.8 (low adherence) (Karve 2008).

Persistence:

The second dependent variable of the study was medication persistence. Medication persistence is defined as "the duration of time from initiation to discontinuation of therapy" (Cramer 2004). For the purpose of the study, medication persistence was defined as the period from the start of the anti-diabetic medication therapy to its discontinuation. Patients with refill gaps were also included in the study since a late refill might indicate lower medication adherence but not necessarily non-persistence. A gap of more than 120 days was considered as discontinued anti-diabetic therapy. In other words, patients with more than 120 days between two medication refills were termed as non-persistent.

Key tested independent variables:

In this study, race was the main independent variable. Race was categorized as Caucasians, African Americans and other races. The information about race was obtained from patients upon initial enrollment in the Medicaid program.

Covariates:

The covariates were selected based on the Andersen's model of healthcare utilization (Andersen 2008, Andersen 2007). According to the model, healthcare utilization can be predicted by predisposing, enabling and need based factors (Andersen 2008, Andersen 1973, Andersen 1995, Andersen 2007). The predisposing covariates that were chosen for this study consisted of age (grouped as 18-30, 31-40, 41-50, 51-60, and 61-64 years) and gender. The enabling factor that could enable patients to access healthcare was the type of health plan (fee-for-service, capitation, and dual). Severity of the disease is a need factor and it was measured in the study by determining the number of prescription refills (2-5, 5-10 and >10), the number of outpatient visits during the pre-index period (yes/no), the number of inpatient visits during the pre-index period (yes/no) and the Charlson comorbidity index during the pre-index period (0 and ≥1). The Charlson comorbidity index was used to control the overall severity of the illness in the study population. The index comprises of 19 different disease conditions and can predict mortality due to the severity of the comorbid disease conditions (Charlson 1987).

Statistical analyses

Patient demographic characteristics were studied using descriptive statistics. A student's t test and chi square test were used to compare MPRm in type 2 diabetic patients with DD by race (Caucasians versus African Americans) and by condition (Cerebral palsy, Autism, Downs

syndrome and Cognitive disability), respectively. A multivariate linear regression and a logistic regression (MPRm $\geq$ 0.8) were employed to assess the racial disparities in type 2 diabetic medication adherence in DD patients respectively, after controlling for other covariates. Medication persistence was measured by conducting survival analysis and a Cox proportional hazards model. The censored time was defined as the time during which patients persistently took anti-diabetic medications during the enrollment period. Racial and condition based differences in the censored time of the DD patients were studied using the unadjusted Kaplan-Meier survival curves. A Cox proportional hazard regression model was used to evaluate the racial differences in the hazards of time associated with discontinuing type 2 diabetic medications, after adjusting for other covariates. Data for the study was analysed using STATA 13 (StataCorp 2013). Statistical significance was attributed to variables with a p value of less than 0.05. The study proposal was approved by the Institutional Review Board (IRB) at the University of Michigan.

Results

The demographic characteristics of the study population are presented in table 4.2. There were a total of 1529 Medicaid enrollees with DD and type 2 diabetes in the study, meeting the inclusion and exclusion criteria. There were 57.49% females, 42.12% African Americans and 75.21% enrolled in the fee for service (FFS) Medicaid plan. During the pre-study period, 97.65% people had an outpatient visit and 26.10% people had an inpatient visit (Figure 4.2).

Table 4.3 describes the racial distribution of type 2 diabetes patients with different types of DD. Among all the races, Caucasians had the highest number of Cerebral palsy patients (57.70%),

Downs syndrome patients (61.18%) and Dognitive disability patients (50.63%) whereas African Americans had the highest number of Autism patients respectively (50%).

Adherence:

Table 4.4 compares the MPRm between Caucasians and African Americans with DD and type 2 diabetes. The MPRm variable is treated as continuous and as dichotomous for this comparison (<0.8 versus ≥0.8). Based on student's t test analysis, African Americans had significantly lower MPRm than Caucasian patients (0.91 vs. 0.88, p<0.01). Also, based on the chi square test, African Americans had significantly lower MPRm than Caucasian patients (0.80 vs. 0.74, p< 0.01).

The multivariate regression model (table 4.5) presents the predictors of medication adherence. MPRm was first analyzed as a continuous variable. Results showed that holding all the other covariates constant, among DD patients with type 2 diabetes, African Americans were negatively associated with the MPRm variable (β = -0.03, SE = 0.01, p<0.05). Also, holding for all the other variables constant, females with DD and type 2 diabetes were negatively associated with the MPRm variable (β = -0.03, SE = 0.01, p<0.05). Then, the MPRm variable was dichotomized as high adherence (MPRm<0.8) and low adherence (MPRm≥0.8). Controlling for all other covariates, compared to DD Caucasian patients with type 2 diabetes, the expected odds for anti-diabetic medication adherence were 29% lower in DD African-American patients with type 2 diabetes (OR=0.71, 95% CI = 0.55-0.93, p<0.05). Also, the adjusted odds of adhering to anti-diabetic medications in DD patients with type 2 diabetes was 25% lower in females compared to males, after controlling for other covariates (OR=0.75, 95% CI = 0.56-0.97, p<0.05).

Persistence:

Figure 4.2 presents the Kaplan-Meier survival curves showing anti-diabetic medication persistence in different races (Caucasians, African Americans and other races). The results of the Log Rank test were not significant even though the Kaplan-Meier survival curves showed that medication persistence in African American DD patients was less that of the Caucasian DD patients. Table 4.6 demonstrates the racial differences in anti-diabetic medication persistence. Compared to African American DD patients, slightly higher number of Caucasian DD patients persistently used anti-diabetics during the study period (30.3% vs. 29.3%). The median duration during which the Caucasian DD patients consumed anti-diabetics was higher than the duration for African American DD patients (189 days vs. 159 days).

Figure 4.3 presents the Kaplan-Meier survival curves showing anti-diabetic medication persistence in different types of DD patients (Cerebral palsy, Autism, Downs syndrome and Cognitive disability). The results of the Log Rank test were not significant even though the Kaplan-Meier survival curves showed that medication persistence in Autistic DD patients was the lowest among the different DD patients. Table 4.7 demonstrates the differences in the medication persistence across different types of DD patients. Patients with Cognitive disability (30.0%) persistently took anti-diabetics more than patients with Cerebral palsy (20.9%), followed by patients with Downs's syndrome (10.5%) and Autism (10.2%) respectively. The median duration during which the Cognitive disability patients (181 days) consumed anti-diabetics was more compared to the Autism patients (157 days), followed by the Downs syndrome patients (124 days) and the Cerebral palsy patients (94 days) respectively.

The results of the Cox-proportional hazards regression analysis can be seen in table 4.8. After

adjusting for all the other covariates, the hazard was higher in African American DD patients compared to Caucasian DD patients (Hazard Ratio = 1.03, 95% CI = 0.91-1.18). The hazard was however, non-significant.

Sensitivity analysis:

Table 4.10 shows medication adherence at different MPRm cut-off points. The cut-off points range from 0.4 to 0.9. The medication adherence decreased as the cut-off range was increased. The adherence drop was the highest (23.9%) when the cut-off point increased from 0.7 to 0.8. In the sensitivity analysis, the drop of 23.9% was the highest compared to any other drop when the MPRm cut-off was increased by 0.1 point.

Discussion

This research showed that African American Medicaid enrollees with DD and type 2 diabetes were less likely to adhere to anti-diabetic medications as well as persistently adhere to anti-diabetic medications compared to Caucasian Medicaid enrollees with DD and type 2 diabetes. The bivariate and multivariate statistics showed that racial disparities in type 2 diabetes medication adherence were significant. However, even though the survival statistics showed that African Americans showed lower persistence in adhering to anti-diabetic medications as well as the Cox-proportional hazards regression analyses suggested that African Americans experienced higher hazards of not persistently taking anti-diabetic medications compared to Caucasian patients respectively, the results for either were not statistically significant.

The results of this research indicating poor medication adherence among racial minorities were similar to a previous study conducted among the North Carolina Medicaid population (Shenolikar 2006). African Americans have a high prevalence of diabetes, poor

metabolic control and worse healthcare outcomes (Schectman 2002). Poorer glycemic control is observed among non-Hispanic blacks and Mexicans compared to non- Hispanic whites. In addition to higher burden of diabetes, treatment affordability, insufficient knowledge, complex medication dosing and desire for quicker relief might be some of the reasons that affect medication adherence in racial minorities (Shenolikar 2006, Dailey 2001, Paes 1997). In African Americans, poor glucose control is also associated with poor diet quality (Betancourt 2013) and social and internal diet temptations (Betancourt 2013). Both African American and Hispanics are significantly more likely to have borderline or poorly controlled hypertension, diabetes associated neuropathy, retinopathy, and diabetes-related amputations than non-Hispanic whites (Bonds 2003, Ness 1999, Harris 1998). In case of DD patients with chronic disease conditions, some of the reasons for medication non adherence are difficulty in communicating symptoms due to reduced cognitive functioning, polypharmacy, vision and hearing impairment, refusal or misuse of medications due to unpleasant side effects, incorrect medication consumption, incorrect medication consumption times, failure to understand the goals of treatment, non-supportive caregivers, insufficient resources, non adherence promoting contingencies (attention seeking behavior or escape tendency) and fragmented care (Juntunen 2012, Wallace 2006). Lower type 2 diabetes medication persistence in DD African Americans compared to DD Caucasians, though not significant, may have important implications in the form of microvascular and macrovascular complications that may have higher likelihood of occurring in racial minorities due to reduced medication persistence (Cramer 2008, Yeaw 2009). The reasons for higher hazards in racial minorities might be not getting their prescriptions refilled within 90 days, the complex medication regimens consisting of multiple medications, consuming free combination pills (multiple agents as separate pills) versus single pill combination (multiple

agents in one pill) and higher medication copayments. The higher hazards found in our study were similar to previous studies conducted in patients with major depressive disorder with comorbid anxiety disorder (Wu 2012) and patients with hypertension (Ferdinand 2013) respectively. The sensitivity analysis indicates that when the cutoff point of MPRm was increased from 0.8 to 0.9, the drop in medication adherence was quite sharp. Generally, in administrative claims database, the conventional cut-off point for medication adherence is considered to be 0.8 (Karve 2008). Higher medication adherence in DD patients with type 2 diabetes aged more than 50 years may indicate better community support and coordinated care for ageing population. (Vasek 2013)

The data for this study represents the Medicaid population from eight states enrolled from 2003 to 2007, contibuting to the generalizability of the study. Based on the generalizability of the study, policy makers can frame health policies to reduce racial disparities in healthcare outcomes experienced by the DD population.

The study is not without its limitations. Due to the observational nature of the study, there is no causal effect. The dataset did not capture variables such beliefs, attitudes or intentions associated with medication intake. These variables might vary by race and could help researchers better understand access to care among different races. Also, the data does not represent patients who have Medicare only, are uninsured, or are dual eligibles. The dual eligible population might have a higher severity of type 2 diabetes and related comorbidities, resulting in different medication intake and healthcare utilization patterns. Patients taking insulin were excluded from the study population since they represent the more severe cases. The assumption that a prescription filled was a prescription taken was made for calculating medication adherence of the study population. There is no measure in the dataset to verify the actual intake of the medications. A questionnaire

such as Morisky scale, asking the patients about their medication intake can be a viable tool for actual medication adherence assessment. Information about the educational background of the patients in not captured in the claims dataset. Due to lack of education, it is possible that patients might face challenges in understanding and following complex medication regimens, leading to lower medication adherence.

Conclusion

In this study, we found that there were racial disparities in anti-diabetic medication adherence among Medicaid enrollees with DD. The studies conducted in the future should look at the predictors that impact access to care, availability of primary and specialized care, social support as well as beliefs of the patients seeking care.

Acknowledgements

Disclosure

This manuscript is part of Ms. Isha Patel's original doctoral dissertation titled "Medication Use and Healthcare outcomes in Developmentally Disabled Medicaid adults with type 2 diabetes: A quantitative race based analysis".

Figure 4.1 The Analytic Framework of Obtaining the Study Population.

Step 1:
There were 213,644 DD patients in the MarketScan® Multi-State Medicaid Database from January 1st, 2003 to December 31st, 2007 (the study duration).

↓

Step 2:
22,093 DD patients (intellectual disability, cerebral palsy, autism) aged 18 to 64 years had a diagnosis of type 2 diabetes from January 1st, 2004 to December 31st, 2006 (the index period) were included. Each patient was assigned to have an index diagnosis date. There were 21,617 patients who had medication information. Patients with dual Medicare and Medicaid eligibility were excluded. There were 8772 patients meeting these exclusion criteria.

↓

Step 3:
Patients who were diagnosed with DD and were prescribed with an OHA during the index period were included in the study. The Medicaid IDs (ENROLID) were used to link the prescription drug claim to the detailed enrollment claim. 4,641 patients met these criteria.

↓

Step 4:
Patients having using any OHA during the pre-index period (12 months before the index diagnosis date) were also excluded. There were 2505 patients excluded in this step. Patients were required to be continuously enrolled from 12 months (the pre-index period) before and 12 months (the study period) after the index diagnosis date. There were 1529 patients who met the criteria and constituted towards the final sample of this study.

Figure 4.2 The Kaplan-Meier Survival Curves of Antidiabetic Persistence between Caucasian and African-American Patients[§]
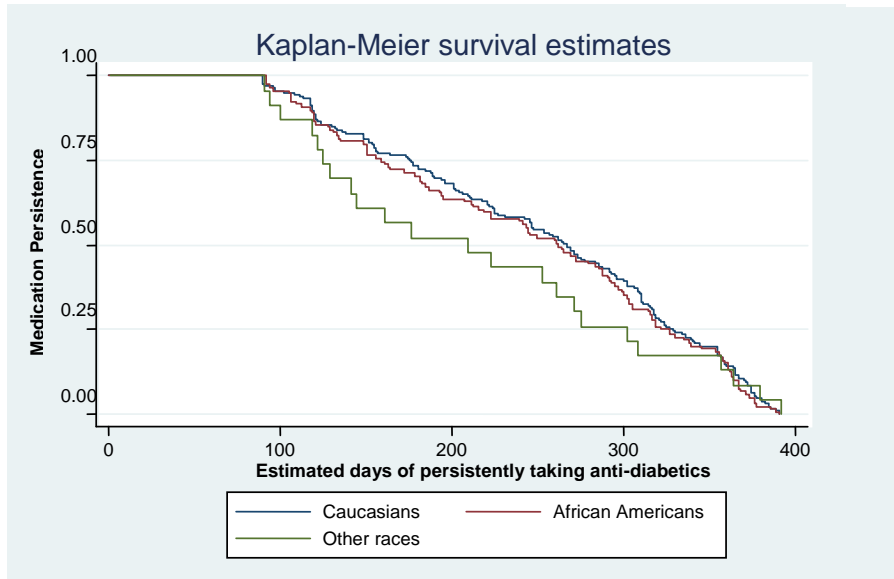
§: Log-Rank Test, p<0.5642

Figure 4.3 The Kaplan-Meier Survival Curves of Antidiabetic Persistence in Patients with different types of DD[§]
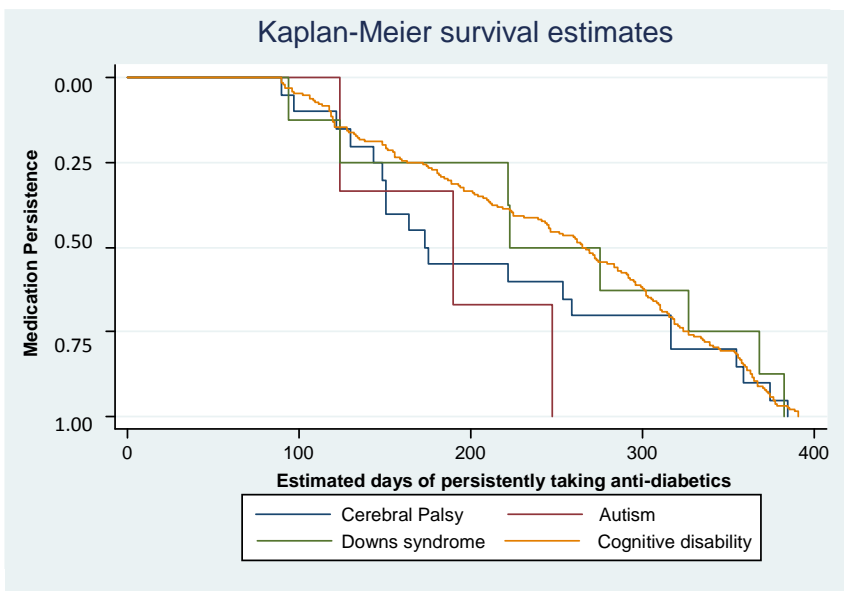
§: Log-Rank Test, p<0.3271

Table 4.1 ICD-9-CM codes*

Disease	Diagnosis	Codes±
Cerebral Palsy	Infantile cerebral palsy	343
	Congenital Diplegia	343.0
	Congenital Hemiplegia	343.1
	Congenital Quadriplegia	343.2
	Congenital Monoplegia	343.3
	Infantile Hemiplegia	343.4
	Other specified infantile cerebral palsy	343.8
	Cerebral Palsy, unspecified	343.9
Autism	Infantile autism	299.0
	Autistic Discord-Current	299.00
	Autistic Discord-Residual	299.01
Downs syndrome	Downs syndrome	758.0
Mental retardation	Mild mental retardation	317
	Moderate mental retardation	318.0
	Severe mental retardation	318.1
	Profound mental retardation	318.2
	Unspecified mental retardation	319

* ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification

Table 4.2 Descriptive Characteristics of the Study Population (N= 1529)

	Frequency	%
Race		
Caucasians	788	51.54
African Americans	644	42.12
Other races	97	6.34
Age (years)		
18-30	443	28.97
31-40	362	23.68
41-50	394	25.77
51-60	275	17.99
61-64	55	3.60
Gender		
Male	650	42.51
Female	879	57.49
FFS vs. Capitation		
FFS	1150	75.21
Capitation	312	20.41
Dual	67	4.38
Comorbidity (Charlson Index)		
0	917	59.97
≥ 1	612	40.03
Comorbidity pre-index period (Charlson Index)		
0	1036	67.76
≥ 1	493	32.24
Inpatient visit pre-index period		
0	1130	73.90
1	399	26.10
Outpatient visit pre-index period		
0	36	2.35
1	1493	97.65
Number of Medication refills		
2-5	1187	77.63
6-10	211	13.80
>10	131	8.57

Table 4.3. Distribution of diabetic population with different types of DD by race (N=1529)

Types of DD → Race ↓	Cerebral Palsy (n=201) Frequency (%)	Autism (n=68) Frequency (%)	Downs syndrome (n=85) Frequency (%)	Cognitive (n=1351) Frequency (%)
Caucasians (n=788)	116 (57.71)	30 (44.12)	52 (61.18)	684 (50.63)
African Americans(n=644)	71 (35.32)	34 (50)	29 (34.12)	578 (42.78)
Other races (n=97)	14 (6.96)	4 (5.88)	4 (4.70)	89 (6.59)

Table 4.4 Comparison of Medication Possession Ratio (MPRm) by race (N=1529)[§]

A: MPRm as a continuous variable:

MPRm$^{\Omega}$	Obs	Mean[#]	SD
Caucasians	788	.91	.18
African Americans	644	.88[**]	.19

$^{\Omega}$: Medication Possession Ratio modified
[§]: MPRm of the study population is 0.90
[#]: Student's T -test of MPRm between Caucasians and African Americans
Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

B: MPRm as a dichotomous variable:

MPRm$^{\Omega}$	Obs	Mean[#]	SD
Caucasians	788	.80	.40
African Americans	644	.74[**]	.44

$^{\Omega}$: Medication Possession Ratio modified
[§]: MPRm of the study population is 0.90
[#]: Student's T -test of MPRm between Caucasians and African Americans
Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 4.5 Predictors of Antidiabetic Adherence in Medicaid Enrollees with Developmental Disabilities: Multivariate Linear Regression Model and Multivariate Logistic Regression Model (N=1529)

| | MPRm[#] | | Odds ratio for medication adherence (80% of MPRm)[±] | |
	Coef.	SE	Odds ratio	95% CI
Race				
Caucasians	Reference	Reference	Reference	Reference
African Americans	-0.03[**]	0.01	0.71[*]	(0.55-0.93)
Other races	-0.00	0.02	1.42	(0.79-2.56)
Age (years)				
18-30	Reference	Reference	Reference	Reference
31-40	-0.01	0.01	0.90	(0.64-1.27)
41-50	0.00	0.01	1.02	(0.73-1.43)
51-60	0.02[*]	0.01	1.43	(0.96-2.14)
61-64	0.02	0.03	2.26	(0.96-5.35)
Gender				
Male	Reference	Reference	Reference	Reference
Female	-0.03[**]	0.01	0.75[*]	(0.57-0.97)
FFS vs. Capitation				
FFS	Reference	Reference	Reference	Reference
Capitation	-0.02	0.01	0.79	(0.58-1.07)
Dual	-0.05[*]	0.02	0.65	(0.39-1.08)
Comorbidity (Charlson Index)				
0	Reference	Reference	Reference	Reference
≥1	0.00	0.00	0.95	(0.85-1.08)
Comorbidity pre-index period (Charlson Index)				
0	Reference	Reference	Reference	Reference
≥1	-0.01	0.01	0.99	(0.84-1.15)
Inpatient visit pre-index period				
0	Reference	Reference	Reference	Reference
1	0.00	0.00	1.02	(0.93-1.12)
Outpatient visit pre-index period				
0	Reference	Reference	Reference	Reference
1	0.00[***]	0.00	1.00[**]	(1.00-1.01)

	MPRm[#]		Odds ratio for medication adherence (80% of MPRm)[±]	
	Coef.	SE	Odds ratio	95% CI
Number of Medication refills				
2-5	Reference	Reference	Reference	Reference
6-10	0.03	0.02	1.13	(0.75-1.69)
>10	0.09[***]	0.02	3.07[***]	(2.20-4.30)
Constant	0.86[***]	0.02	1.89[**]	(1.25-2.87)
Adjusted R^2	0.07		0.07	

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
#: Multivariate linear regression analysis
±: Multivariate logistic regression analysis

Table 4.6 Comparisons of medication persistence between Caucasian and African-American Patients with MDD (N=1529)[Ω]

Races	Censored(cases,%)[#¤]	Median time(days,95%CI)[§]
Caucasians (n=788)	239(30.33%)	189(154-221)
African Americans (n=644)	189(29.34%)	159(121-196)
Other races (n=97)	36(36.11%)	123(66-189)

#: No. of patients who persistently used antidepressants until the end of the follow-up period
¤: The follow-up period is one year (365 days)
§: Estimated median time that patients persistently used antidepressants
Ω: Log -Rank test, p<0.0946

Table 4.7 Comparisons of medication persistence between MDD Patients with and without Comorbid Anxiety Disorders (N=1529)[Ω]

Races	Censored(cases,%)[#¤]	Median time(days,95%CI)[§]
CP(n=201)	42(20.90%)	94(62-150)
Autism(n=68)	7(10.29%)	157(68-247)
Downs syndrome(n=85)	9(10.59%)	124(49-306)
Cognitive(n=1351)	406(30.06%)	181(155-207)

#: No. of patients who persistently used antidepressants until the end of the follow-up period
¤: The follow-up period is one year (365 days)
§: Estimated median time that patients persistently used antidepressants
Ω: Log -Rank test, p<0.3271

Table 4.8 Factors Associated with Antidiabetic Persistence in Medicaid Enrollees with Developmental Disabilities: Cox-proportional Hazard Regression Analysis (N=1529)

| | Cox Proportional Hazard Analysis | |
	Hazard Ratio	95% CI
Race		
Caucasians	Reference	Reference
African Americans	1.03	(0.91-1.18)
Other races	1.10	(0.81-1.49)
Age (years)		
18-30	Reference	Reference
31-40	0.87	(0.72-1.05)
41-50	0.86	(0.72-1.04)
51-60	0.80[*]	(0.66-0.97)
61-64	0.73	(0.53-1.00)
Gender		
Male	Reference	Reference
Female	0.95	(0.84-1.09)
FFS vs. Capitation		
FFS	Reference	Reference
Capitation	0.99	(0.84-1.17)
Dual	0.81	(0.64-1.03)
Comorbidity (Charlson Index)		
0	Reference	Reference
≥1	0.92[*]	(0.86-0.99)
Comorbidity pre-index period (Charlson Index)		
0	Reference	Reference
≥1	1.06	(0.98-1.14)
Inpatient visit pre-index period		
0	Reference	Reference
1	1.02	(0.97-1.07)
Outpatient visit pre-index period		
0	Reference	Reference
1	1.00[*]	(1.00-1.00)
Number of Medication refills		
2-5	Reference	Reference
6-10	0.88	(0.53-1.46)
>10	0.50[***]	(0.38-0.66)

Note: * p < 0.05, ** p < 0.01, *** p < 0.001

Table 4.9 Results of Sensitivity Analysis for Adherence
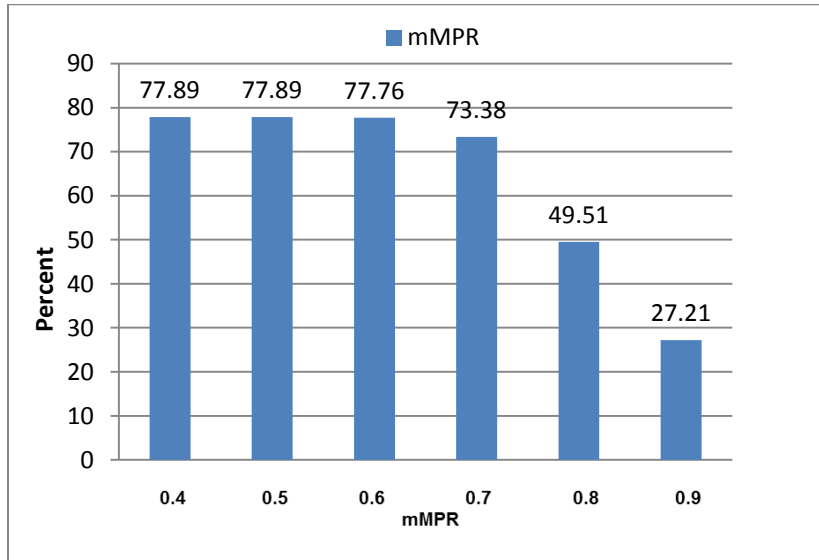
Chapter 5 Manuscript Two

Title: Association of Race and Medication Adherence with Healthcare Utilization and Healthcare costs in Medicaid Enrollees with Developmental Disabilities and type 2 diabetes

Abstract

Objective:

Adults with developmental disabilities have higher prevalence of chronic disease conditions such as diabetes, obesity, high blood pressure, arthritis, CVD and chronic pain. They also have poor healthcare utilization and screened less for chronic disease conditions. Very few studies have looked at the diabetes related health outcomes in developmentally disabled adults. The objective of this study was to examine the association of race, and medication adherence, and their interaction with healthcare utilization and healthcare costs in Medicaid enrollees with developmental disabilities (DD) and type 2 diabetes.

Methods:

This was a retrospective cohort study that identified the DD adults with type 2 diabetes from the MarketScan® Multi-State Medicaid Database. Enrollees aged 18-64 years who received new anti-diabetic medications from January 1, 2004 and December 31, 2006 were included. An index diagnosis date was assigned to each patient and adults with a continuous enrollment for at least 12 months were included. Probabilities of anti diabetic healthcare utilization (inpatient,outpatient

and emergency department visits) in DD adults were computed using multivariate logistic regression models. Multivariate negative binomial regression was used to measure the rate of change in type 2 diabetes related healthcare utilization in DD patients. Multivariate linear regression with log-transformation was used to determine type 2 diabetes related healthcare costs in DD Medicaid enrollees.

Results:

The study population comprised of 1529 patients. After controlling for all the covariates, compared to DD Caucasians, DD African Americans were more likely to have type diabetes related inpatient (OR=1.71; 95% CI, 1.02-2.85) and emergency department visits (OR, 1.67; 95% CI, 1.02-2.73). African Americans with DD and type 2 diabetes had significantly higher healthcare costs compared to Caucasians with DD and type 2 diabetes.

Conclusion:

Racial disparities exist in healthcare utilization in DD Medicaid patients with type 2 diabetes. Access to culturally competent healthcare providers, providers who accept Medicaid patients and continuous care can reduce inpatient visits and emergency room visits in racial minorities. More attention should be given to designing culturally appropriate health prevention and health promotion interventions for minorities.

Introduction

Diabetes Mellitus, a serious metabolic disorder is the seventh leading cause of death in the United States (US) (CDC 2011, Wild 2004, U.S. Census Bureau, Huang 2009, Deshpande 2008, Narayan 2006). The cost of diabetes related healthcare places a huge burden on the US economy with treatment costs and loss of productivity accounting for $174 billion in 2007. These costs are estimated to rise to $336 billion in 2034 (CDC 2011, Deshpande 2008, Huang 2009, Narayan 2006, Wild 2004, Huang 2009). About 15% of children in the agegroup of 3-17 years have disabilities like ADHD, cerebral palsy, (CP) hearing loss, intellectual disability, Downs syndrome, learning disability, vision impairment, autism spectrum disorders (ASDs) and other developmental delays (Boyle 2011). According to CDC, the lifetime cost to care for an individual with CP is nearly $1 million (2003) dollars (CDC 2004). According to CDC estimates, in U.S., around 6000 babies are born each year with Downs syndrome (Parker 2010). People with ASD have higher medical expenditure than those without ASDs. The mean expenditure for people with ASDs is 4.1-6.2 times ($4,110-$6,200/year) greater than those without ASDs (Shimabukuro 2008). Sedentary lifestyle, poor nutrition and high rates of obesity lead to increased risk of type 2 diabetes in patients with DD (Yamaki 2005, Rimmer 2006). When DD patients live independently, there is a higher likelihood of an unhealthy lifestyle with less dietary restrictions (Taggart 2012). Patients with developmental disabilities (DD) have a higher risk of developing type 2 diabetes. In 2006, the prevalence of diabetes in adults with cognitive disabilities was 19.4% compared to 3.8% in patients without cognitive disabilities respectively (Reichard 2011).

A study conducted using the 2001 North Carolina Behavioral Risk Factor Surveillance System and the North Carolina National Core Indicators survey showed that compared to

disabled adults with DD, adults without DD performed less amount of physical activity, received seven times less emotional support, had high health risk behaviors and had low breast cancer and cervical cancer screenings (Havercamp 2004, Ouellette-Kuntz 2005). The comorbid conditions associated with DD are more likely to be found among adults with low income, who also face socioeconomic disparities in access to healthcare (Surgeon General Report 2002). In North America, the prevalence of type 2 diabetes in the DD population can vary from 7.1% to 14%. (Havercamp 2004, Shiremen 2010, McDermott 2006, Lunsky 2011) A study in Northern Sydney showed that among people with DD, prevalence of type 2 diabetes complications, medical consultations, hospitalizations and mortality were higher compared to the people without DD. The study population also had many undetected conditions. Out of the 5.4 medical conditions that each patient had on an average, half the conditions remained undetected during previous physician visits (Beange 1995).

A study exploring relationships between access to diabetes care and health outcomes demonstrated that patients with restricted access to healthcare had higher Hba1c levels than those using acute care facilities. Also, patients without a usual source of care reported significantly higher Hba1c levels than patients receiving care at doctor's clinics (Rhee 2005). Medication adherence has been associated with fewer hospitalizations (Lau 2005) and lower health-care costs (Sokol 2005, Hepke 2004). Some of the common causes of non-adherence among adults with DD are fragmentation of care, comorbidity, polypharmacy, and consideration of medication side effects (Ince 2009). Paying for healthcare and prescriptions may compete with other basic needs and priorities and may create strong bottlenecks for access and adherence. Exploring the nature of these bottlenecks, a study by Heisler et al (2005) found that racial minorities were

twice as likely to cut down on necessities and incur debt in order to cope with medication costs compared to the white respondents (Heisler, 2005).

Medicaid covers uninsured and unemployed individuals, mainly comprising of pregnant women, children, adults with physical and developmental disabilities, and elderly and frail individuals. Individuals with disabilities make up just 14% of all the Medicaid enrollees and yet are accountable for 42% of the total Medicaid expenses. Research has shown that people with disabilities have higher rates of diabetes, depending on the type of disability (McDermott 2007, McDermott 2006). Among people with disabilities, rates of diabetes in patients with sensory or psychiatric disabilities are 31.6% and 24.7% respectively compared to 15.8% in patients without disabilities. Compared to patients with sensory or psychiatric disabilities, diabetes is seen in only 10.4% patients with DD. The rates of obesity are seen in 67% patients with DD, sensory and psychiatric disabilities. Chronic disease conditions including diabetes, are not managed properly in patients with DD (Beange 1995). Adults with DD have a higher risk of having multiple chronic disease conditions, generally four or higher (Reichard 2011). Two studies assessing health outcomes in Medicaid patients DD with diabetes have been conducted in Kansas. Results from one study state that the quality of care received by DD patients with diabetes was lower than the national recommended standards (Shiremen 2010). The other study showed that adults with physical disabilities and diabetes had better screening rates for chronic disease conditions compared to the national recommended rates (Reichard 2012). With increase in life expectancy of the patients with DD, their burden of morbidity and challenges in accessing care have also increased. The literature looking at healthcare utilization and costs in DD patients with type 2 diabetes is scarce. This study determines the racial disparities in healthcare utilization, primarily inpatient visits, outpatient visits, ER visits and healthcare costs in DD patients with type 2

diabetes enrolled in Medicaid. It also looks at the association of interaction of race and medication adherence with healthcare utilization and costs in the diabetic DD population enrolled in Medicaid.

Methods

Data sources:

The Marketscan Multi-State Medicaid database was used for conducting this study. It is a pooled Medicaid dataset that consists of claims from eight states in the United States and has variables that provide information about disease conditions, clinical outcomes and demography of the enrolled subjects. The dataset also has information about the enrollment periods of the enrollees, claims for inpatient visits, outpatient visits and prescriptions. The diagnoses in the dataset were identified using the ICD-9-CM codes. Each patient is assigned a confidential enrollee identifier and this identifier can be used to track patients longitudinally. The identifier is also same across different sets of claims (Thomson Reuters 2007).

Sample selection:

This retrospective cohort study was conducted with data from January 1st, 2003 to December 31st, 2007. Patients aged 18-64 years with diagnosis of developmental disabilities (DD) and a new prescription of oral hypoglycemic medications during January 1st, 2004 and December 31st, 2006 were included in the study. Each patient was assigned an index diagnosis date. Only drug naïve patients, i.e. patients who did not have any drug claims during the 12 months before the index diagnosis date, were included in the study. If patients were drug naïve, it was an indication that the patients were new users. Patients with continuous Medicaid enrollment for 12 months before and after the index diagnosis date were included in the study. Patients with claims for

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insulin and patients who were dual eligibles were excluded. After applying inclusion and exclusion criteria, the total sample size was 1,529. Table 5.1 represents the ICD-9-CM codes for DD.

Study variables:

Dependent variables:

The main dependent variables were type 2 diabetes related healthcare utilization and type 2 diabetes healthcare costs. Type 2 diabetes related healthcare utilization variables included inpatient visits, outpatient visits and ER visits respectively. Type 2 diabetes related healthcare costs included medication costs, medical costs (inpatient costs + outpatient costs) and overall costs (medication costs + medical costs) respectively. The term "type 2 diabetes related DD patients" comprised of patients with a primary diagnosis of DD (autism, cerebral palsy, downs syndrome, cognitive disability) and a secondary diagnosis of type 2 diabetes. The ICD-9-CM codes for DD were 299.0x (autism, where x=0-2), 317, 318.x and 319 (intellectual disabilities, where x=0-2), 343.x (cerebral palsy, where x=0-9) and 758 (Downs syndrome) and for type 2 diabetes were 250.x (where x=0,2). All the patient healthcare utilization with the above ICD-9-CM codes were defined as type 2 diabetes related healthcare utilization in patients with DD. Each healthcare utilization variable was coded dichotomously (yes/no). For example, type 2 diabetes related outpatient visits were coded 'yes' for patients having at least one outpatient visit (yes) and 'no' for patients having no outpatient visits during the study period. The healthcare costs variable was defined as the healthcare costs incurred by the patients during the study period. Healthcare costs were categorized as medication costs, medical costs and overall costs.

Key independent variables:

Race, medication adherence and the interaction of race and medication adherence were the three main independent variables in the study. The variable race was obtained from the participants upon enrollment into Medicaid. Race was categorized as Caucasians, African Americans, and other races. Claims for type 2 diabetes medications were identified in DD patients during the enrollment period after their index diagnosis date. DD patients with type 2 diabetes diagnosis were identified as having comorbid type 2 diabetes. The interaction term was the interaction between race and medication adherence. Since race might not completely account for the differences in healthcare outcomes and medication adherence is low in racial minorities, the interaction term was one of the main independent variables.

Covariates:

The covariates in this study were based on Andersen's model of healthcare utilization (Andersen 2008, Andersen 2007). According to this model, predisposing factors, enabling factors and need factors can predict healthcare utilization (Andersen 2008, Andersen 1973, Andersen 1995, Andersen 2007). For the purposes of this study, predisposing factors included age (grouped as 18-30, 31-40, 41-50, 51-60, and 61-64 years) and gender. The enabling factors determine access to healthcare. In this study, the enabling factor was the type of health plan (fee-for-service, capitation, and dual). The need factors in the study were number of prescription refills (2-5, 5-10 and >10) and severity of the disease, which was measured by the number of outpatient visits during the pre-index period (yes/no), the number of inpatient visits during the pre-index period (yes/no), the Charlson comorbidity index during the pre-index period (0 and ≥1) and the

Charlson comorbidity index during the study duration (Andersen 1973, Andersen 1995). This study used the Charlson comorbidity index, an index consisting of 17 different disease conditions used to predict mortality associated with the severity of comorbid conditions. This index was used as a measure to assess the overall severity of the illness in the study population (Charlson 1987). The modified MPR (MPRm) that includes the patient's last day of anti diabetic medication supply was also one of the covariates in the study. MPRm was categorized as high adherence if the value was greater than 0.8 and low adherence if the value was less than or equal to 0.8 (Hess 2006, Karve 2009).

Statistical analyses

Descriptive statistics were computed to study the patient characteristics. Healthcare utilization (outpatient visits, inpatient visits and ER visits) was compared using student's t-test. Comparison between Caucasians and African Americans on healthcare costs (medication costs, medical costs and overall costs) was also conducted using student's t-test. Multivariate regression analysis was performed to determine the association between type 2 diabetes related healthcare utilization (number of outpatient visits, number of inpatient visits, and number of ER visits), and race, medication adherence and their interaction. First, multivariate logistic regression analyses were done to estimate the probability of occurrence of any of the healthcare utilization independent variables (outpatient visits, inpatient visits and ER visits). Then, multivariate negative binominal regression analyses were performed to determine the change in outpatient visits given the patients had at least one outpatient visit. Similarly, multivariate zero negative binominal regression analyses were conducted to determine the change in inpatient and ER visits, given the patients had at least one inpatient and ER visit respectively. Multivariate linear regression analyses were used to predict log-transformed healthcare costs as a function of race, medication

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adherence, their interaction, and other covariates. In the study, data management was performed using SAS v.9.3 (SAS Institute 2011). All the data analysis was completed using STATA 13 (StataCorp 2013) Statistical significance was determined by obtaining a 0.05 level of significance in two tailed tests and other analyses. This study was approved by the Institutional Review Board (IRB) at the University of Michigan.

Results

Table 5.2 describes the demographic characteristics of the study population. Among 1529 Medicaid enrollees with DD and type 2 diabetes, 28.97% people were aged 18-30 years, 57.49% were females, 42.12% were African Americans, 97.65% had an outpatient visit during the pre-index period and 26.10% had an inpatient visit during the pre-index period.

Table 5.3 illustrates the mean differences in healthcare utilization (number of outpatient visits, number of inpatient visits and number of ER visits) among different races with DD and type 2 diabetes. Compared to Caucasians with DD and type 2 diabetes, African Americans with DD and type 2 diabetes had significantly less number of outpatient visits (125.67 versus 10.7.93, p<0,05). Also, among DD patients with type 2 diabetes, compared to Caucasians, African Americans had higher number of inpatient visits (0.77 versus 1.02) and ER visits (2.66 versus 3.17) respectively, even though these differences were not statistically significant.

Table 5.4 presents the mean differences in healthcare costs (medication costs, medical costs and overall costs) among different races with DD and type 2 diabetes. Compared to Caucasians with DD and type 2 diabetes, African Americans with DD and type 2 diabetes had significantly higher medication costs ($1284.69 versus $1114.85, p<0,05). Similarly, among DD patients with type 2 diabetes, compared to Caucasians, African Americans had higher medical costs ($39248.37

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versus $43423.2) and overall costs ($40363.22 versus $44707.89) respectively, even though these differences were not statistically significant.

Table 5.5 shows the association between race, medication adherence and their interaction with type 2 diabetes related healthcare utilization in DD patients enrolled in Medicaid using multivariate logistic regression models. Controlling for all the other covariates, the adjusted odds of having type 2 diabetes related inpatient visits in African Americans with DD were 1.70 times greater than the adjusted odds of having type 2 diabetes related inpatient visits in Caucasians with DD (OR =1.71, 95% CI = 0.53-1.16, p<0.05). Controlling for all the other covariates, the adjusted odds of having type 2 diabetes related outpatient visits in African Americans with DD were 19% lower than the adjusted odds of having type 2 diabetes related inpatient visits in Caucasians with DD (OR =0.81, 95% CI=0.38-1.76). Controlling for all the other covariates, the adjusted odds of having type 2 diabetes related ER visits in African Americans with DD were 1.67 times greater than the adjusted odds of having type 2 diabetes related inpatient visits in Caucasians with DD (OR =1.62, 95% CI=1.03-2.73, p<0.05). The interaction between race and medication adherence was significant. After controlling for all the other covariates, DD African American with lower medication adherence had higher probability of having type 2 diabetes related ER visits compared to DD African Americans with higher medication adherence, Caucasians with higher medication adherence, and Caucasians with lower medication adherence (OR = 2.05, 95% CI =1.19-3.55, p<0.05).

Tables 5.6 shows the association between race, medication adherence and their interaction with type 2 diabetes related healthcare utilization in DD patients enrolled in Medicaid. These associations were computed using multivariate negative binomial regression models. The expected number of type 2 diabetes related inpatient visits in African Americans with DD was

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72% (RR =1.77, 95% CI = 1.12-2.63, p<0.05) greater compared to the expected number of type 2 diabetes related inpatient visits in Caucasians, after controlling for other covariates. The expected number of type 2 diabetes related outpatient visits in African Americans with DD was 5% (RR =0.95, 95% CI = 0.76-1.19) lower compared to the expected number of type 2 diabetes related inpatient visits in Caucasians, after controlling for other covariates. The expected number of type 2 diabetes related ER visits in African Americans with DD were significantly higher than the expected number of type 2 diabetes related inpatient visits in Caucasians, after controlling for other covariates (RR =1.76, 95% CI = 1.18-2.61, p<0.01). After controlling for all the other covariates, compared to DD African Americans with higher medication adherence, Caucasians with higher medication adherence and Caucasians with lower medication adherence, DD African Americans with lower medication adherence had higher probability of having type 2 diabetes related ER visits (RR =1.88, 95% CI = 1.22-2.91, p<0.01).

Table 5.7 presents the associations between race, medication adherence, and the interaction between race and medication adherence with log-transformed healthcare costs (medication costs, medical costs and overall costs). Among DD patients with type 2 diabetes, after holding all the other covariates constant, higher medication adherence (≥80%) was negatively associated with medication costs (β = -0.32, p<0.01), medical costs (β = -0.48, p<0.001) and overall healthcare costs (β = -0.52, p<0.001). After holding all the other covariates constant, among DD patients with type 2 diabetes, compared to Caucasians, African American patients had 23% higher medication costs, 26% higher medical costs and 21% higher overall costs respectively. The interaction between medication adherence and race was not statistically significant for any of the three types of costs (medication costs, medical costs or overall costs).

Discussion

This study found that African Americans with DD and type 2 diabetes had higher healthcare expenditures, ER visits and inpatient visits compared to Caucasians with DD and type 2 diabetes. There is a need for establishing local outpatient healthcare facilities that can specifically fulfill mental and physical health needs in adults with DD. Patients with DD going for a physical examination can require three times more time as compared to patients without cognitive disabilities due to barriers such as difficulty in communicating symptoms, inability to tolerate longer waiting times, displaying aggressive behavior or reluctance to get a physical, fear of needles, fear of examination of private areas, fear of new physicians and need for physical assistance for many procedures (Doostan 1999). Adults with DD visit the ED department to a far larger extent than adults without DD; this can be attributed to the lack of sufficient centers providing specialized outpatient services to this unique group of patients and lack of continuity of primary and specialist care (Lunsky 2012). Previous research on healthcare access in minorities shows that minorities tend to drop out more from community programs, receive less comprehensive services, lack access to trained culturally competent or bilingual healthcare providers, and are more underserved (National Council on Disability website). The risk of higher healthcare utilization can be reduced by increasing the number of primary and specialty providers who accept Medicaid patients, improving access to culturally sensitive and competent minority healthcare providers with cultural backgrounds similar to minority patients', physicians using respectful language and terminologies during patient encounters, providing language assistance to patients, and increasing rates of out of home placement for minority DD patients with chronic diseases. (National Center for Cultural Competence website, Smedley 2002, Hsu 2007(b), McGuire 2008, University of California at San Francisco website)

In this study, 26% patients had an inpatient visit and 32% patients had comorbidities during the pre-study period. This shows that the DD Medicaid enrollees in this study were vulnerable and had poor health status. Medicaid population is generally less educated and has lower SES. Compared to Caucasians, lower medication adherence in African Americans might be associated with a higher prevalence of diabetes, limited access to multi drug regimen and higher HbA1c levels (Schectman 2002). Some of the reasons for low medication adherence in DD patients are incorrect medication intake, wrong medication intake times, failure or refusal to consume medications, failure to understand the goals of treatment, insufficient resources and failure to comply with medication therapy (Wallace 2006). It can be quite challenging for minority DD patients with chronic disease conditions to access and utilize healthcare services. Hence the interaction term (being African American and having low medication adherence) shows a reduced effect on healthcare utilization.

This study found that DD patients enrolled in capitated Medicaid plans had lower anti diabetic medication adherence, higher inpatient visits, lower outpatient visits and higher ER visits compared to DD patients enrolled in FFS Medicaid plans. These findings were similar to a previous study conducted in Medicaid patients with type 2 diabetes, who were enrolled in capitated and FFS plans. Medicaid enrollees have very low copayments and out of pocket expenditures ($1-$3) for most of the services. Patients in capitated plans have limited prescription drug benefits due to presence of a cap on medication related spending. Out of pocket expenditures increase once the cap is reached and this may lead to reduced medication adherence or discontinuation of therapy. In capitated plans, reduced adherence, inadequately provided health services, shorter treatment periods, limited patient follow up, and poor treatment can contribute to higher healthcare utilization (Pawaskar 2010, Cox 2001, Tseng 2004).

This study provides important implications for health research and policy. The study has high generalizability since the Medicaid population chosen as the study population represents eight states enrolled from 2003 to 2007. The study findings provide important information about the association of race, medication adherence, and their interaction with healthcare outcomes in Medicaid enrollees with DD and type 2 diabetes. One of the advantages of conducting this study was that the study variables were based on the Aday Andersen's model of healthcare utilization which made it feasible to determine the predictors of medication usage and related healthcare utilization (Andersen 2007). The usage of the model helped in controlling predisposing, enabling, and need factors so that the association between race, medication adherence and its interaction with healthcare utilization could be determined.

The study has a few limitations. Causation cannot be attributed due to the observational nature of the study. Variables such as beliefs, attitudes or intentions that are associated with healthcare utilization were not captured in this study. The study does not represent the people enrolled in Medicare, commercial insurers or dual eligibles. Claims data also does not have clinical measures such as HbA1c levels which are a measure of diabetes severity level. Hence, the healthcare utilization in the pre-study period was used as a proxy to determine the severity of type 2 diabetes. It is not possible to capture patient satisfaction using claims data. While information about primary and specialized care can be obtained from the claims dataset, collaboration between different types of providers for a particular patient cannot be measured. In case of developmentally disabled individuals, coordination of care can reduce hospitalization (Criscione 1995, Pincus 1987, Walsh 1997). Activities that are not reimbursed such as care coordination by social workers or the extent of caregiving provided by family members cannot be captured by claims dataset.

Conclusion

Racial disparities were existent in healthcare utilization and healthcare costs in type 2 diabetes patients with DD enrolled in Medicaid. African Americans were more likely to have inpatient and ER visits respectively. Also, African Americans were more likely to have higher type 2 related healthcare costs compared to Caucasians. Future studies should focus on determining the effect of interventions involving access to culturally competent providers, continuity of care and coordinated care on healthcare utilization in racial minorities. Studies should also assess the healthcare utilization and healthcare costs in DD patients with other chronic disease conditions such as CVD, hypertension, chronic kidney disease, asthma, etc.

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Table 5.1 ICD-9-CM codes*

Disease	Diagnosis	Codes±
Cerebral Palsy	Infantile cerebral palsy	343
	Congenital Diplegia	343.0
	Congenital Hemiplegia	343.1
	Congenital Quadriplegia	343.2
	Congenital Monoplegia	343.3
	Infantile Hemiplegia	343.4
	Other specified infantile cerebral palsy	343.8
	Cerebral Palsy, unspecified	343.9
Autism	Infantile autism	299.0
	Autistic Discord-Current	299.00
	Autistic Discord-Residual	299.01
Downs syndrome	Downs syndrome	758.0
Mental retardation	Mild mental retardation	317
	Moderate mental retardation	318.0
	Severe mental retardation	318.1
	Profound mental retardation	318.2
	Unspecified mental retardation	319

* ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification

Table 5.2 Descriptive Characteristics of the Study Population (N= 1529)

	Frequency	%
Race		
Caucasians	788	51.54
African Americans	644	42.12
Other races	97	6.44
Age (years)		
18-30	443	28.97
31-40	362	23.68
41-50	394	25.77
51-60	275	17.99
61-64	55	3.60
Gender		
Male	650	42.51
Female	879	57.49
FFS vs. Capitation		
FFS	1150	75.21
Capitation	312	20.41
Dual	67	4.38
Comorbidity (Charlson Index)		
0	917	59.97
≥ 1	612	40.03
Comorbidity pre-index period (Charlson Index)		
0	1036	67.76
≥ 1	493	32.24
Inpatient visit pre-index period		
0	1130	73.90
1	399	26.10
Outpatient visit pre-index period		
0	36	2.35
1	1493	97.65
Number of Medication refills		
2-5	1187	77.63
6-10	211	13.80
>10	131	8.57

Table 5.3 Racial differences in healthcare utilization in type 2 diabetes patients with DD (N= 1529)

Healthcare Utilization	Caucasians Mean	SD (N=788)	African Americans Mean	SD (N=644)
No. of outpatient visits	125.67	195.39	107.93[*]	178.30
No. of inpatient visits	0.77	1.83	1.02	2.96
No. of ER visits	2.66	4.98	3.17	7.66

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
Student's T -test of healthcare utilization between Caucasians and African Americans

Table 5.4 Racial differences in healthcare costs in type 2 diabetes patients with DD (N= 1529)

Healthcare Costs	Caucasians Mean	SD (N=788)	African Americans Mean	SD (N=644)
Cost of medications	1114.85	1687.92	1284.69[*]	1822.73
Medical costs	39248.37	2520.66	43423.2	2586.64
Overall costs	40363.22	2530.09	44707.89	2601.27

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
Medical costs = Inpatient costs + Outpatient costs
Overall costs = Cost of medications + Medical costs
Student's T -test of healthcare costs between Caucasians and African Americans

Table 5.5 Predictors of healthcare utilization in type 2 diabetes patients with DD: Multivariate logistic regression models (N=1529)

	Inpatient visits		Outpatient visits		ER visits	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Adherence						
MPRm<80%	Reference	Reference	Reference	Reference	Reference	Reference
MPRm≥80%	0.78	(0.53-1.16)	1.05	(0.57-1.94)	0.59**	(0.40-0.87)
Race						
Caucasians	Reference	Reference	Reference	Reference	Reference	Reference
African Americans	1.71*	(1.02-2.85)	0.82	(0.38-1.76)	1.67*	(1.02-2.73)
Other races	1.64	(0.82-3.31)	1.12	(0.40-3.16)	1.66	(0.88-3.11)
Interaction between race and MPRm						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	1.35	(0.75-2.42)	0.60	(0.25-1.46)	2.05*	(1.18-3.55)
Age (years)						
18-30	Reference	Reference	Reference	Reference	Reference	Reference
31-40	0.99	(0.69-1.42)	0.77	(0.45-1.35)	0.99	(0.74-1.35)
41-50	1.46*	(1.06-2.02)	0.69	(0.40-1.19)	1.06	(0.79-1.44)
51-60	1.37	(0.95-1.97)	0.38**	(0.21-0.68)	0.86	(0.61-1.21)
61-64	2.76***	(1.57-4.85)	1.19	(0.32-4.42)	1.47	(0.80-2.71)
Gender						
Male	Reference	Reference	Reference	Reference	Reference	Reference
Female	0.96	(0.75-1.23)	1.32*	(0.89-1.95)	1.42**	(1.14-1.78)
FFS vs. Capitation						
FFS	Reference	Reference	Reference	Reference	Reference	Reference
Capitation	1.15	(0.83-1.58)	1.01	(0.64-1.58)	1.47**	(1.11-1.96)
Dual	1.49	(0.87-2.54)	1.00	(omitted)	1.73	(0.99-3.03)
Comorbidity (Charlson Index)						
0	Reference	Reference	Reference	Reference	Reference	Reference
≥1	1.61***	(1.38-1.86)	1.66**	(1.16-2.36)	1.62***	(1.34-1.96)
Comorbidity pre-index period (Charlson Index)						
0	Reference	Reference	Reference	Reference	Reference	Reference
≥1	1.00	(0.83-1.21)	0.85	(0.57-1.26)	1.06	(0.85-1.32)
Inpatient visit pre-index period						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	1.85***	(1.57-2.18)	0.98	(0.81-1.18)	2.06***	(1.67-2.54)
Outpatient visit pre-index period						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	1.00**	(1.00-1.00)	1.06***	(1.05-1.08)	1.00**	(1.00-1.00)
Number of Medication refills						
2-5	Reference	Reference	Reference	Reference	Reference	Reference
6-10	1.28	(0.78-2.08)	2.36**	(1.38-4.05)	1.15	(0.76-1.75)
>10	1.63*	(1.10-2.40)	12.38***	(7.32-20.92)	1.53*	(1.10-2.14)
Constant	0.09***	(0.05-0.16)	0.55	(0.25-1.19)	0.43***	(0.21-0.54)
Adjusted R^2	0.16		0.29		0.13	

Table 5.6 Predictors of healthcare utilization in type 2 diabetes patients with DD: Multivariate negative binomial regression models (N=1529)

	Inpatient visits		Outpatient visits		ER visits	
	Relative$^{\Omega}$ Risk	95% CI	Relative$^{\Omega}$ Risk	95% CI	Relative$^{\Omega}$ Risk	95% CI
Adherence						
MPRm<80%	Reference	Reference	Reference	Reference	Reference	Reference
MPRm≥80%	0.80	(0.60-1.07)	1.13	(0.93-1.35)	0.50***	(0.38-0.67)
Race						
Caucasians	Reference	Reference	Reference	Reference	Reference	Reference
African Americans	1.72*	(1.12-2.63)	0.95	(0.76-1.19)	1.76**	(1.18-2.61)
Other races	1.27	(0.73-2.22)	0.78	(0.59-1.03)	1.39	(0.85-2.28)
Interaction between race and MPRm						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	1.47	(0.90-2.39)	0.96	(0.75-1.24)	1.88**	(1.22-2.91)
Age (years)						
18-30	Reference	Reference	Reference	Reference	Reference	Reference
31-40	1.08	(0.78-1.48)	1.17*	(1.00-1.36)	0.92	(0.72-1.17)
41-50	1.18	(0.89-1.57)	1.12	(0.96-1.30)	0.90	(0.71-1.14)
51-60	1.14	(0.82-1.57)	0.99	(0.85-1.15)	0.73*	(0.56-0.95)
61-64	1.57*	(1.03-2.45)	1.07	(0.79-1.47)	0.85	(0.52-1.38)
Gender						
Male	Reference	Reference	Reference	Reference	Reference	Reference
Female	0.96	(0.78-1.19)	1.17**	(1.04-1.30)	1.20*	(1.00-1.43)
FFS vs. Capitation						
FFS	Reference	Reference	Reference	Reference	Reference	Reference
Capitation	1.08	(0.83-1.40)	0.79***	(0.69-0.90)	1.57***	(1.26-1.95)
Dual	1.30	(0.88-1.93)	1.38*	(1.08-1.77)	1.78**	(1.22-2.60)
Comorbidity (Charlson Index)						
0	Reference	Reference	Reference	Reference	Reference	Reference
≥1	1.51***	(1.37-1.67)	1.15***	(1.09-1.21)	1.40***	(1.28-1.53)
Comorbidity pre-index period (Charlson Index)						
0	Reference	Reference	Reference	Reference	Reference	Reference
≥1	0.97*	(0.87-1.07)	0.92**	(0.86-0.98)	1.01	(0.91-1.11)
Inpatient visit pre-index period						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	1.47***	(1.37-1.58)	1.03	(0.99-1.07)	1.33***	(1.24-1.42)
Outpatient visit pre-index period						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	1.00**	(1.00-1.00)	1.01***	(1.01-1.01)	1.00***	(1.00-1.00)

	Inpatient visits		Outpatient visits		ER visits	
	Relative$^{\Omega}$ Risk	95% CI	Relative$^{\Omega}$ Risk	95% CI	Relative$^{\Omega}$ Risk	95% CI
Number of Medication refills						
2-5	Reference	Reference	Reference	Reference	Reference	Reference
6-10	1.09	(0.74-1.60)	1.20	(1.00-1.45)	0.98	(0.70-1.38)
>10	1.92***	(1.38-2.66)	3.21***	(2.75-3.75)	1.74***	(1.31-2.31)
Constant	0.15***	(0.09-0.25)	15.16***	(12.13-18.96)	0.83	(0.55-1.25)
Alpha	1.83	(1.52-2.22)	0.67	(0.62-0.73)	1.77	(1.57-1.99)
Likelihood-ratio (LR)	Chibar^2(01) = 860.88		Chibar^2(01) = 3.15e+05		Chibar^2(01) = 4492.06	
Test of alpha=0	Prob>=Chibar^2 = 0.000		Prob>=Chibar^2 = 0.000		Prob>=Chibar^2 = 0.000	
Vuong test	Z = 5.53; Prob>z=0.054		Z = -14.2; Prob>z =0.054		Z = 4.70; Prob>z=0.052	
Log likelihood	-1677.45		-8044.52		-3027.41	

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
$^{\Omega}$: Negative binomial regression model

Table 5.7 Predictors of healthcare costs in type 2 diabetes patients with DD: Multivariate linear regression models (N=1529)

	Medication costs		Medical costs		Overall costs	
	β coefficient	SE	β coefficient	SE	β coefficient	SE
Adherence						
MPRm<80%	Reference	Reference	Reference	Reference	Reference	Reference
MPRm≥80%	-0.32**	0.11	-0.48***	0.12	-0.52***	0.11
Race						
Caucasians	Reference	Reference	Reference	Reference	Reference	Reference
African Americans	0.23**	0.08	0.26**	0.09	0.21*	0.09
Other races	0.08	0.13	0.19	0.17	0.14	0.16
Interaction between race and MPRm						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	-0.27	0.16	-0.11	0.18	-0.09	0.17
Age (years)						
18-30	Reference	Reference	Reference	Reference	Reference	Reference
31-40	0.01	0.09	-0.04	0.11	-0.01	0.10
41-50	0.10	0.09	-0.04	0.11	0.04	0.10
51-60	0.08	0.10	-0.16	0.13	-0.07	0.11
61-64	0.22	0.16	0.25	0.19	0.24	0.18
Gender						
Male	Reference	Reference	Reference	Reference	Reference	Reference
Female	-0.01	0.07	0.02	0.08	-0.03	0.07
FFS vs. Capitation						
FFS	Reference	Reference	Reference	Reference	Reference	Reference
Capitation	0.07	0.08	-0.70***	0.10	-0.69***	0.09
Dual	0.24	0.14	0.29	0.05	0.24	0.16
Comorbidity (Charlson Index)						
0	Reference	Reference	Reference	Reference	Reference	Reference
≥1	0.12***	0.03	0.29***	0.04	0.25***	0.04
Comorbidity pre-index period (Charlson Index)						
0	Reference	Reference	Reference	Reference	Reference	Reference
≥1	-0.10*	0.04	-0.08	0.05	-0.08	0.05
Inpatient visit pre-index period						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	0.02	0.02	0.13***	0.03	0.12***	0.03
Outpatient visit pre-index period						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	-0.00**	0.00	0.01***	0.00	0.01***	0.00
Number of Medication refills						
2-5	Reference	Reference	Reference	Reference	Reference	Reference
6-10	1.21***	0.11	0.94***	0.13	1.04***	0.12
>10	2.77***	0.08	2.25***	0.10	2.47***	0.09
Constant	3.96***	0.13	7.17***	0.15	7.26***	0.14

Adjusted R^2	0.44	0.37	0.43

Note: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Chapter 6 Overall Conclusions

6.1 Study Conclusion

The prevalence of chronic disease conditions in DD patients is high. Racial disparities are existent in developmentally disabled individuals with type 2 diabetes. Since the study population has Medicaid insurance, their socioeconomic status is lower and disease severity is more as compared to individuals with private insurance coverage or Medicare. The care process of DD patients is complex and factors such as medication intake can help researchers to better understand this process. The aim of this study was to understand the role of race and other predictors that determine medication adherence and medication persistence in type 2 diabetic DD patients with Medicaid coverage. In the Medicaid population, compared to Caucasians, the type 2 diabetes medication adherence was lower in African Americans. Also, African Americans had lower anti diabeticmedication persistence and a higher hazard of not persistently taking type 2 diabetes medications, though the results were not statistically significant.

The study also looked at the predictors of the type 2 diabetes related healthcare utilization and healthcare costs in the DD population respectively. Race was interacted with medication adherence of the DD population to study its effect on type 2 diabetes related healthcare utilization outcomes such as inpatient visits, outpatient visits and ER visits as well as type 2 diabetes related healthcare costs such as medication costs, medical costs and overall costs

respectively. Type 2 diabetic African American adults with DD enrolled in Medicaid were more likely to have higher inpatient visits and ER visits and lower outpatient visits (non-significant) compared to type 2 diabetic Caucasian adults with DD enrolled in Medicaid. Also, among adults enrolled in Medicaid, the likelihood of higher medication, medical and overall expenditure were more in African American adults with DD and type 2 diabetes compared to their Caucasian counterparts.

6.2 Overall Implications

This study provides important implications for health research and policy. The study has high generalizability since the Medicaid population chosen as the study population represents eight states enrolled from 2003 to 2007. One of the strengths of the study was that the study variables were based on the Andersen's model of healthcare utilization. This model provided a theoretical background for the study. It allowed the researchers to control the predisposing, enabling, and need factors that helped in explaining the racial disparities in medication use outcomes and healthcare utilization in Medicaid enrollees with DD and type 2 diabetes. This study has important implications for the association of race, medication adherence, and their interaction with healthcare outcomes in Medicaid enrollees with DD and type 2 diabetes.

6.2.1 Access to care

Families of minority patients with DD face many difficulties in their search for primary care and specialty physicians that they can trust (Caudle 1993, Cornelius 1993, Friedman 1994, Kindig 1993). Since many physicians are unaware about providing the appropriate treatment for DD patients, accessing care is an issue in this population, especially for non-English speaking patients with cultural values differing from the physicians' (Scott 1993, Woloshin 1995, Riddick, 1998, Vasquez 1991). Many a times, minority patients with DD also

face physical barriers when they go for their examination. These barriers comprise of lack of wheel chair friendly examination rooms, enlarged door frames, ramps or additional bathroom equipment. Lack of the right equipment at home prevents these patients from performing day to day activities (Reichard 2004). Lack of transportation in rural areas, longer travelling distances, longer waiting times, limited access to specialized services and family members missing work for taking patients for physician visits can lead to social exclusion in patients by limiting their access to healthcare services, physical activity, recreation and attending health appointments (Rask 1994, Smith 1996, Crain 1998, Harbaugh 1998).

Patients with DD going for a physical examination can require three times more time as compared to patients without DD due to barriers such as difficulty in communicating symptoms, inability to tolerate longer waiting times, displaying aggressive behavior and reluctance to get a physical, fear of needles, fear of examination of private areas, fear of new physicians and need for physical assistance for many procedures. Patients with physical impairment, when they go for an examination might be mistaken for cognitively impaired patients due to their disheveled appearance, communication difficulties, need physical assistance for an examination and equipment that can elevate them from the ground (Doostan 1999). This study found that African Americans with DD and type 2 diabetes had higher ER visits and inpatient visits compared to Caucasians with DD and type 2 diabetes. This risk of higher healthcare utilization can be reduced by increasing the number of primary and specialty providers who accept Medicaid patients, improving access to culturally competent minority healthcare providers with cultural backgrounds similar to minority patients' and increasing rates of out of home placement for minority DD patients with chronic diseases (National Center for Cultural Competence website, Smedley 2002, Hsu 2007(b), McGuire 2008).

In some cases, DD patients are unable to communicate their symptoms clearly to their healthcare practitioner which restricts their relationship with their practitioner. Many healthcare practitioners might assume that it is the patient's responsibility to discuss their health issues (Boyer & Lutfey,2010). As a result, the symptoms of the DD patients might worsen. Attempts to initiate effective communication with DD patients by physicians can help the physicians better understand the problems faced by these patients on a daily basis and they might allow some extra time for consultaion for them during future visits. Patients with DD have more complex health problems than the general population and are in need of more access to medical resources indicated by higher number of healthcare visits as found in this study. Medicaid coverage for the general population and the DD population is the same. Compared to the general population enrolled in Medicaid, Medicaid enrollees with DD require more resources due to the different types of issues occurring at different rates in this population. There is a need for developing policies which are based on a deeper understanding of the health issues and the health status of the DD population and which can provide the necessary resources to the DD population (Boyer & Lutfey,2010).

Care provided to ethnic minorities- Role of cultural sensitivity

Healthcare providers should keep in mind about the social norms followed by people coming from different racial/ethnic backgrounds. African Americans and Latinos tend to utilize services that provide less social support since they depend on their family members for love and support. Latinos who are migrants tend to face linguistic barriers in seeking care (Cabellero 2007, Gavin 2007). Native American people are unable to access care from state or local agencies since they are often provided referrals for reservation agencies or the Bureau of

Indian Affairs. Many of these minorities distrust the government programs and healthcare professionals (Glassheim 2009). As opposed to the Western perception of attaining autonomy and self-reliance for children with DD, Japanese people tend to value interdependence, belongingness and reciprocity during the course of provision of care for their DD children (Hsu 2007(a)). Seeking assistance for social or emotional issues, even though visualized as constructive among Caucasians, it may seem shameful in Chinese or Indian culture (Hsu 2007). Generally, in these cultures, there is reluctance in discussing about disability due to the stigma associated with it and help is sought only when the problems are assumed to be of somatic nature (Glassheim 2009). This study showed that medication adherence and healthcare utilization was less in African Americans compared to Caucasians. These findings are supported by previous research on healthcare access in minorities which states that minorities tend to drop out more often from community programs, receive less comprehensive services, lack access to trained culturally competent or bilingual healthcare providers and are more underserved (National Council on Disability website).

Minority DD patients face cultural insensitivity just like minority patients without DD. However, in addition to cultural insensitivity, DD patients also have to face prejudice and tolerate negative social attitudes associated with their disability (Reichard 2004). Cultural sensitivity can be taught to providers and caregivers by training them to display culturally appropriate behavior that takes into account the disability culture, use of respectful language and terminologies related to patient's condition, and providing language assistance when communicating with the patient (University of California at San Francisco website). Practices followed by physicians such as delaying treatment, providing wrong treatment, spending insufficient time with patients and withholding important information from DD patients or their

families can be considered inappropriate by caregivers of DD patients (Ebert 1995, McEwen 1988, Welner, 1998, Brooks 1997, Barnett 1988, Grabois 1999, Reichard 2001, Nosek 1995, Ralston 1996). Showing respect for the needs of the DD patient, including patients and their families in the decision making process and harboring a patient and family centered attitude can foster trust and confidence about the healthcare provider.

6.2.2 Fragmented care

One of the unique challenges that the DD population faces is fragmented care. This is further compounded by additional challenges such as co-occurring chronic conditions, limited coverage of care and restricted funding. There is inadequate identification of comorbid conditions in DD patients. 20-30% individuals with cognitive disabilities also have comorbid psychiatric disorders. However, these disorders upon surfacing tend to get shadowed due to communication limitations faced by the DD patients. Diagnostic shadowing is often seen in DD patients. It is a phenomenon whereby comorbid conditions in DD patients are overlooked and DD patients, due to their inability to communicate their emotional or physical distress tend to manifest it through non specific actions such as head banging (Reiss 1982). Families of the DD patients, if provided with the appropriate training and information, can help healthcare professionals in identifying a baseline behavior in DD children which can, in turn help in diagnosing comorbid disorders (Jacobstein 2004).

The challenges in DD patients are not limited to detection of chronic conditions alone. Even after, the comorbid conditions get detected in DD patients, procuring care is a tedious process for both the patient and the family. There is lack of collaboration between healthcare providers such as physicians, caregivers, case managers, etc. Effective communication between healthcare

professionals and the DD patients and their families can aid in proper disease diagnosis and the right referrals to improve continuity of care. Physicians can find catering to the complex health care needs of the DD population an arduous task, partly due to lack of training and partly due to the communication barriers faced by the patients. Hence, a curriculum focused on cross systems training for healthcare professionals can bring to light the barriers and facilitators encountered by the medical professionals at different stages of the care process of the DD patients (Jacobstein 2004).

In case of children with DD, procuring services is age specific and eligibility criteria might be different for different age brackets. Healthcare services for DD patients vary from state to state based on the funding availability. The severity of chronic conditions is especially higher for DD patients in foster care. There is lack of synchronization in the working of the local welfare agencies and the governmental agencies (American Academy of Pediatrics 2002). Due to fragmented care, DD patients tend to have limited healthcare services, respite care, home support and rehabilitation facilities. There are limited transition services and intensive behavioral treatment centers for DD individuals who drop out from schools before the age of 21. Care provided in welfare programs for DD patients is often not sufficient for managing physical and mental chronic conditions. Training provided to DD children in special education classes in schools might focus on just one of all the co-occurring conditions. All the above reasons indicate that adults who receive fragmented care since childhood might have a greater severity of chronic disease conditions (Jacobstein 2004). Adults who are not supported by their families face additional challenges in procuring services through government programs. Public insurance programs do not provide comprehensive care like private insurance programs. Eligibility for patients and reimbursement for providers mainly depend on the financial capacity of the states

which drives access to continuous care. These challenges alongwith disparities characteristic to the minority populations of all ages makes access to care really challenging (U.S. Department of Health & Human Services 2002).

6.2.3 Coordination of care

According to the National Committee for quality assurance, employing HEDIS quality measures by health plans for diabetes management can result in improved screening of HbA1c, better glycemic control, lower healthcare costs and less healthcare utilization (inpatient visits and ER visits) (National Committee for quality assurance 2005). Even though national guidelines exist for treating type 2 diabetes, caring for patients with DD and type 2 diabetes gets more complex. Evidence based guidelines for treating DD patients are often established by local institutions and due to lack of standardization; it might not be possible to judge the appropriateness of primary and specialist care that the patient receives (Epilepsy Action Australia website, Glassheim 2009). Lack of evidence based guidelines for chronic disease conditions calls attention to the need for funding to conduct research and develop interventions that can improve patient outcomes for chronic disease conditions such as diabetes, CVD, hypertension, asthma, etc. (Kronick 2007).

The ability of the primary care provider to communicate and collaborate with DD patient's caregivers, specialty providers and case coordinators can improve the patient's access to comprehensive care (Meuwese-Jongejeugd 2005). In absence of case managers, families struggle with finding the appropriate care for the DD minority patients and tend to rely on friends and acquaintances to direct them towards community based organizations funded by Medicaid, for obtaining information and referrals (Reichard 2004). Continuous care is important in

minority DD patients and can be associated with the following factors: presence of trust between the patient and the provider, affordable care, referrals for specialist care, absence of the need to explain patient history repeatedly by family members, specialty providers avoiding moving the health records of the DD patient every time they change a primary healthcare provider, improved patient health and bedside mannerisms. Collaboration among all the care providers can ensure that they are well informed, have the DD patient's treatment plan, and are better prepared to constantly cater to the emotional and physical needs of the patient (Meuwese-Jongejeugd 2005).

Physicians should observe DD patients' behavior, have the ability to notice the slight changes in the patient's behavior and communicate with the caregiver to procure more information about the patient. Providing medical attention to the patients with DD can be time consuming and demanding but openness on part of the physician can go a long way in establishing trust with the patient. The acute conditions that the DD patients experience from time to time might not be detected by a new primary care provider since the symptoms of acute conditions often get blanketed by the chronic diseases that DD patients have and the new provider might not have updated information about the patient (Lubin 2012). Recognizing special needs of the patients with DD such as patients wanting to undergo physical in their homes, arranging special diagnostic equipment suitable for screening or examining and convincing and assisting patients to undergo examinations can require preplanning and investment of extra time on healthcare provider's behalf. Improving access to medical homes and incentivizing case management by providing reimbursement can add to Medicaid costs but in turn be cost-effective in the long run by reducing health related disparities, improving continuity of care and health outcomes in minority patients with chronic disease conditions such as diabetes (Beal 2007).

Pharmacist as a liaison between the DD patients and other healthcare providers, caregivers and family members

We found in this study that there were racial disparities in medication adherence in DD patients with type 2 diabetes. Some of the reasons for low medication adherence in DD patients are incorrect medication consumption, incorrect medication consumption times, failure or refusal to consume medications, failure to understand the goals of treatment, non-supportive caregivers, insufficient resources, non adherence promoting contingencies (attention seeking behavior or escape tendency), failure to comply with medication therapy and resisting routine examinations (Wallace 2006). Pharmacists can provide their cognitive services and expertise to create a difference in the disease management of patients with DD and chronic conditions. Pharmacists can serve as liaisons between the patients and their care givers and other healthcare providers. Rather than meeting the DD patient's caregiver, family member or case manager who are responsible for providing medications to the DD patients, communicating directly with the DD patients can provide an insight into the complex care that these patients need on a continuous basis and the role of each care provider in their lives (Raleigh 2003). In spite of pharmacists encountering communication barriers with DD patients, these patients have varying range of intelligence and might not be deaf. Hence, asking open ended questions and providing advice to the patients can be an effective way of understanding their health issues and conveying useful information that can aid the patient/the caregivers in their disease management. Pharmacists can assist caregivers aiming to provide high quality of life to their clients by teaching them to detect any medication related adverse events early on, by answering medication queries for chronic disease therapy, by simplifying complicated multiple medication therapy in lay terms and by

training caregivers to improve medication adherence. Caregivers aim to understand and work towards the overall well being of the DD patients and collaborating with them can provide pharmacists with valuable information about the success of the medication therapy and medication intake patterns of the patients (Raleigh 2003).

Intervention strategies used with elderly patients or patients with linguistic barriers might be beneficial in case of patients with DD as well. In particular, techniques that can be employed to enhance medication adherence among DD patients with chronic disease conditions are, a) antecedent control manipulations, b) reinforcement procedures, and c) extinction. Antecedent control manipulations comprise of interventions such as i) providing additional prompts to attain or improve adherence (color coding medication containers and putting pictorial labels on medication bottles of "spoon and dish" for intake during meals or of "moon and stars" for intake at bedtime), ii) creating conditions that motivate adherence (providing DD patients' access to a activity they crave), iii) reducing the response effort related to adherence (keeping health foods handy at home) and iv) eliminating the motivation for nonadherence using behavioral momentum (making the DD patients feel special prior to engaging in an activity that they resist). Reinforcement procedures comprise of interventions such as i) using reinforcers contingent upon the fulfilment of the intended action (making DD patients behave favorably using tokens) and ii) using reinforcers contingent upon elimination or reduction of non-adherence (using verbal praise and providing foods or engaging in activites that DD patients desire). Extinction consists of eliminating reinforcers contingent upon the maintainence of adherent behavior (terminating activities that the DD patients prefer or improving their tolerance for aversive side effects of medications and avoiding scolding or providing attention) (Wallace 2006). Pharmacists should also keep in mind cultural

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considerations while interacting with DD patients from racial minorities. It is very important to maintain eye contact when listening to or communicating with African Americans. It might be difficult to establish trust with the African American patients due to their general distrust in the healthcare system, embarrassment arising from less awareness about disease conditions, fear of receiving distressing news about their own health, discriminatory treatment experienced by their family or friends and lack of sufficient funds. African Americans are very religious and might be of the belief that their spiritual faith has more healing power than consuming medications. They might believe that praying with the spiritual leader in the church and not acknowledging diabetes can rid the body of diabetes, thereby healing the body (Gavin 2007).

Latinos perceive people with plump or overweight bodies as healthy individuals who are very well cared for as opposed to people with thin bodies who they perceive might be neglected or undernourished. In the Latino culture, as a gesture of endearment, "healthy" individuals are often called "gorda" i.e. fat one or "gordito" i.e. little fat one. Similar to the Asian culture, for Latinos, their traditional meals connect them to their homelands. Asking Latinos to substitute their diet for a healthier diet might be perceived by them that the healthcare professionals are asking them to make a major sacrifice. Instead, culturally acceptable dietary interventions such as not using the excess grease after cooking meats with high fat content, using healthier oils instead of lard and using corn flour instead of refined white flour can be applied with more probability of success. It is important to keep in mind that Latinos uses herbal supplements with their medications and might be scared of being scolded which prevents them from disclosing about it in front of healthcare professionals. Latinos also might be of the belief that diabetes can be caused by susceptibility to susto i.e. anger, fright and emotional nature. Latinos believe that emotions impact physical health and feelings or episodes of fear and terror

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(susto) can make the body more susceptible to developing diabetes. Latinos also have an attitude of "fatalism" and many of them assume that since their family members have diabetes, they are bound to get it as well and cannot prevent or delay it (Cabellero 2007)

Among Asians, more importance is placed on maintaining harmony i.e. yin and yang while cooking meals. Importance is placed on the texture, color and quality of meals rather than counting the calories in the meals prepared. Seating down for meals is often seen as a custom that brings the family together and cooking food is symbolic of expressing care for an individual. When Asians fall sick, rather than giving medications, the caregiver in the family provides teas or soups that can restore vitality. Asians believe that imbalances in the body make a person ill and the right diet, instead of strong medications can help the ill person regain his/her strength back (Hsu 2007(a)).

DD patients visit several physicians for their multiple health issues and generally spend 15 minutes or less with their physicians which might not be sufficient to tend to all their problems. Also, in case of DD patients seeing a new physician or multiple physicians, the physician/s might not be aware of all the medications that the patient receives from the older or other physicians. However, a pharmacy might hold all the records of medications that the DD patients receive from different physicians, if they go to the same pharmacy. In such instances, pharmacists can provide their expertise with linking multiple diagnoses, detecting drug interactions and answering any health concerns that might have been overlooked unintentionally or due to lack of time during the physician visit (Raleigh 2003). Education based interventions that focus on improving awareness about disease management such as continuing education provided to healthcare professionals with videos of interaction with patients and educational

materials provided to the DD patients or caregivers can lead to improved health outcomes among the DD patients (Martínez-Moreno 2013, Aman 2007).

6.2.4 Prevention and early intervention

This study found that DD patients enrolled in capitated Medicaid plans had lower outpatient visits and higher ER visits compared to DD patients enrolled in FFS Medicaid plans. These findings were similar to a previous study conducted in Medicaid adults with type 2 diabetes enrolled in capitated and FFS plans. Medicaid enrollees have very low copayments and out of pocket expenditures ($1-$3) for most of the services. Patients in capitated plans have limited prescription drug benefits due to presence of a cap on medication related spending. Out of pocket expenditures increase once the cap is reached and this may lead to less medication adherence or discontinuation of therapy. Children and young adults staying with parents might be able to support themselves and get the necessary healthcare but there is a possibility that older adults living by themselves might stop taking medication or utilizing healthcare services if they cannot afford copayments due to lack of employment. Reduced adherence, inadequately provided health services, shorter treatment periods, limited patient followup and poor treatment can contribute to higher healthcare utilization (Pawaskar 2010). The impact of capitated Medicaid plans on outpatient visits is inconclusive. Studies have shown both to improve (Deck 2000) and reduce outpatient visits in patients enrolled in capitated plans (Balkrishnan 2002).

Interventions such as educating women during pregnancy about getting immunization for rubella or measles, abstaining from alcohol to prevent fetal defects and taking folic acid supplements to avoid neural tube defects can contribute to preventing developmental disabilities. DDs are generally visible at an early age in children and parents' alongwith

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healthcare providers, can play an important role in their early diagnosis. Parents can proactively inquire about DD during well child and sick child visits with pediatricians as well as with healthcare professionals other than physicians such as social workers, speech therapists, pathologists, nurses, daycare providers, early intervention specialists, occupational therapists, school personnel and pharmacists, many of whom come in contact with their children on a regular basis and who have the ability to diagnose DD. Early diagnosis of DD in children can mean early access to educational and behavioral interventions. As a result, positive outcomes such as reduced severity of DD, lesser learning delays, reduced dependence, less social isolation, and better self-esteem and productivity can be achieved as these children grow into adults. Interventions provided at an early age can be cost-effective, children can require less long term services, and the family members can better interact with their children and understand their disability (Glassheim 2009).

There are many organizations that focus on educational and behavioral interventions in children and youth with DD. Programs such as LEAP (Learning Experiences: An Alternative Program for Preschoolers and Parents) and UCLA YAP (Young Autism Project) assist children and youth with autism. LEAP is 2-3 year program that focuses on improving functional, behavioral and social skills, increasing independence and preventing or reducing linguistic impediment in children aged 3-5 years and their families. Autisitc children enrolled in LEAP experience better health outcomes and display complex developmental skills (Research Autism website (b)). The UCLA YAP is similar to LEAP and consists of a 3 year program that focuses on discrete trail training for pre-school children and detailed monitoring of the child's developmental progress by parents and therapists. The YAP participants have shown an increase in IQ and better school adjustment (Research Autism website (a)). The Early and Periodic

Screening, Diagnosis, and Treatment (EPSDT) is a federally mandated Medicaid program in Michigan for enrollees under 21 years that provides screening to children who are at a risk of developing DD or who already have development delays. Parents can take benefit of this program during well child visits to healthcare providers (Health Resources and Services Administration website). CEDEN (Center for Development, Education and Nutrition) is part of the Substance Abuse and Mental Health Services Administration (SAMHSA) and assists children from families with low SES. CEDEN is for children less than 5 years old and includes interventions that focus on improving birth outcomes for mothers, delivering home and community services based on the need of the family, providing educational materials to enhance child development and reducing social isolation of mothers. CEDEN has been known to improve immunization rates in children and enhance parent's satisfaction from learning to care for their children and understanding them (U.S. Department of Justice website).

6.3 Testing the theoretical model

The theoretical model was based on the Health belief model and Aday-Andersen's model for healthcare utilization (Andersen 2007, Andersen 2008, Andersen 1973). According to the model, the predisposing, modifying and the enabling factors impact medication adherence which in turn affect the healthcare utilization and healthcare costs. Patients display willingness to adhere to their medications on the basis of their perceptions about disease severity, susceptibility to adverse health conditions due to the disease condition, benefits derived from adhering to medications and barriers faced in adhering to medications. The researchers faced some limitations using the Marketscan Medicaid dataset since the above variables were not available in the dataset and so their influence on medication outcomes could not be determined. In this study, among the predisposing variables, race was a variable of interest. This study showed that

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the patient's race and gender were associated with medication adherence and healthcare utilization. Also, enabling factor such as the type of plan was associated with the likelihood of ER visits and need factor such as the number of comorbidities was associated with healthcare utilization such as emergency room visits, outpatient visits and inpatient visits and healthcare costs. Patients with certain characteristics had a higher probability of higher ER visits or inpatient visits. As proposed by the model, this study showed that higher medication adherence was associated with lower risk of ER visits and higher risk of inpatient visits. Higher medication adherence was also related to lower medication costs, lower medical (inpatient and outpatient) costs and lower overall (medical and medication) costs. Both the Health belief model and Aday Andersen's model of healthcare utilization seem appropriate for explaining the predictors of the main outcomes of this study. However, there is need to explore more measurement tools to study the impact of the variables that could not be captured using the Marketscan Medicaid dataset.

6.4 Testing the analytical model

The Shapiro Wilk test was significant (p<0.000) which indicated that the data was not normal. Also, a probability of <0.000 obtained in the Breusch-Pagan-Godfrey test indicated presence of heteroscedasticity. Hence MPRm was log transformed for stabilizing the variance. White-Huber robust standard errors were computed while running the negative binomial regression models. A VIF value of less than 1.44 for each independent variable showed absence of multicollinearity among the study variables. In this study, the Durbin Watson statistic of 1.98 showed the absence of autocorrelation among the variables. The Hosmer-lemeshow chi square test was non-significant for the multiple logistic regression models which indicated that the models were well-fitted. Also, the squared prediction in the model specification link test was not significant, indicating lack of specification errors. The ROC of 0.63 indicated fair discrimination. The

Likelihood ratio test of alpha was significant for negative binomial regression models but the Vuong test was not significant. Due to the retrospective nature of the study, it has selection bias. In the future studies, this bias can be controlled by using propensity scores to compare the diabetic DD population with the non diabetic DD population.

6.5 Limitations

The study is not without its limitations. Due to the observational nature of the study, there is no causal effect. The dataset did not capture variables such beliefs, attitudes or intentions associated with medication intake. These variables might vary by race and could help the researchers to better understand access to care among different races. The data does not represent patients who have Medicare only, are uninsured or are dual eligibles. The dual eligible population might have a higher severity of type 2 diabetes and related comorbidities, resulting in patterns differing in medication intake and healthcare utilization.

Patients taking insulin were excluded from the study population since they represent the more severe cases. The assumption that a prescription filled was a prescription taken was made for calculating medication adherence of the study population. However, there is no measure in the dataset to verify the actual intake of the medications. A questionnaire such as Morisky scale, asking the patients about their medication intake can be a viable tool for actual medication adherence assessment. Information about the educational background of the patients was not captured in the claims dataset. Due to lack of education, it is possible that patients might face challenges in understanding and following complex medication regimens, leading to lower medication adherence.

Claims data also does not have clinical measures such as HbA1c levels which are a measure of diabetes severity level. Hence, the healthcare utilization in the pre-study period was used as a proxy to determine the severity of type 2 diabetes. It was not possible to capture patient satisfaction using claims data. While information about primary and specialized care can be obtained from the claims dataset, collaboration between the different types of providers for a particular patient cannot be measured. In case of DD individuals, coordination of care can reduce hospitalization (Criscione 1995, Pincus 1987, Walsh 1997). Activities that are not reimbursed such as care coordination by social workers or the extent of caregiving provided by family members cannot be captured by claims dataset.

6.6 Future directions

This study provides the first comprehensive account about healthcare outcomes in diabetic adults with DD and opens up new areas of potential research. Medicaid programs differ from state to state in terms of service eligibility and reimbursement systems. Studies' comparing the Medicaid claims data across individual states can provide information about geographic disparities in delivery of care. Future studies could be conducted in DD adults with diabetes with Medicare coverage or dual eligibility or commercial insurance or with no insurance. Studies can also be replicated in DD adults with chronic disease conditions such as congestive heart failure, obesity, hypertension, hyperlipidemia and chronic kidney disease. Understanding the predictors of healthcare outcomes associated with different chronic disease conditions can help in the comprehensive management of the adults with DD. Alongwith analyzing claims data, data should also be collected via survey instruments or focus groups to understand the medication intake beliefs, attitudes, intentions and other psychological predictors among different racial minorities. Inclusion of variables such as care coordination, extent of caregiving, degree of

independence exhibited by the patients and adherence to prescribing practices recommended by evidence based guidelines can provide an insight about access to quality care in the DD population. Studies can also look at hospital length of stay and hospital readmissions to understand the severity and treatment efficacy of the DD population. Environmental variables such as the zip code of the patients and physicians can help researchers understand geographic disparities in access to care, availability of specialized and primary care physicians, variations in treatment in rural versus urban areas and the nature of accommodation of the patient (shared medical home or living with family members). The literature determining quality of care in DD patients with type 2 diabetes is scarce (Shiremen 2010). There is need for more studies assessing whether the quality of care provided to the DD patients with type 2 diabetes confirms to the standards set by HEDIS or not.

Appendix: A

NDC Codes used for the identifying OHAs used as part of analysis of the study:

NDC Codes	Medication NDC Codes			
Metformin	00087606005	00087606010	51129415501	11532002102
	00087607005	00087607010	51129415502	11532002201
	00087607111	00087607112	54868550000	54868550001
	64764015514	64764015565	64764015560	64764015518
	64764015814	64764015865	64764015860	64764015818
	00173316418	00173316461	53873316302	53873316301
	53873316300	53873316303	00007316318	00007316361
	00007316320	00007316418	00007316420	00007316461
	00007316718	00007316720	00007316761	00007316820
	00007316818	00007316861	00173316318	00173316361
	00173316718	00173316761	00173316818	00173316861
	30256316300	30256316400	30256316700	30256316800
	51129305801	51129305802	51129305901	51129305902
	53873316400	53873316401	53873316402	53873316700
	53873316701	53873316702	53873316800	53873316801
	53873316802	54868515700	54868515701	59742316300
	59742316301	59742316302	59742316304	59742316400
	59742316401	59742316402	59742316404	59742316700
	59742316701	59742316702	59742316704	59742316800
	59742316801	59742316802	59742316804	51129411301
Sulfonylureas	00009007002	00009010011	00009014101	00009017105
	00009034101	00009035201	00009344901	00009344903
	00039005110	00039005210	00039005250	00039005270
	00039005305	00039022110	00039022210	00039022310
	00047046324	00047046330	00049155066	00049155073
	00049156066	00049156073	00049162030	00049411066
	00049411073	00049412066	00093936401	00049412073
	00093936405	00069393066	00093936410	00069394066
	00093943301	00078035205	00093943305	00087606313
	00093947753	00087607211	00169008181	00087607311
	00169008281	00087607411	00169008481	00093104801
	00172224560	00093104901	00172297860	00093803501
	00172297960	00093803505	00172298060	00093803601
	00172364960	00093834201	00172364970	00093834301

	00172365060	00093834310	00172365070	00093834401
	00093834405	00093834410	00172433060	00781505201
	00781145601	52544046010	59762372603	00781505201
	00172433160	00781145701	52544046101	59762372704
	00172443260	00781145705	52544046105	59762372706
	00182199501	00781145710	52544046110	59762372707
	00182264701	00781505001	52544055901	59762378201
	00185021301	00781505101	52544055905	59762378203
	00185021501	00781505201	52544056001	97623783010
	00185022101	00904507780	53489046701	59762378302
	00228271811	00904792580	53700506070	60951071170
	00247144330	38245036410	55370050608	60951071185
	00378021001	00185022105	00228265711	3824506420
	0904792440	55953003540	62037067401	59930159201
	59930162201	59930163901	59930163903	62037067501
	62037067601	62269029129	62269029224	62269029229
	62939323100	00378110505	49884073601	59762372501
	00378112501	00536346501	00536466805	3489046901
	5370014607	5370014707	5370014708	5953003570
	5953003640	5953034240	5953034340	5953034370
	5953034440	5953034470	0378111001	0111037201
	0781145310	1285059902	2544046001	0904792460
	0904792480	0904792540	8245036450	8245038110
	8245038120	8245038150	8245043310	8245043350
	8245047749	5953034480	0378111005	0111037301
	0378114201	0536346510	00228265750	00228271511
	00378021010	00378021501	00378023401	00378024001
	00378024401	00378055101	00378110501	49884045201
	57664039788	00378111301	50111037303	51285059904
	52544046005	005364739	00591245501	00536564201
	00591245505	00536564301	00591271301	00536569701
	00591271305	00603283628	0536569801	0536570205
	0591277501	00603375621	0536570201	536570301
	00603376321	00536575101	00536575201	00603612121
	00555038502	00662411066	00555038602	00662411073
	00555038702	00662412066	00591046001	00663394066
	00591046005	00677154501	00591046010	00781145201
	00591046101	00781145210	00591046110	00781145301
Thiazolidinedione	64764015104	64764030100	64764015105	64764045125
	64764045100	64764015106	11532001100	64764030115
	64764030114	11532001216	11532001300	64764030116
	51129177709	64764045124	51129178206	54868434301
	64764045126	66332001125	64764015118	66332001201
	66332001309	000293158 61	00029315918	00029316001
	05112916220	05974231592	05974231609	05112916218
	05974231581	00007315113	00007315213	00173315200
	00173315213	00173315265	00173315313	00173315365
	00173315113	00173315165	00007315213	00007315265
	00007315266	00007314913	00007314965	00007314966
	00007314813	00007314865	00007314866	00173314813
	00173314865	00173314913	00173314965	54868537900

49990935030	00029315825	00029315838	00029315813
00029315818	00029315820	00029315822	00029315866
00029315938	00029315913	00029315918	00029315920
00029315922	00029315966	00029315925	00029316038

Appendix: B

Exemption of IRB

Subject: Notice of Exemption for [HUM00074825]

SUBMISSION INFORMATION:
Title: Diabetes Mellitus outcomes and healthcare utilization in Medicaid adults with
Developmental Disabilities
Full Study Title (if applicable): Diabetes Mellitus outcomes and healthcare utilization in Medicaid
adults with Developmental Disabilities: A look at Intellectual disabilities, Cerebral Palsy and
Autism
Study eResearch ID: HUM00074825
Date of this Notification from IRB: 5/10/2013
Date of IRB Exempt Determination: 5/10/2013
UM Federalwide Assurance: FWA00004969 (For the current FWA expiration date, please visit
the UM HRPP Webpage)
OHRP IRB Registration Number(s): IRB00000246

IRB EXEMPTION STATUS:
The IRB HSBS has reviewed the study referenced above and determined that, as currently
described, it is exempt from ongoing IRB review, per the following federal exemption category:

EXEMPTION #4 of the 45 CFR 46.101.(b):
Research involving the collection or study of existing data, documents, records, pathological
specimens, or diagnostic specimens, if these sources are publicly available or if the information
is recorded by the investigator in such a manner that subjects cannot be identified, directly or
through identifiers linked to the subjects. Note that the study is considered exempt as long as any
changes to the use of human subjects (including their data) remain within the scope of the
exemption category above. Any proposed changes that may exceed the scope of this category,
or the approval conditions of any other non-IRB reviewing committees, must be submitted as an
amendment through eResearch. Although an exemption determination eliminates the need for
ongoing IRB review and approval, you still have an obligation to understand and abide by
generally accepted principles of responsible and ethical conduct of research. Examples of these
principles can be found in the Belmont Report as well as in guidance from professional societies
and scientific organizations.

SUBMITTING AMENDMENTS VIA eRESEARCH:
You can access the online forms for amendments in the eResearch workspace for this exempt
study, referenced above.

ACCESSING EXEMPT STUDIES IN eRESEARCH:
Click the "Exempt and Not Regulated" tab in your eResearch home workspace to access this
exempt study.

Richard Redman
Chair, IRB HSBS

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