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Evaluation of the Relationship between Body Mass Index (BMI) and Healthcare Cost, Utilization and Health-Related Quality of Life in Adult Diabetic Patients

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Evaluation of the Relationship between Body Mass Index (BMI) and Healthcare Cost, Utilization and Health-Related Quality of Life in Adult Diabetic Patients

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Dedication

To Ade Orimi- Abiola, for making this dream a reality, thank you!

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Evaluation of the Relationship between Body Mass Index (BMI) and Healthcare Cost, Utilization and Health-Related Quality of Life in Adult Diabetic Patients

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Abstract

The present study assessed the relationship between Body Mass Index (BMI) and healthcare cost, utilization and health-related quality of life (HRQoL) of type 2 diabetes patients using the Medical Expenditure Panel Survey (MEPS) database. Study subjects were at least 18 years of age, diagnosed with diabetes and taking ≥1 oral antidiabetic medication. Data were extracted over a 5-year period (01/01/2006-12/31/2010). The main study outcomes were healthcare costs and utilization and HRQoL. The study covariates were age, gender, race, smoking status, census region of residence, marital status, insurance status, Charlson comorbidity index score and additional bed days. Study

objectives were addressed using generalized linear model, negative binomial and multivariate regression analyses.

A final un-weighted sample size of 7,003 patients was obtained. Mean age (±SE) was 61.2 (±0.24) years, mean BMI (±SE) was 32.2 (±0.12), and 50.4% were males. The majority was white (77.4%), did not smoke (84.5%), and were married (60.4%). Based on BMI categories, 12.6% had normal weight (BMI: 18.0-24.9); 29.2% were overweight (BMI: 25.0-29.9); 45.6% were obese (BMI: 30.0-39.9), and 12.6% were morbidly obese (BMI$\geq$ 40.0).

Compared to normal-weight patients; overweight, obese or morbidly obese patients had significantly higher ($p<0.05$) diabetes-related direct medical costs. However, overweight patients had significantly lower ($p=0.021$) all-cause direct medical costs. Furthermore, compared to normal weight patients, obese patients had a significantly higher ($p=0.009$) number of ambulatory care visits, while overweight patients had a significantly lower ($p=0.035$) number of emergency department visits. In addition, being obese or morbidly obese was associated with a significantly higher ($p<0.0001$) number of prescribed medicines compared to normal-weight patients.

Compared to normal-weight patients; being obese or morbidly obese was also significantly ($p<0.0001$) associated with lower physical component summary (PCS-12) scores (i.e., worse quality of life) while being overweight was significantly ($p=0.038$) associated with higher mental component summary (MCS-12) scores (i.e., better quality of life).

In conclusion, the present study suggests that among type 2 diabetes patients, being obese may be associated with negative consequences (in terms of healthcare costs, utilization and outcomes). Hence, there is the need to address obesity among type 2 diabetes patients in order to improve their health outcomes and significantly reduce healthcare costs and resource utilization.

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CHAPTER ONE: INTRODUCTION

1.0 STATEMENT OF THE PROBLEM

As of 2008, obesity was the second most common cause of preventable deaths in the US after smoking; it is also the 6th most common factor responsible for increasing the burden of disease world-wide.[1-3] Overweight and obesity are defined in relation to a person's body mass index (BMI). This is the ratio of a person's weight in kilograms (kgs) to the square of the person's height in meters. A person with a BMI value that falls between 25.0 and 29.9 is considered overweight while those with values that are equal to or above 30.0 are considered obese.[4] The Centers for Disease Control and Prevention (CDC) reported that between 2009 and 2010, obesity prevalence estimates in the US adult population were 35.7 percent and almost 17 percent in children respectively, with prevalence rates not significantly different among men and women but higher among boys compared to girls.[5] Overall, the prevalence of obesity has increased by several folds between the 1990s and the present, thus causing public health concerns due to its adverse effects on general health status. Furthermore, the economic burden of obesity to the US has been reported to have doubled in the last 10 years, with medical care costs estimated to be $147 billion in 2008 dollars.[6] The CDC reported that on average, obese patients spent about 42 percent more ($1,429) than their non-obese peers on medical care in 2008.[7]

Obesity has been reported to increase morbidity and mortality rates, as well as adversely affect obese patients and the society at large in several ways. These include patients' increased exposure to other comorbid diseases, increased medical costs, and worsened health-related quality of life (HRQoL) compared to their non-obese peers. [8-9]

Overweight and obesity are important risk factors for several chronic diseases such as type 2 diabetes, hypertension, cardiovascular diseases, stroke and certain types of cancer. The global rise in the prevalence of obesity has been reported to have produced a simultaneous increase in the prevalence of type 2 diabetes.[7, 10] In 2011, about 25.8 million people in the US aged 20 years and over were estimated to present with diabetes, of which 7 million people were unaware that they have the disease.[11] World-wide, diabetes is the 5th leading cause of death; in the US it is the 7th leading cause of death. Diabetes has been associated with significant utilization of healthcare services and costs.[12] The economic cost of type 2 diabetes in the US as of 2007 was about $174 billion, of which 67 percent was accounted for by direct medical costs, while about 33 percent was due to indirect costs such as productivity loss.[13] On average, a patient diagnosed with diabetes spends $11,744 annually on healthcare, of which 57 percent of it is spent on diabetes-related costs.[14] Overall, the economic burden of diabetes on society costs each adult an average of $700 annually. The high levels of healthcare utilization and costs stem from treatments for the management of this chronic disease, treatment of its complications, and the presence of co-morbid conditions. Also, type 2 diabetes has been reported to adversely affect the HRQoL of its patients, mainly due to the management of the disease and its complications.[15]

With reports showing that over 85 percent of patients presenting with type 2 diabetes are either overweight or obese, it seems logical that obese diabetic patients will be more exposed to diabetes-related complications, have more co-morbidities, consume more healthcare resources and have lower HRQoL compared to their non-obese peers. A study that used a nationally representative database, (i.e., the Medical Expenditure Panel Survey [MEPS]) between 2000 and 2002, concluded that obesity and type 2 diabetes are among the cardio-metabolic risk factor clusters responsible for significant healthcare costs – estimated at 80 billion dollars per year.[16] Although a number of studies have been carried out in the attempt to estimate the economic implications of comorbid obesity in diabetic patients, mixed conclusions have been reached.

While some studies reported no significant difference in medical expenditures by BMI status, other studies have reported otherwise.[17-20] In fact, a study involving elderly Veteran Health Administration diabetic patients reported that patients with normal weight had significantly higher expenses compared to their overweight or obese peers.[21] While cost estimates of the impact of obesity on type 2 diabetes have been made in a number of populations outside the US, little has been reported on such estimates in the US. [22-24]

Furthermore, while it is expected that patients with either type 2 diabetes or obesity generally have poorer HRQoL compared to their healthy peers, little is known about the severity of the joint impact of type 2 diabetes and obesity on the HRQoL of patients compared to their non-obese counterparts.[25] Some studies have evaluated the HRQoL of adult patients presenting with either type 2 diabetes or obesity without taking into account how both conditions jointly influence patients' HRQoL.[15, 26] However, a few studies have reported significantly poorer HRQoL and greater utilization of healthcare resources in adult obese patients presenting with a number of comorbid diseases compared to their non-obese peers.[27-28]

Results of studies that examined the influence of obesity on the HRQoL of type 2 diabetic patients in different populations are also mixed. Some studies reported significantly poorer HRQoL in overweight/obese diabetic patients compared to their non-obese peers,[15, 25, 28-29] whereas Wexler et al. reported that obesity was not significantly correlated with low quality of life in patients with type 2 diabetes.[30] This finding is further supported by another study which found no significant difference in HRQoL measures in the obese when diabetic patients were compared against their non-diabetic peers. However, this study was targeted towards adult obese patients seeking weight-loss interventions instead of diabetes management, hence the HRQoL of patients in this study was considerably poorer compared to their obese peers in the community not seeking weight loss intervention.[31]

1.1 Study aim

This study seeks to evaluate the relationship between BMI and healthcare costs, healthcare utilization and Health-Related Quality of life (HRQoL) in the type 2 diabetic MEPS population.

1.2 Study significance

The joint management of obesity and type 2 diabetes has several health and economic implications for patients, healthcare providers, and the society at large as it impacts treatment choices, healthcare resource utilization, as well as the HRQoL of patients. It therefore becomes important to estimate the economic burden of the management of obese type 2 diabetic patients compared to their non-obese peers and evaluate how the HRQoL of patients are influenced. These findings may lend more support to the fact that the rising prevalence of overweight and obesity needs to be addressed more urgently and promptly given its deleterious effect on the already poor health of diabetic patients. Furthermore, it is not clear if healthcare utilization disparities exist in type 2 diabetes patients by patient-level and clinical characteristics, such as BMI.[32]

1.3 LITERATURE REVIEW

1.3.1 Overview of Literature review

This chapter provides a summary of important information in the literature regarding the focus of this study, i.e., obesity and diabetes. Definitions, epidemiology, economic burdens, risk factors of the two diseases, as well as the relationship between the two conditions are provided in this chapter. Also included are the individual influences of these two conditions on healthcare use, costs, as well as on the Health-Related Quality of Life of patients and measures that may be taken to reduce the incidence of these conditions. Finally, the chapter concludes with the rationale for and the significance of the present study.

1.3.2 Obesity

1.3.2.1 Definition of overweight and obesity

Generally, overweight and obesity are defined in terms of the excess amount of body fat a person has, and the calculation of body mass index (BMI) is commonly used as a proxy to assess this. BMI is calculated as the ratio of the weight in kilograms to the height in meters squared. While the BMI is the most widely used measure of body fat because it is commonly believed to correlate with a person's body fat, this may not always be true as some people, such as athletes, may have high BMI values yet have no excess fat. Hence, there are other anthropometric methods of measuring body fat which include:1) waist circumference (in cm); 2) weight (in kg); 3) the ratio of the waist circumference to hip circumference; 4) the ratio of waist circumference to height (known as Body Adiposity Index (BAI)); and 5) skin fold thickness.[33] The BAI is the least common of the body fat measurements listed above. This index is derived from measurements of the waist circumference and height. The skin fold thickness measurement involves the measurement of skin fold thickness in several regions of a person's body; a person's skin is pinched and the thickness of this pinched area is measured with the use of calipers.

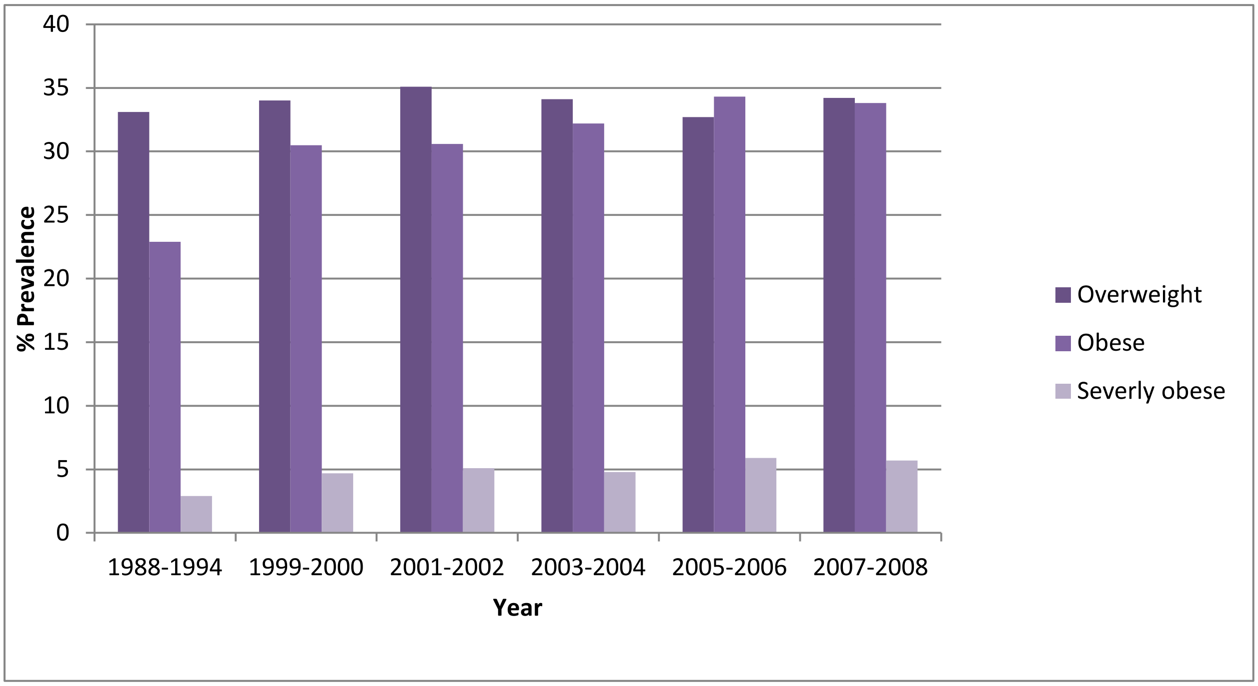
The World Health Organization (WHO) classifies people with BMI values in kg/m^2 that fall between 25.0 and 29.9 as overweight while people with BMI values at and above 30.0 are considered obese.[4, 34] Overweight and obesity in the pediatric population are usually defined based on whether a child's BMI falls above the 85th percentile of children in the same sex and age categories. Children with BMI values between the 85th and 95th percentile are termed overweight, and children with BMI values above the 95th percentile are considered obese.

1.3.2.2 Prevalence of obesity

After smoking, obesity remains the second most common cause of preventable deaths in the US.[3] The Centers for Disease Control (CDC) reported that between 1980 and 2008, the prevalence of obesity across population groups doubled and tripled in adults and children, respectively. By 2010, 78 million adults i.e., about one in three adults were obese and 12.5 million children and adolescents were considered obese in the US.[35-37] In 2010, obesity prevalence rates across states ranged from 21 to 35 percent, making obesity a national epidemic as no state was able to achieve the target goal of less than the 15 percent prevalence rate set by the Healthy People 2010.[2, 38] In 2000, obesity prevalence rates were less than 30 percent in all US states; however, in 2009, nine states in the US had prevalence rates above 30 percent, and in 2012, 13 states were reported to have obesity prevalence rates above 30 percent.[4] Furthermore, obesity prevalence rates in the US have been projected to rise to 75 percent by 2020 if this trend continues.[39] In 2008, 1.46 billion adults were considered at least overweight worldwide, and about 34 percent (500 million) of them were obese.[39] The World Health Organization (WHO) has also projected that at this rate, 2.3 billion adults will be at least overweight in 2015 and 700 million of them obese. As of 2010, study reports show that 40 million children below the age of 5 years are overweight worldwide,[40]and that the prevalence of obesity among children between 6 and 11 years more than doubled between 1960 and 1980. Likewise, the prevalence of obesity among adolescents between 12 and 17 years increased from 5 to 13 percent in boys and from 5 to 9 percent among girls.[41] This evidence, in addition to reports that globally, almost 3 million lives are lost annually due to overweight and obesity, support the notion that overweight and obesity is a pandemic affecting the whole world.[40] Furthermore, WHO reports that about 65 percent of the world's population lives in countries where overweight and obesity contribute more to mortality rates than being underweight.[40] Wang et al. projected that by 2030, 65 million more adults will become obese, with a corresponding 6-8.5 million new diabetic cases. Also, the joint costs associated with the management of these preventable diseases has been projected to increase by $48-$66 billion annually by 2030 in the US with a similar trend reported for the UK.[39]

Nationally, obesity cuts across all ages, races and socioeconomic status levels. In 2012, the CDC reported that obesity prevalence rates were 49.5, 39.1 and 34.3 percent in Blacks, Hispanics and Whites, respectively.[42] By socioeconomic status (SES), non-Hispanic blacks and Mexican-American men with higher incomes had a higher likelihood of being obese compared to their low income earning peers. On the other hand, women with a higher SES were less likely to be obese compared to women of low SES. Overall, between 1988-1994 and 2007-2008, obesity prevalence rates among adults increased irrespective of income and education levels.[43] By age, the CDC reported that between 1978 and 2008, obesity prevalence rates increased by almost four-fold in children between 12 and 19 years.[2] More recently, the American Heart Association (AHA) reported that in 2009, at least one in every three children/adolescents (between 2 and 19 years) was overweight or obese, and about 70 percent of these children will be obese as adults.[44] In general, the rising prevalence of obesity in the general population has been attributed to environmental factors and genetics.[45] Earlier studies have reported the need to reduce the rising prevalence of obesity. Yet, despite available interventions, recent studies have shown no significant decline in these rates either in the adult or pediatric populations.[46-47] Figure 1.1 shows the prevalence of overweight and obesity in adults over a 20-year timeframe.

Figure 1.1: Age-adjusted prevalence of overweight, obesity and severe obesity among US adults above 20 years between 1988 and 2008.[48]



1.3.2.3 Economic burden of obesity

In 2000, a study reported that the economic impact of obesity in the US was $117 billion, of which direct and indirect costs were responsible for $61 billion and $56 billion (52 and 48 percent), respectively (indirect costs included costs of productivity loss due to disability, illness and premature mortality).[49] Furthermore, in 2002, medical expenses for the problems of overweight and obesity in the US accounted for almost $93 billion, and with the rising prevalence of the disease, Finkelstein et al. estimated that $147 billion (about 9.1 percent of medical expenditures) was spent in direct costs in 2008. [2, 6] Based on 2012 estimates, adolescent obesity was responsible for $254 billion in total costs ($46 billion in direct medical costs and $208 billion in lost productivity). At this rate, it has been estimated that up to $957 billion, that is, almost 18 percent of US healthcare costs will be spent on obesity by 2030.[44] In a systematic review, Withrow and Alter supported this projection by reporting that the current economic burden of obesity may account for up to 2.8 percent of the nation's healthcare spending, and this may increase to 18 percent of US healthcare costs by 2030.[50-51] Although recent indirect cost estimates of obesity in the US are not numerous, it has been suggested that these costs are substantial.[52] In 2002, a study attributed $70 billion in medical costs, 40 million missed work days, 63 million physician office visits, and 90 million bed-restricted days to obesity.[49]

1.3.2.4 Impact of obesity on healthcare utilization and costs

The rising economic burden of obesity has been attributed to the healthcare costs required to manage diseases associated with obesity, as obese patients are more likely to present with cardiovascular, asthmatic, ulcerative, and diabetic disease conditions. Hence, these patients are more likely to utilize more healthcare costs due to increased hospitalizations, office-based visits, outpatient hospital care, and prescription medications compared to non-obese patients.[52,53] Raebel et al. reported that obese patients were significantly more likely to incur healthcare costs based on more prescription medications, hospitalizations, and outpatient visits compared to their non-obese peers. Moreover, obesity-related diseases have been estimated to cost as high as $209 billion in 2008 dollars in the US.[54] Obesity remains a risk factor for many diseases; in fact, obesity has been reported to be the single strongest predictor of the incidence of type 2 diabetes.[12, 55] Even in the pediatric population, a number of studies have associated obesity with diabetes and several adult onset diseases.[56] Buescher et al., using a Medicaid dataset, reported that adolescents who are overweight are more likely to use more healthcare services by filling more asthma and diabetes-related prescriptions compared to their peers of normal weight.[18] Trasande et al. also reported a significant increase ($125.9 million to $237.6 million) in hospitalization costs of obesity-related disease conditions from 2001 to 2005 among children between 6 and 17 years.[57] Another study involving Canadian children reported that healthcare costs were 21 percent higher in obese children compared to their normal weight peers and that this difference was evident in children as early as age 3.[58] Evidence shows that there is a 70-80 percent chance of overweight adolescents remaining overweight as adults. There is also increasing evidence that obesity increases the risk of developing several comorbid conditions such as hypertension, cardiovascular diseases, type 2 diabetes, sleep apnea, and even some cancers during adolescence and much later on in life.[1-2, 44, 59]

1.3.2.5 Types of obesity

Obesity-related complications have been specifically associated with the region of fat distribution; hence, depending on where excess fat is deposited, two main types of obesity exist. These include central and peripheral obesity.

Peripheral obesity: this refers to the distribution of fat around the limbs and hips. This is more common among females and has been reported to be associated with an increase in insulin sensitivity.[33]

Central obesity: commonly known as abdominal obesity, refers to the distribution of adipose tissues around the trunk. This type of fat distribution increases the likelihood of presenting with visceral obesity which has been closely linked with glucose intolerance and decreased insulin sensitivity, which, if unresolved, may result in diabetes.[12]

Compared to females with the same BMI, more males have been reported to present with central adiposity; thus, they are more likely to present with diabetes and even cardiovascular diseases such as myocardial infarction.[12] Even among women, females with central obesity reported significantly greater clinical and laboratory risk factors of diabetes compared to their peers with peripheral obesity.[60]

1.3.2.6 Impact of obesity on health-related quality of life

Health-related quality of life (HRQoL) generally refers to the state of an individual's health and the effect of a disease on a person's physical, mental, and social well-being, usually reported from the patient's perspective.[61] Generally, the physical functioning, social functioning and mental status are the main aspects assessed through self-report when health-related quality of life of a patient is evaluated.[61] The SF-12 is a quality of life instrument with 12 items which evaluates 8 main domains: physical functioning, mental functioning, role limitations as a result of physical health problems, role limitations as a result of emotional health problems, social functioning, body pain and general health and vitality.[62] These domains are collapsed into two components, that is, the physical component summary scale (PCS-12) and the mental component summary scale (MCS-12) – both of which are included in the Medical Expenditure Panel Survey (MEPS) data used in this study.

While obesity has been reported to decrease life expectancy by at least six years, obese patients have also been reported as having significantly poorer HRQoL compared to their non-obese peers, and this is not only because activities of daily living such as walking, dressing and eating are usually severely affected by the excess weight.[12, 63-64] Generally, most obese people (particularly older adults) present with a number of chronic disease conditions such as cardiovascular diseases, diabetes, musculoskeletal diseases such as osteoarthritis, and cancers such as endometrial and colon cancers, and are at risk of suffering from the associated symptoms of these diseases in addition to the side-effects of therapy.[65] A study involving 70-year old adults concluded that obesity significantly decreased the number of disability-free years, increased healthcare costs and increased the risks of chronic diseases such as diabetes and cardiovascular diseases among this elderly population.[66] Furthermore, overweight and obese patients have been known to suffer from self-esteem and self-image issues particularly in adolescents, thus eventually presenting with anxiety, depression and other disease conditions as the condition worsens.[67-69] A study reported that the weight-related quality of life of obese patients, either with or without diabetes, who sought treatment was significantly poorer compared to their peers in the community.[31] Another study reported significantly poorer quality of life in obese US adults even when they did not present with any other chronic comorbid conditions, as utility scores were found to be significantly lower in obese patients irrespective of their diabetes status.[70] Furthermore, a study involving adult obese patients presenting with both diabetes and cardiovascular disease (CVD) reported that there was a significant reduction in quality of life as BMI increased, independent of diabetes and CVD.[28] In obese children between 5 and 18 years, studies have reported that both the physical and psychosocial aspects of the health-related quality of life of this population were severely affected by being obese.[71-73]

With these reports, the importance of healthy weight cannot be overstated. Kolotkin et al. further corroborated these findings by reporting that obese patients who lost a significant amount of weight had significantly improved HRQoL compared to those who remained obese, while another study reported that HRQoL among an English population significantly declined as BMI increased.[74-75]

1.3.2.7 Risk factors for obesity

Generally, the rising prevalence of obesity has been associated with several factors which include but are not limited to individual health behaviors, environmental factors, diseases, medications, genetics and certain socio-demographic charateristics.[12, 45]

1) Individual health behaviors

This factor includes individuals' attitudes towards physical exercise and healthy dietary habits. Obesity is known to develop due to the gradual and consistent accumulation of calories (through diet) without an equal or greater depletion of such calories (through physical activity). Individuals who have poor, unhealthy dietary habits coupled with sedentary lifestyles are more likely to be overweight or obese.[12, 76-77]

2) Environmental factors

It is generally believed that the environment greatly influences certain behaviors in people. Communities with facilities that foster physical activity (walking, biking, swimming, etc.) will more likely encourage people to engage in physical exercises compared to communities that do not make such provisions.[40] Whereas, communities that directly or indirectly promote poor dietary habits by encouraging the growth of several fast food restaurants that promote unhealthy dietary habits through commercials will most likely encourage the consumption of unhealthy dietary choices, hence, increase the incidence of obesity.[77-78]

3) Genetics

The prevalence of obesity has also been linked to genetics. Studies have also shown that up to 80 percent of children born of obese parents are more likely to become obese later on in life.[12, 44] Genetics also influences the rate of metabolism and fat distribution, and these two factors significantly determine whether a person will be overweight or not.[63]

4) Diseases

Certain disease conditions such as Cushing's syndrome; a disorder that occurs as a result of excessive production of the hormone cortisol (which may either be as a result of tumors that produce the adrenocorticotropic hormone, cortisol or the use of medications such as glucocorticoids) is known to predispose people to obesity. Eventual weight gain is also known to be caused by hypothyroidism, an endocrine disorder which occurs as a result of a reduced production of the thyroid hormone (which is necessary for metabolism). Polycystic Ovarian Syndrome and menopause have also been associated with unintentional weight gain.

5) Medications

One of the side effects of certain medications is weight gain, which may eventually result in obesity. Such medications include atypical antipsychotics such as clozapine and olanzapine,[79] anti-depressants such as tricyclic antidepressants and a number of antidiabetic medications (e.g., insulin, thiazolidinediones, sulfonylureas and meglitinide analogs).[76, 80] The use of such medications, especially in patients who are prone to being overweight or obese, therefore requires some caution.

6) Age

Overall, it has been observed that the prevalence of obesity increases significantly after age 60.[5,36] This may be due to a decrease in metabolism and physical activity with age, especially in menopausal women.[81] Also, in children, adolescents were more likely to be obese compared to their younger, pre-school aged peers.[36, 44] Possible reasons for this include increased sedentary lifestyle (video games), poor dietary habits, poor physical activity, family and peer problems, depression, low self-esteem and the adolescents' new independence from parents which mostly reflects on their dietary habits and exercise or the lack of it.[76, 82]

7) Race

It has been reported that non-Hispanic blacks and Hispanics are more susceptible to overweight and obesity compared to their non-Hispanic white peers.[5, 42, 64]

8) Socioeconomic status

It has been shown that there is no significant difference in obesity prevalence rates by gender. However, regarding income, men with higher income levels were more likely to be obese, conversely, obesity prevalence rates increased as income levels declined in women.[12, 83]

1.3.2.8 Obesity: A risk factor for other diseases

Obesity, irrespective of age and race, has been associated with a number of diseases, including cardiovascular diseases, dyslipidemia, type 2 diabetes, sleep apnea and certain cancers.[52] A strong association has been reported between overweight and diabetes, such that overweight persons are three times more likely to develop diabetes compared to their peers of normal weight. Moreover, the likelihood of developing diabetes in persons considered to be within the obese class I (BMI: 30.0-34.9) is 20 times that of their normal-weight peers.[12] A study involving a 10-year study period found a significant association between the severity of overweight and the risk of developing chronic diseases such as diabetes, heart disease and hypertension in adults, irrespective of gender.[84] Many of these disease conditions present as comorbid factors in the same patient; hence, it may be difficult to isolate the effect of one from the other. Associations that have been commonly reported in the literature are provided in some detail below.

1.3.2.9 Obesity and the metabolic syndrome:

Although the pathogenesis of the metabolic syndrome is not yet well understood, the main risk factors that characterize this syndrome are dyslipidemia, hypertension, abdominal obesity and insulin resistance.[85] A significant association between abdominal obesity and the metabolic syndrome has been reported, which highly predisposes one to type 2 diabetes.[86] Metabolic syndrome includes certain factors that highly predispose a person to diabetes and cardiovascular diseases. This syndrome cuts across both the pediatric and adult populations and its definition is population-specific.[10] Metabolic syndrome in children between 10 and 16 years is defined by the International Diabetes Federation (IDF) as "the presence of abdominal obesity (abdominal circumference that is greater than the 90th percentile by gender) combined with the presence of any two of the following factors: triglyceride levels above 150mg/dl, high density lipids below 40 mg/dl, blood pressure levels above 130/85 mmHg and fasting plasma glucose levels above 100mg/dl or the presence of type 2 diabetes that was previously diagnosed." [10, 87] A study reported that almost 8 out of 10 adolescents with type 2 diabetes fulfilled at least two of the five criteria for the metabolic syndrome.[88] Moreover, in the adult population, the IDF defines the metabolic syndrome similar to that in the pediatric population but with a different definition of abdominal obesity, which is defined as a waist circumference greater than 80 cm and 94 cm for women and men, respectively.[89] The IDF reported that globally, one in every four adults presents with metabolic syndrome. This population is two times more likely to die from a myocardial infarction and three times more likely to have a stroke compared to their peers without this syndrome. Furthermore, the likelihood of presenting with type 2 diabetes in this group of patients is five times that of their normal peers and 80 percent of type 2 diabetes patients die from the disease.[90]

1.3.2.10 Obesity and cardiovascular diseases

Cikim et al. reported a significant relationship between abdominal obesity and indicators of cardiovascular diseases in women.[60] Another study reported that obese patients had a 60 percent higher risk of presenting with cardiovascular diseases and cancer compared to their peers who were of normal weight.[91] The development of cardio-metabolic risk factors (impaired glucose tolerance, reduced high density lipoproteins, increased blood triglycerides and increased blood pressure) were significantly associated with an increase in BMI even in normal-weight subjects.[92] A UK-based study of men between 60 and 79 years reached the conclusion that overweight and obese men were at increased risks of disability, insulin resistance, diabetes and cardiovascular conditions.[93] Moreover, a Japanese study found that multiple cardiovascular risk factors increased significantly in patients presenting with abdominal obesity.[94] Furthermore, a study used a model to assess the lifetime impact of obesity on health, and estimated that adult obese patients had significantly higher risks of presenting with hypertension and coronary heart disease compared to their non-obese peers. Life expectancy was also observed to decrease by one year.[95] It is therefore apparent that the incidence of several diseases may be significantly minimized or avoided once the prevalence of obesity is reduced.[12]

1.3.2.11 Obesity and cancers

Overweight and obesity have been reported to account for one in five cancers. Breast, endometrial and colon cancers are common types of cancers that have been associated with obesity.[96] A study by Field et al. found a significant association between increased BMI and colon cancer in adult females.[84] While there are a number of studies that have reached mixed conclusions regarding this association, a definite association between physical activity in the obese with cancers and improved quality of life has been reported.[96] Poorer prognoses have also been reported in obese patients with breast cancer compared to their non-obese peers.[96] Calle et al. further suggested that between 14-20 percent of cancer deaths could be associated with being at least overweight.[97]

1.3.2.12 Obesity and osteoarthritis

The weight borne by the joints of the body increasingly becomes burdensome with an increase in BMI, resulting in the painful, active wear and tear of cartilages that provide support to joints responsible for carrying out activities of daily living. More overweight and obese patients have been reported to present with osteoarthritis compared to their peers of normal weight. A study estimated that obese patients were two times more likely to report having osteoarthritis compared to their non-obese peers.[98]

1.3.2.13 Management of obesity

In general, studies have demonstrated the importance of weight loss in overweight and obese patients by the significant decrease in the incidence of the risk factors associated with obesity such as dyslipidemia, type 2 diabetes, osteoarthritis and cardiovascular diseases. Sjostrom et al. reported a significant decrease in the prevalence of diabetes, hypertension and dyslipidemia over a period of 2 years in obese patients who lost more than 12 percent of their body weight and sustained this weight loss compared to those who did not lose weight.[99] Likewise, other studies have reported that hypertension and cardiovascular risk factors were significantly reduced in patients placed on weight reduction programs.[100-101] The successful treatment of obesity is, however, multifaceted. Lifestyle modification is a key factor in the adequate management of obesity such that dietary changes (healthy dietary habits) and an increase in physical activity are required to maintain a healthy balance between the intake and expenditure of calories. Medications may also be required to complement lifestyle changes,[102] while surgery is considered an option of last resort if the previous options are found ineffective in adequately managing obesity; this is especially the case in severely obese patients or in overweight patients with comorbidities.[103] However, it has been reported that only one in five people who are obese are able to achieve and maintain significant weight loss (that is, at least 10 percent of their original body weight) for at least a year. Hence, the need for pharmacological treatment options may arise in many obese patients.

1.3.2.14 Pharmacological management of obesity

Medications commonly used for managing obesity include phentermine, orlistat, sibutramine, exenatide and metformin (exenatide and metformin are usually used in obese patients with type 2 diabetes).[104] The use of these medications has been reportedly associated with weight loss as well as improvement of risk factors.[105] However, due to reports of adverse cardiac events associated with the use of sibutramine, it was withdrawn in 2010 by the US Food and Drug Administration (FDA).[106-107] Hence, there are only three anti-obesity medications in the US currently approved by the FDA (phentermine, orlistat and lorcaserin).

1) Phentermine:

Phentermine is an appetite suppressant which has been approved for use as an anti-obesity medication since the 1950s; however, its use is limited to 12 weeks due to long-term use safety issues such as increases in both blood pressure and heart rate. It is effective at inducing up to 10 percent weight loss within this period.[106]

2) Orlistat:

Orlistat is a lipase inhibitor, approved by the FDA in 1999, which acts by interfering with digestion by inhibiting the absorption of ingested fat.[108] Its use is limited in many patients due to possible gastrointestinal side-effects such as diarrhea and steatorrhea.[104, 106] Following 12 months of therapy, it has been reported that merely 15 to 30 percent of patients on orlistat can achieve weight loss greater than 5 percent. However, its effectiveness was further demonstrated by Maetzel et al. who reported the cost-effectiveness of orlistat in increasing event-free (these include the decrease in the incidence of type 2 diabetes-associated microvascular and macrovascular complications) life-years gained over an 11-year period in obese type 2 diabetic patients.[109]

3) Lorcaserin:

Lorcaserin is a 5HT-2c receptor agonist that was recently approved by the FDA in 2012.[110] Weight loss results in obese patients have been assessed in a number of clinical trials involving uncomplicated obesity and also in obese type 2 diabetic patients.[102] These studies reported that ≥5% weight loss was observed in more than 20 percent of patients in both categories after 12 months of therapy.[111-112] This medication is contraindicated in pregnancy and should be used with caution in patients with congestive heart failure due to the increased risk of valvulopathy as a result of its ability to increase the number of serotonin 2B (5HT-2b) receptors.[110] Its common side-effects include dizziness, blurred vision, headaches, gastrointestinal disturbances and nausea.[113-114]

4) Topiramate/Phentermine:

Topiramate/Phentermine is a fixed dosed combination that was recently approved for use in conjunction with lifestyle modification by the FDA in 2012 for patients in need of chronic weight management.[115] Topiramate is an anti-epileptic medication; although the mechanism of action whereby weight-loss is achieved is not yet understood, additive weight loss actions are observed with phentermine which is a non-selective monoamine releasing agent.[102, 108] Clinical trial results have shown that about 40 percent of patients placed on this fixed-dose combination had at least a 10% decrease in weight, which is higher than the weight loss reported for either rimonabant or sibutramine. Although this combination has been observed to be even more effective at weight-loss compared to locarserin, its side-effects include dry mouth, insomnia, dizziness, alopecia and palpitations. Its teratogenic effects make it unsuitable for use in pregnancy.[115]

Pharmacologic treatment options for obesity have been observed to be limited due to very few available medications that have been approved by the FDA. This may be due to the poor safety profiles of previously approved anti-obesity medications. Fenfluramine, dexfenfluramine, and rimonabant are examples of anti-obesity medications that were withdrawn from the market due to possible cardiovascular and psychiatric side effects.[102, 106, 116] A new anti-obesity pharmacological agent (explained below) in the form of combination therapy, is presently undergoing development, and may be approved by the FDA if it can fulfill the required efficacy and safety profiles.[103, 106]

1) Bupropion/Naltrexone:

Bupropion/Naltrexone is another combination product in the clinical trial stage of development. Bupropion is a weak dopamine reuptake inhibitor commonly used in aiding smoking cessation, while naltrexone is a non-selective opioid receptor antagonist used in the treatment of opioid and alcohol dependence. This medication, in conjunction with lifestyle modification, has been observed to induce weight-loss. Its side-effects include dry mouth, headaches, dizziness and insomnia. Safety concerns that may impede its approval by the FDA are its tendency to increase blood pressure, incidence of hypertension and palpitations. [117-118]

There are other medications (not specifically anti-obesity drugs) that have been found to be effective at inducing weight loss in certain patients. Exenatide, a synthetic glucagon-like peptide 1(GLP-1) agonist, was approved by the FDA in 2005 as an anti-hyperglycemic agent. It has also been found to be effective in reducing body weight in obese patients due to its appetite suppressing ability and the feeling of satiety it promotes.[108] Likewise, pramlintide, an analog of amylin (amylin is produced by the beta islet cells as insulin) has been found effective at inducing weight loss by decreasing food intake and increasing satiety.[103] Metformin, a biguanide, is commonly prescribed in the management of type 2 diabetes, and it is the only oral antidiabetic medication approved for use in the pediatric population. Metformin is prescribed particularly to obese type 2 diabetic patients due to its weight-loss inducing property.[80] A number of antidepressants have also been observed to have weight loss properties, including sertraline and fluoxetine.[108]

1.3.2.15 Non-pharmacological management of obesity

The restricted use of pharmacological treatment options of obesity due to safety/efficacy profiles, high cost, restricted conditions for use and the absence of insurance coverage for most of these medications makes it important to explore other avenues.

1.3.2.15a Lifestyle modification:

This includes dietary changes and physical exercise.

Dietary changes

A number of low-carbohydrate diets such the Atkins, Dukan, South Beach and Stillman diets have received considerable attention, and have been recommended for people who desire to lose a modest amount of weight. Some of these programs include diets low in carbohydrates, such that the body derives its glucose by the breakdown of fat rather than carbohydrates, a state known as ketosis. This process occurs due to lipolysis (the breakdown of fat) which results in the production of ketone bodies when insulin levels in the blood are low.[63] In addition, diets that are high in fiber, with low glycemic index, lean protein, low polysaturated and trans fat, with increased monounsaturated fat are desired. The Weight Watchers and Subway diet plans are also popular diet plans that involve the ingestion of food in the right portions and diets low in fats (and absence of saturated fats). These diets may be recommended in conjunction with intensive or gradually increased, yet regulated, physical activity to ensure that weight-loss is achieved and maintained.[63, 119]

Physical activity

A number of studies have associated increased, regulated and consistent physical activity with sustained weight loss. Physical activity such as brisk walking and swimming for a minimum of 150-minutes a week has been recommended in conjunction with dietary changes in achieving sustained weight loss. The intensity of the activity should however be individualized based on age, fitness and the presence/ absence of disabilities.

Lifestyle modification is an important option that needs to be aggressively explored to curb the problem of obesity, especially in the pediatric population whose use of medication in managing obesity is severely limited. A number of studies have been carried out to determine the effect of dietary changes and physical exercise on obesity in several populations. Improved cardio-respiratory fitness was found in a population of obese adolescents who were subjected to a 6-month lifestyle modification program.[120] Significantly improved body weight, blood pressure and aerobic fitness were also reported in a population of overweight adults placed on a lifestyle intervention program.[121]

1.3.2.15b Bariatric surgery

Bariatric surgery has been shown to significantly improve patients' health status and quality of life as obesity-related diseases are mostly resolved when a significant amount of weight is lost. However, the effectiveness of bariatric surgery is largely dependent on lifestyle modification after surgery. Four main types of bariatric surgery exist, and several factors (such as the patient's BMI, age, presence of obesity-related diseases, and eating habits) largely dictate the type of bariatric surgery most appropriate for a patient.

1) Adjustable gastric band: this involves the use of an adjustable band placed around the crown of the stomach such that the opening between the throat and stomach is reduced as needed, resulting in a decrease in the amount of food ingested.
2) Roux-en-Y gastric bypass: this involves the creation of a pouch in the stomach wherein food passes through to the small intestine, bypassing the stomach and upper intestine such that food intake is restricted and food absorption reduced. A study reported that normoglycemia was achieved 14-months post-surgery in about 43 percent of type 2 diabetic patients who underwent this surgery.[122]
3) Bilopancreatic diversion with a duodena switch: this type of bariatric surgery is characterized by three features to ensure significant weight loss. These include: the exclusion of a major part of the stomach; the bypass of a major part of the small intestine to ensure that food absorption is minimized; and also the ability of the body to process food affected by the digestive juices such as bile. This drastic reduction in absorption usually results in the malabsorption of vital nutrients and vitamins; hence increasing the likelihood of anemia and osteoporosis in patients.
4) Vertical sleeve gastrectomy: this involves the removal of a major part of the stomach, which may result in the reduction of the secretion of the hormone ghrelin, which is responsible for appetite levels. Generally believed to be the most ineffective type of bariatric surgery, this surgery is usually recommended in patients prone to high surgical risks.

Common side-effects of bariatric surgery include bleeding, neuropathy, infection and diarrhea.[123-124] Bariatric surgery has also been found effective in youths who qualify for this surgery. Currently accepted guidelines recommend that adults and adolescents who have attempted other weight loss options for at least 6 months with no significant improvement, who have attained their adult height, have BMI values equal to or greater than 40 and have diseases such as type 2 diabetes or sleep apnea, may qualify for bariatric surgery.[125-126] In addition, eligible adults are required to be 1) willing to lose excess weight; 2) aware of the risks and benefits of both surgery and treatment post-surgery; and 3) aware of and committed to lifestyle modification procedures post-surgery.[123]

1.3.3 Diabetes

1.3.3.1 Definition of Diabetes

Diabetes is an endocrine metabolic disease condition arising due to a partial or complete damage of the pancreatic beta cells in the body; these beta cells are responsible for the production of the hormone, insulin. This hormone ensures that glucose is converted to energy for use by the body. Insulin is therefore responsible for regulating the amount of glucose and fat in the bloodstream and its lack will result in inadequate blood glucose regulation, hence, hyperglycemia. A decrease in the body's sensitivity to insulin combined with an impairment in the body's ability to produce insulin greatly increases the risk of presenting with diabetes.[127]

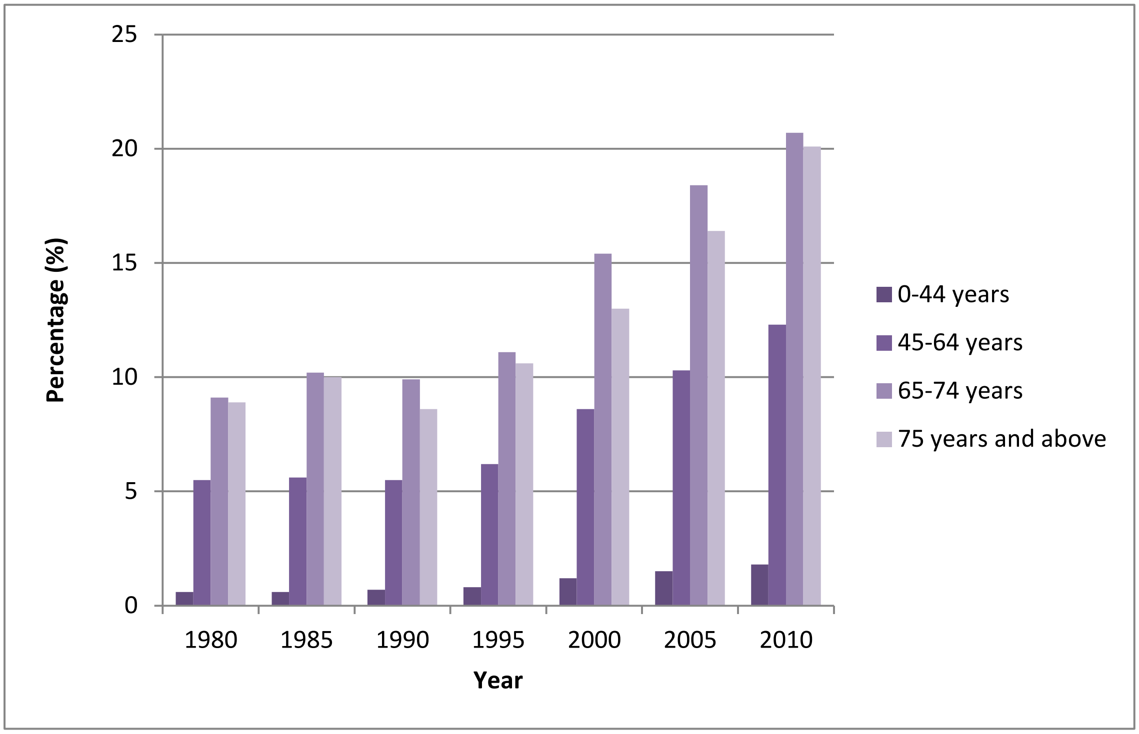
1.3.3.2 Epidemiology of Diabetes

Diabetes is the 7th leading cause of death in the US and the Centers for Disease Prevention and Control (CDC) reported that as of 2010, the number of people affected by diabetes in the US was 25.8 million, amounting to about 8.3 percent of the US population. Of these, 18.8 million cases of diabetes have been diagnosed and currently, about 7 million people live with diabetes but are yet to be diagnosed with the disease. The management of diagnosed diabetes and its complications in 2007 was responsible for about $174 billion, accounting for up to 10 percent of all healthcare expenditures.[128] Overall, pre-diabetes and diabetes accounted for $218 billion in 2007.[13]

Generally, reports have shown that patients with diabetes spend more than 2 times as much on healthcare compared to their non-diabetic peers. [129, 130-131] Recently, the incidence of this chronic disease has been reported in children and youths, particularly in Hispanics and blacks, mainly due to the concurrent increase in the prevalence of obesity. Shrestha et al. reported that on average, youths presenting with diabetes spend 84 percent more in medical expenditures compared to their non-diabetic peers. [132-133]

Reports indicate that the number of patients newly diagnosed with diabetes increases by at least 1 million yearly, with the year 2010 recording almost 2 million new cases of diabetes.[129] Figure 1.2 shows the rising prevalence of diabetes in the US. This increase has mainly been associated with the rising average age of the population and the rising prevalence of obesity in the population. The prevalence of diabetes has been found to increase with age and low socioeconomic status (SES). However, diabetes prevalence has been observed to cut across all racial groups. Based on 2007-2009 national survey data, diabetes prevalence rates in non-Hispanic whites, Asian-Americans, Hispanics and non-Hispanic blacks were 7.1, 8.4, 11.8 and 12.6 percent, respectively.[129] Diabetic patients are twice as likely to die compared to their non-diabetic peers and worldwide, 8 out of ten diabetic patients are likely to die from the disease.[89, 129]

Figure 1.2: Percentage of civilian non-institutionalized population with diagnosed diabetes by age between 1980 and 2010.[134]



1.3.3.3 Types of diabetes

Diabetes may be broadly classified into two groups depending on the nature and extent of the destruction of the beta cells of the pancreas. These include type 1 and type 2 diabetes.

1.3.3.3a Type 1 diabetes

Type 1 diabetes is an auto-immune disease condition that results in the destruction of the body's own beta-cells responsible for the production of insulin; sometimes, this self-destruction does not have a cause.[135] The damage to these beta-cells results in a shortage or absence of insulin, requiring that an external source of insulin be provided for survival. This is because the gradual and chronic destruction of insulin-producing beta cells results in the damage of vital organs of the body due to chronic hyperglycemia; therefore, to avoid such destruction, the use of an external source of insulin is mandatory. Type 1 diabetes is therefore termed Insulin Dependent Diabetes Mellitus (IDDM), and accounts for almost 6 percent of people with diabetes.[127,131] In 2007, almost $15 billion was spent on healthcare costs to manage the approximately 1 million people diagnosed with type 1 diabetes, most of whom were children and adolescents. The prevalence of IDDM in non-Hispanic whites has been reported to be higher compared to peers of other racial groups.[13] Genetics has been closely linked to type 1 diabetes and presently, there are no preventative measures that may be taken against this disease. [136]

1.3.3.3b Type 1.5 diabetes

Commonly known as Latent Autoimmune Diabetes of Adults (LADA), this variant of diabetes is known to present in adults usually above 35 years of age. The symptoms of this disease are a combination of symptoms of types 1 and 2 diabetes, making diagnosis difficult. In fact, it has been suggested that up to 20% of patients diagnosed with type 2 diabetes actually have LADA. Usually found in non-obese adults, this variant of diabetes presents with increased likelihood of ketosis, uncontrolled blood glucose and the presence of serum islet auto antibodies. Although the management of LADA initially responds to diet and oral antidiabetic (OAD) medications, most patients with this type of diabetes eventually require insulin; usually within a shorter period compared to their peers with type 2 diabetes. Some levels of insulin resistance (not as common as in type 2) have also been reported in patients presenting with LADA.[137]

1.3.3.3c Type 2 diabetes

Also known as Non-Insulin Dependent Diabetes Mellitus (NIDDM), type 2 diabetes is the most common form of diabetes. As of 2010, almost 19 million people in the US were diagnosed with this variant of the disease. Approximately 92 percent of the $174 billion spent on diabetes was spent on the management and complications of type 2 diabetes.[13] Due to the strong association between the onset of type 2 diabetes and older age, it is commonly believed to be a disease of adulthood. Its development results from impaired production of insulin and/or reduced sensitivity of the cells to insulin. Usually, patients with type 2 diabetes have some functioning insulin-producing beta cells, and typically do not require insulin for survival. Patients with type 2 diabetes are regularly placed on oral antidiabetic (OAD) medication therapy in combination with lifestyle modification to achieve and maintain glycemic control.[138] However, patients who are difficult to manage with only oral antidiabetic medications may be concurrently placed on insulin. Due to the initially symptomless nature of the disease and its gradual progression, patients suffering from Type 2 diabetes may go undiagnosed for a protracted period of time before the disease symptoms (usually in form of complications such as hypoglycemia, retinopathy, neuropathy, diabetic foot ulcers and nephropathy) manifest.[138] The rising incidence of type 2 diabetes has been associated with an increase in the prevalence of obesity, an aging population, and improvements in health technology for easier detection of the disease. Among patients with type 2 diabetes, the management of elderly patients is especially challenging due to physiological changes attributable to old age, presence of comorbid conditions, as well as the burden of taking several medications as a result of these comorbid conditions.[131] These challenges ultimately result in significantly higher healthcare costs in this population compared to their non-diabetic peers.[11]

1.3.3.3d Other types of diabetes

Among other types of diabetes are those with a variety of causes/links: genetic abnormalities (e.g., maturity onset diabetes mellitus of the young [MODY]), surgeries, infections, gestational diabetes and the use of certain medications. Gestational diabetes is presented more commonly in non-whites, that is, African-American, Hispanic and American–

Indian women in the form of glucose intolerance. Obesity and a family history of diabetes are common factors that predispose women to gestational diabetes in women. Gestational diabetes costs totaled an estimated $636 million in 2007 and accounted for up to nine out of 10 complications caused by diabetes during pregnancy.[13, 127, 130] Gestational diabetes is commonly known as diabetes during pregnancy and has been reported to affect almost 2 out of ten pregnancies.[129] Reports have shown that the probability of a woman with gestational diabetes developing type 2 diabetes right after birth is up to ten percent. Furthermore, there is about a 35 – 60 percent chance of such women developing type 2 diabetes at least 10 years post-partum.[129] During pregnancy, it is therefore imperative to alleviate rising glucose levels in women with hyperglycemia to prevent possible complications during and after delivery to the mother and the child. [56, 138]

Infections, such as congenital rubella, may also result in diabetes, while exposure to certain medications, such as glucocorticoids, predisposes a patient to diabetes because they induce insulin resistance.[135] Maturity onset diabetes of the young (MODY) is also a form of diabetes which may occur as a result of genetic defects of the beta cells. This disease arises due to a defective gene with a high probability of mutating, eventually resulting in hyperglycemia due to a shortage in the amount of insulin produced.[130, 139] MODY is more commonly reported among non-Hispanic white youths usually below the age of 25.

1.3.3.4 Glucose Intolerance

In 2010, glucose intolerance, also known as prediabetes, was reported in about 79 million adults who presented with hyperglycemia.[129] The chances of presenting with diabetes are significantly high in patients with glucose tolerance; in 2007, the cost of healthcare in people presenting with glucose intolerance accounted for $25 billion .[13, 130]

1.3.3.5 Risk factors for type 2 diabetes

1) Overweight/Obesity (BMI>25): being at least overweight has been strongly associated with presenting with type 2 diabetes and the literature reports an increased risk of developing type 2 diabetes in people presenting with abdominal obesity.[86]

2) Age (>45 years): type 2 diabetes is commonly known as an adult-onset disease; hence, the risk of presenting with the disease increases with age.

3) Metabolic syndrome (hypertension, dyslipidemia, history of vascular disease, insulin resistance): increased insulin resistance is one important feature of the metabolic syndrome and persistent insulin resistance eventually results in type 2 diabetes.[140]

4) Polycystic Ovarian Syndrome (PCOS): has been strongly associated with the development of type 2 diabetes particularly in adolescent females.[141]

5) Genetics: a person with a family history of diabetes is more likely to present with the disease compared to someone without this history.

6) Certain racial groups: the CDC has reported that compared to whites, African-Americans, Hispanics, and American-Indians have a higher risk of presenting with type 2 diabetes.[127]

7) Gestational diabetes and in-utero exposure to gestational diabetes are also common risk factors that predispose to diabetes: the risk of presenting with diabetes post-partum increases (by about 50 percent) in mothers who presented with gestational diabetes, while there is also an increased risk of developing type 2 diabetes later on in life in children born of mothers with gestational diabetes.[56, 140, 142]

1.3.3.6 Treatment guidelines

While the management of type 2 diabetes is typically individualized, it is generally recommended that overweight or obese patients with risk factors of diabetes be placed on lifestyle interventions, which include diet restrictions (medical nutrition therapy), reduction in sedentary lifestyle and an increase in physical exercise.[138 10] However, reports show that lifestyle interventions alone in symptomatic patients (patients with diabetes-related complications) are only effective in less than 10 percent of adults; hence, OAD medication use is recommended in conjunction with lifestyle modifications at the time of diagnosis.[143] Depending on outcomes, insulin, mono-, dual- or multiple-therapy may be required to achieve desired outcomes. This is especially true in patients without satisfactory glycemic control after 3-6 months (e.g., patients with poorly controlled hyperglycemia having HbA1c levels above 7 percent).[144 145]

1.3.3.7 Diabetes management

1.3.3.7a Non-pharmacological management of diabetes

Diet and nutrition:

Like the non-pharmacological management of overweight and obesity, the non-pharmacological management of diabetes is focused on weight loss such that an improvement in glucose sensitivity and glycemic control is achieved either in obese type 2 diabetes patients or in high risk groups (people presenting with prediabetes). While caloric-intake suggestions have been recommended based on weight, a gradual yet constant deficit in calorie intake relative to expenditure is needed to ensure sustained weight loss. The use of low-fat, low carbohydrate and low glycemic index diets (such as fruits and vegetables) have been reported to aid in weight loss.[143] The effectiveness of diet in achieving adequate weight loss is, however, dependent on individual adherence to medical nutrition therapy (MNT).[138]

Physical activity:

Ensuring regular and sustained physical activity, which is not necessarily required to be regimented or structured, may result in weight loss, especially when coupled with a restriction in diet. Usually engaging in at least 150-minutes per week of exercise has been recommended to improve insulin sensitivity and glycemic control. In the management of diabetes, a key non-pharmacological factor is regular patient counseling by healthcare providers, which ensures that patients are adequately informed about their disease and its management. This is relevant in achieving and maintaining glycemic control as well as preventing complications. Furthermore, involving patients in the active management of their disease condition and providing education for self-management such as ability to self-monitor blood glucose levels, in conjunction with regular examinations by their physician for complications and adverse effects, have also been recommended.[146] Since age is a known risk factor for diabetes, screening is recommended in adults at least 45 years of age.[144] Finally, since adherence to diabetes management options are greatly influenced by family/social support, their importance to patients need to be emphasized.[147]

A 30 to 40 percent decrease in diabetes-related morbidities has been associated with at least a 10 percent weight loss; therefore, these non-pharmacological recommendations should also be called to attention in patients presenting with glucose intolerance, impaired blood glucose or asymptomatic hyperglycemia. Finally, an annual screening of patients is recommended to detect and manage the development of complications associated with diabetes as soon as they occur (these include eye dilation and foot exams).[1, 138]

1.3.3.7b Pharmacological management of diabetes

Early management of diabetes has been strongly associated with better outcomes; hence, it is recommended that medication therapy be considered if non-pharmacological forms of intervention have proven unsatisfactory after 3-6months.[135] Generally, patients whose blood glucose levels are adequately controlled with oral antidiabetic medications, do not require insulin; however, this is required in patients with poorly controlled type 2 diabetes presenting with ketoacidosis. Typically, such patients are weaned off insulin and placed on metformin once glucose levels are normalized.[135] Metformin is currently the first line of therapy recommended by the American Diabetes Association (ADA). In addition to lifestyle modification in patients with uncomplicated diabetes, metformin is usually used as monotherapy, particularly when glucose levels are not adequately controlled by lifestyle modification alone.[148-150] Commonly used oral antidiabetic medications include metformin, sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors, and meglitinide analogs.[80] In the event of inadequate glycemic control with metformin, other OADs are combined as dual or triple therapy to improve outcomes.[148]

Oral antidiabetic (OAD) agents

Commonly used OAD medications can be classified into three major groups based on their modes of action: insulin sensitizers, insulin secretagogues and alpha-glucosidase inhibitors. Newer classes of OAD medications include the glucagon-like agonists (GLP-1) and Amylin analogs.

Insulin sensitizers

Biguanides and thiazolidinediones are common examples of insulin sensitizers. Their mode of action is based on their ability to increase muscle cell glucose utilization while minimizing glucose production by the hepatic cells.

Biguanides

Biguanides improve insulin sensitivity of storage cells in the muscles and liver by preventing free fatty acids from being released from adipose tissues. Biguanides therefore decrease the amount of glucose produced in the blood.[151] Metformin is the only biguanide approved in the US.[150] The weight-loss inducing tendency of metformin has been found to be advantageous in obese patients; however, it is contraindicated in patients with hepatic, renal or cardiopulmonary dysfunctions due to risks of lactic acidosis. Gastrointestinal disturbances, such as diarrhea, are a common side-effect of metformin. Metformin as monotherapy is first-line therapy in patients with blood glucose levels that are not adequately controlled by lifestyle modification.[80, 152] A United Kingdom Prospective Diabetes Study (UKPDS) reported significantly lower costs of complications and increased life expectancy in overweight patients with type 2 diabetes who were placed on metformin as first line therapy compared to patients on conventional treatment (mainly dietary restrictions).[153] Depending on patients' needs, dosages range from 500mg to 2000mg daily. [80]

Thiazolidinediones

Thiazolidinediones reduce insulin resistance by increasing the influx of glucose into storage cells such as muscles, liver, and fatty tissues. Rosiglitazone and pioglitazone are common examples of thiazolidinediones. Weight gain and increased risks of fractures of the wrists and hips in adults on long-term therapy are common side effects. Pioglitazone was observed to reduce the risk of progression to type 2 diabetes by 72 percent in patients with insulin resistance.[154] Although thiazolidinediones have a slow onset of action, they may be used as monotherapy. While the risk of hypoglycemia is higher when combined with other OAD medications, such as metformin, these combinations are often more effective at achieving glycemic control.[80, 155] Caution is required in the use of pioglitazone and rosiglitazone due to concerns about the increased risk of renal failure reported in troglitazone (a withdrawn thiazolidinedione).[156] Thiazolidinediones are contraindicated in patients presenting with elevated alanine aminotransferase levels, especially in young patients with type 2 diabetes. Usually, daily dose ranges for rosiglitazone are 15 to 45 mg, with lower doses required when used in combination with other classes of OADs.[80]

Insulin secretagogues

Sulfonylureas and meglitinides are common examples of insulin secretagogues.

Sulfonylureas

The mode of action of sulfonylureas is dependent on their ability to bind to adenosine triphosphate (ATP) sensitive potassium channels located on surviving beta cell membranes; this action enhances insulin secretion. Sulfonylureas have a quick onset of action and are well tolerated; however, common side effects observed include hypoglycemic episodes and weight gain. Common examples of sulfonylureas include tolbutamide, glyburide, glipizide and glimepiride. [80, 157]

Meglitinide analogs

This group of OAD medications has been reported effective at stabilizing post-prandial glucose variations. Like sulfonylureas, meglitinide analogs improve insulin secretion using different binding sites. Repaglinide, an example of meglitinide analogs has a faster onset of action with a longer duration of effects compared to sulfonylureas. This class of antidiabetic medications is also known for its cardio-protective properties.[154] However, common side effects include hypoglycemia and weight gain. The daily recommended adult dosing regimen range from 0.5 to 4mg before meals.[80]

Alpha-glucosidase inhibitors

Alpha-glucosidase inhibitors' mechanism of action is dependent on their ability to stop the breakdown and absorption of ingested carbohydrates in the gastrointestinal tract. Acarbose and miglitol have been reported to have good safety profiles and do not have the tendency to induce weight gain (an advantage in obese patients) or loss. Abdominal pain, diarrhea and flatulence are common side-effects. [80]

Other classes of OAD medications used by adults include glucagon-like peptide-1 agonists (GLP-1) (e.g., exenatide), amylin analogs, and dipeptidyl peptidase-4 inhibitors (DPP-4). These classes of medications were recently approved for use.[80]

Insulin

In poorly controlled hyperglycemia in type 2 diabetes patients, insulin may be administered. Usually the use of insulin is mandatory in type 2 diabetic patients presenting with ketoacidosis.[127] Once glycemic control has been achieved, these patients are gradually taken off insulin and are subsequently managed with an OAD medication, usually metformin.[80] The mode of administration of insulin is subcutaneous, and it is available in several forms depending on its source and duration of action.[156] Although human sources of insulin are the most commonly prescribed, other sources of insulin are beef and pork sources. Based on the duration of action, insulin categories include regular (short- and rapid-acting), intermediate, or long-acting.[146] Insulin analogs, such as insulin aspart and insulin glargine, are products of the chemical alterations of the human insulin which result in insulin forms that have faster onset of action and longer duration of effects.[158] Weight gain and hypoglycemia are common side-effects of insulin.[80]

1.3.3.8 Diabetic complications

In order to minimize the progression of type 2 diabetes, adequate disease management, which involves tight glycemic control, is required. However, the progressive nature and long duration of the disease have been linked to several complications which have been associated with significant loss of productivity, as well as high rates of morbidity and mortality.[56] In 2007, [in the US] about $58 billion was spent on the management of both short- and long-term diabetic complications.[159] Common examples of short-term complications associated with high morbidity and mortality rates include hypoglycemia and diabetic ketoacidosis.[56, 135] Long-term diabetic complications are more common and can be broadly classified into microvascular and macrovascular complications.[160] While intensive glycemic control has been strongly associated with a low occurrence of microvascular complications in diabetes, a clear-cut relationship between controlled blood glucose levels and macrovascular complications has not been established.[154, 161-162]

Neuropathy, nephropathy, retinopathy, and renal failure are examples of microvascular complications of diabetes. A number of large clinical studies have reported that ensuring intensive glycemic control has been observed to be essential in preventing these complications; however, patients who have had the disease for at least ten years are at risk of developing these complications.[163] [56, 164] It has been reported that between 60 to 70 percent of mild to severe forms of neuropathies are related to diabetes; these neuropathies result in pain, foot ulcers and increased risks of amputations.[165] The CDC reported that as of 2005, diabetes was the leading cause of renal failure in more than 4 out of 10 patients; also, about 6 out of 10 non-traumatic lower-limb amputations have been associated with diabetes.[139] Furthermore, as of 2007, up to 24,000 new cases of blindness were related to diabetic retinopathy every year.[166] [167-168] Atherosclerosis, hypertension, myocardial infarction, stroke and coronary heart disease are examples of macrovascular complications that are associated with diabetes. These complications are the major causes of mortality in diabetic patients.[160] Atherosclerosis, a narrowing of the arterial walls due to the irreversible deposition of lipids in the arterial walls is a major cause of death in diabetic patients. Furthermore, it was estimated by the CDC in 2007 that almost 8 out of ten patients with blood pressure readings at and above 130/80 Hg mm have type 2 diabetes.

Compared to microvascular complications, macrovascular complications are seventy times more likely to result in mortality in patients with diabetes.[169]

1.3.3.9 Impact of type 2 diabetes on health-related quality of life

Although type 2 diabetes is an asymptomatic disease, it has been reported that people presenting with this disease have poorer HRQoL compared to their non-diabetic peers and several factors are responsible for this.[52] In order to achieve optimal glycemic control, many diabetic patients are usually placed on dietary restrictions and multiple medications. In turn, such patients are more likely to suffer from the side-effects of the medications, and face the challenge of chronically adhering to these medications which may be expensive. When patients fail to adhere to their disease management options, the disease progresses and several complications set in; these complications which may be microvascular or macrovascular in nature, further increase the burden of the disease and worsens patients' quality of life. Type 2 diabetes has also been reported to be accompanied by other chronic comorbid conditions such as cardiovascular diseases, hypertension, and obesity (including medication-related obesity), hence, several factors are responsible for adversely affecting the QoL of diabetic patients.[170]

1.3.4 Diabesity: Type 2 diabetes and comorbid obesity

The strong relationship between type 2 diabetes and obesity led to the creation of the term "diabesity" in the 1970s.[171] It is estimated that more than 8 out of every ten type 2 diabetic patients are at least overweight.[1, 31] Compared to the individual disease conditions (either type 2 diabetes or obesity alone), the presence of these comorbid conditions in a patient implies significantly higher healthcare consumption and expenditure, loss of productivity, increased disability, premature morbidity and mortality.[56, 172] Obesity has been reported to increase the risks of cardiovascular diseases, hence the risks of morbidity and mortality in patients with comorbid type 2 diabetes increases. Moreover, the increased risks of dylipidemia and other cardiac disease conditions associated with obesity are intensified in obese type 2 diabetic patients.[173]

1.3.4.1 Risks of Diabetes due to Obesity

Studies have reported that obesity (particularly abdominal obesity) is one single factor that strongly predisposes patients to developing type 2 diabetes (it is reported that about 67 percent of type 2 diabetes cases is associated with obesity). It is also widely reported that being at least overweight is associated with insulin resistance, which in itself is an indication of the impending development of type 2 diabetes.[6, 174-175] Whereas, an increase in insulin sensitivity has been associated with a reduction in body weight, insulin sensitivity may be improved through the incorporation of healthy dietary changes, active participation in physical exercise and a cutback on inactive lifestyles.[1, 10] The relationship between BMI status and diabetes has been explained in several ways such that remission of diabetes has been reported in 64 to 83 percent of obese diabetic patients who lost a significant amount of weight through bariatric surgery.[33, 176] The joint presence of these two conditions in an individual greatly increases the risks of other diseases and complications of diabetes such as blindness, nephropathy, and diabetic ulcers, all of which have also been linked with poor disease management and long duration of disease.[138, 175]

1.3.4.2 Common comorbid/predisposing factors to diabesity

Provided below are three other factors known to either be common comorbid disease conditions of 'diabesity' or diseases that predispose patients to 'diabesity', apart from the diseases that make up the metabolic syndrome previously explained.

1.3.4.2a Depression

A number of studies have reported a significant relationship between depression and type 2 diabetes and between obesity and depression.[68, 177-178] The likelihood of presenting with depression in diabetic patients was reported to be triple compared to non-diabetic patients.[68, 178] Likewise, the risk of the obese and overweight patients developing depression later on in life, as well as the risk of the depressed patient becoming at least overweight has also been reported in a meta-analysis.[177]

1.3.4.2b Chronic stress

When the physiological anabolic-catabolic hormonal balance of the body is disturbed as a result of prolonged psychological stress, there is an increase in visceral fat deposition, as well as insulin resistance. Also, chronic stress promotes the activation of autonomic and neuro-endocrine systems which increases the risk of pre-diabetes. [52]

1.3.4.2c Sleep deprivation

The perpetual lack of or reduction in sleep has been reported to be associated with increased glucose intolerance, thus increasing the risk for diabetes. Sleep deprivation has also been associated with an increase in the secretion of ghrelin, an appetite stimulating hormone, hence, increasing appetite, food consumption and thus promoting weight gain.[179]

1.3.4.3 Management of the obese diabetic patient

A distinctive feature in the obese prior to presenting with diabetes is insulin resistance, which is brought about by glucose intolerance, and this has commonly been found in people presenting with abdominal obesity. Glucose intolerance in the obese is due to the presence of excess adipose tissues in the abdominal region, which stimulates an increase in insulin resistance in the liver and muscles.[173, 180] Hence the management of the obese diabetic patient is challenging and there is a need to strategically focus on improving insulin resistance through medication use and weight loss. Lifestyle modifications, in terms of diet and physical exercise that results in a weight loss of at least 5 percent, have been reported to improve insulin sensitivity considerably; hence, in the management of the obese diabetic patient, intentional weight loss is mandatory.[105] A systematic review suggested that a decreased risk of developing diabetes, a decreased level of low density lipoprotein, a decreased total cholesterol reading, and a decrease in blood pressure were all associated with intentional weight loss.[105] Kumar et al. also reported a significant decrease in the number and doses of OAD medications and insulin obese diabetic patients were placed on following an intentional weight loss of at least 7 percent, which also resulted in an improvement in insulin sensitivity.[181] Since it has also been reported that type 2 diabetes prevalence rate is about 5 times higher in the obese compared to those with healthy weight, the goal towards achieving healthy weight cannot be overemphasized.[143]

It is also important to consider the type of medications used to manage this set of patients, so as to avoid complications such as weight gain in already obese patients, thus worsening the comorbid conditions. While the use of insulin and/or sulphonylureas may induce weight gain, the addition of metformin, which counters the weight gain problem, may also have negative effects on insulin resistance and hypertension in at-risk patients.[173, 182] Hence, a cautious balance is required in the pharmacologic treatment of an obese diabetic patient. Early detection and management is of great importance as it has been reported that obese patients who have had diabetes for less than 5 years experience greater success with diabetes remission after bariatric surgery compared to their peers who have longer duration of the disease.[33] Overall, the goals of treatment are centered on achieving and sustaining glycemic levels below 7 percent in order to minimize the likelihood of presenting with microvascular complications.[144, 152] With studies reporting that about 85 percent of type 2 diabetic patients are at least overweight, it is imperative to address the excess weight in order to improve the chances of adequate glycemic control, especially since an increase in insulin sensitivity has been associated with weight loss.[143] Consequently, insulin sensitivity may be improved through diet, involvement in active yet controlled physical exercise, and a reduction in sedentary lifestyles.[1, 10] The strong association between type 2 diabetes and an increase in the incidence of macrovascular complications, such as hypertension and dyslipidemia, makes it necessary to screen for hypertension and dyslipidemia at diagnosis and every other year following diagnosis in order to minimize risks of morbidity and mortality due to high blood pressure and lipid levels.[56] Generally, blood glucose tests are conducted twice a year in patients with adequate glycemic control, while it is recommended that such tests be carried out every quarter in patients with poor glycemic control or in patients who changed therapy.[135, 138, 152] Fasting plasma glucose (FPG) screening is recommended every two to three years in children and adults who present with certain risk factors, such as overweight/obesity or other risk factors. [144]

Most importantly, implementing adequate yet realistic treatment goals is necessary in order to delay the occurrence of, or reduce the progression of microvascular complications such as retinopathy, nephropathy, neuropathy, and diabetic ulcers (and eventual limb amputations).[138] An increase in complications has been associated with poor glycemic control and a longer duration of diabetes.[161, 164] Ensuring adequate glycemic control through efficient disease management will significantly improve the patient's quality of life and reduce rates of morbidity and mortality. [138]

Finally, there are three main methods for managing diabesity. These include lifestyle modification, use of medication, and surgery (all mentioned previously). It has been noted that a significant proportion (up to 90 percent) of obese patients do not respond to either lifestyle modifications or treatment with medications due to the severity of their obesity or due to the presence of diseases associated with obesity. Such patients who are morbidly obese with BMI values ≥40 or who present with obesity-related diseases (such as type 2 diabetes, sleep apnea and cardiovascular diseases) with BMI values ≥ 35 are candidates for bariatric surgery. [175]

1.3.4.4 Issues with the management of the obese diabetic patient

Although the management options of obesity and type 2 diabetes have been separately discussed in previous sections, these management options are inter-related. It is therefore expected that the management of the obese diabetic patient will involve a combination of both disease management measures. However, there are a number of factors that make this co-morbid disease management a challenge.

Several factors have been considered barriers to optimal management in 'diabesity' patients. These include: patient-related factors (e.g., demographic factors such as age, race, gender, literacy levels, in addition to psychosocial factors such as anxiety and depression); environmental factors (e.g., family/peer support, and socioeconomic status); disease-related factors (e.g., the severity of symptoms, duration of disease and the presence of comorbidities); medication-related factors (e.g., the complexity of dosing regimen (frequency and duration), side effects and cost of medication); and health care provider-related factors). [183]

1.3.4.4a Disease-related factors

Diabetes and obesity have been reported to significantly influence both the pharmacokinetics (the way the body works on medications) and pharmacodynamics (the way the drug works in the body) of medications in the body.[184]The pharmacokinetic aspects which include absorption, distribution, metabolism and excretion are all influenced in a number of ways.

Generally, absorption is greatly influenced by changes in muscle and subcutaneous adipose blood flow as well as gastric emptying. Patients who are obese or are insulin resistant have poor blood flow in the subcutaneous adipose tissues, and hence, have slow absorption. The distribution of medications, on the other hand, is affected in diabetic patients basically due to the non-enzymatic glycosylation of the protein, albumin, leading to serum albumin abnormalities. Metabolism is affected in that diabetes affects the regulation of enzymes required for the breakdown of medications. This is because diabetes influences the metabolism of lipids and proteins, as well as complex sugars. Abnormal liver functions, such as non-alcohol steato-hepatitis and liver fibrosis, which affect metabolism, are seen in diabetic patients. Finally, excretion is severely affected in patients who present with kidney problems, usually nephropathy, a diabetic complication which is not uncommon among diabetic patients as it presents in 4 out of every 10 diabetic patients. Nephropathy affects the glomerular filtration rate and eventually results in end-stage renal disease.[184]

Other disease-related factors are centered on the presence of comorbidities, duration of disease, severity of disease and symptoms, and the development of complications. These factors have all been associated with poor adherence to disease management therapy. [185] Likewise, the presence of co-morbid factors, which is associated with a high comorbidity index, has also been associated with poor disease management.[186] While the progression of type 2 diabetes in the obese patient has also been associated with the development of complications and comorbidities, these factors eventually result in an increase in the number of medications required by the patient, thus worsening adherence as pill burden increases. [185]

1.3.4.4b Treatment-related factors

High costs of medications and surgery, medication side-effects, and pill burden (frequency and the number of medications used) have all been reported to adversely influence adherence, especially in patients with comorbid disease conditions.[185, 187] Challenges with discipline and self-motivation to maintain the continuous balance required in caloric intake and expenditure also present as a problem in adequate disease management.[81, 173] However, studies have been inconclusive on the association between adherence and pill burden. While a study found no significant association between adherence and the number of medications used, Donnan et al. reported better adherence with monotherapy in diabetic patients, a negative association between adherence and unreported side-effects was also reported. [188-189] The high cost of medication has also been regarded as an important factor for low adherence to medications.[190] Furthermore, studies have reported an association between poor adherence and dosing complexity of medications prescribed.[189, 191] In 2003, the WHO gave recommendations centered on the need to reduce dosing frequency and medication side effects, in order to ultimately improve adherence.[189, 192] This is of great importance in patients with co-morbid diseases, such as the obese diabetic patient, whose medication taking regimen may already be complicated as a result of the presence of more than one disease condition.

1.3.4.4c Patient-related factors

Demographic factors like gender, age and race are commonly known to influence adherence to therapy.[186] Adherence rates based on these three factors are not clear cut. Being male, younger and black was reported to be associated with low adherence to OAD medications in one study, while another study associated being female, older, and non-white with poor adherence among Medicare Part D patients above 65 years of age.[186, 193] Sociocultural beliefs and norms have also been found to have a significant influence on body weight and image as many still consider the attention given to weight loss in overweight and obese people as cosmetic in nature;[32] hence, there is a need to incorporate these considerations in therapy to optimize individual patient management.[81, 194] Age may also be interrelated with barriers to adequate management of these diseases and should be given serious consideration with regard to patient management. Lifestyle modifications such as adequate physical exercise may also be more difficult to accomplish as the patient ages, while surgery may not be a good option for older patients for fear of severe complications or even death.

Other factors that significantly influence adherence to therapy include the patient's knowledge and beliefs about the disease and its implications, as well as the belief in the efficacy of the treatment regimen. [188, 195]

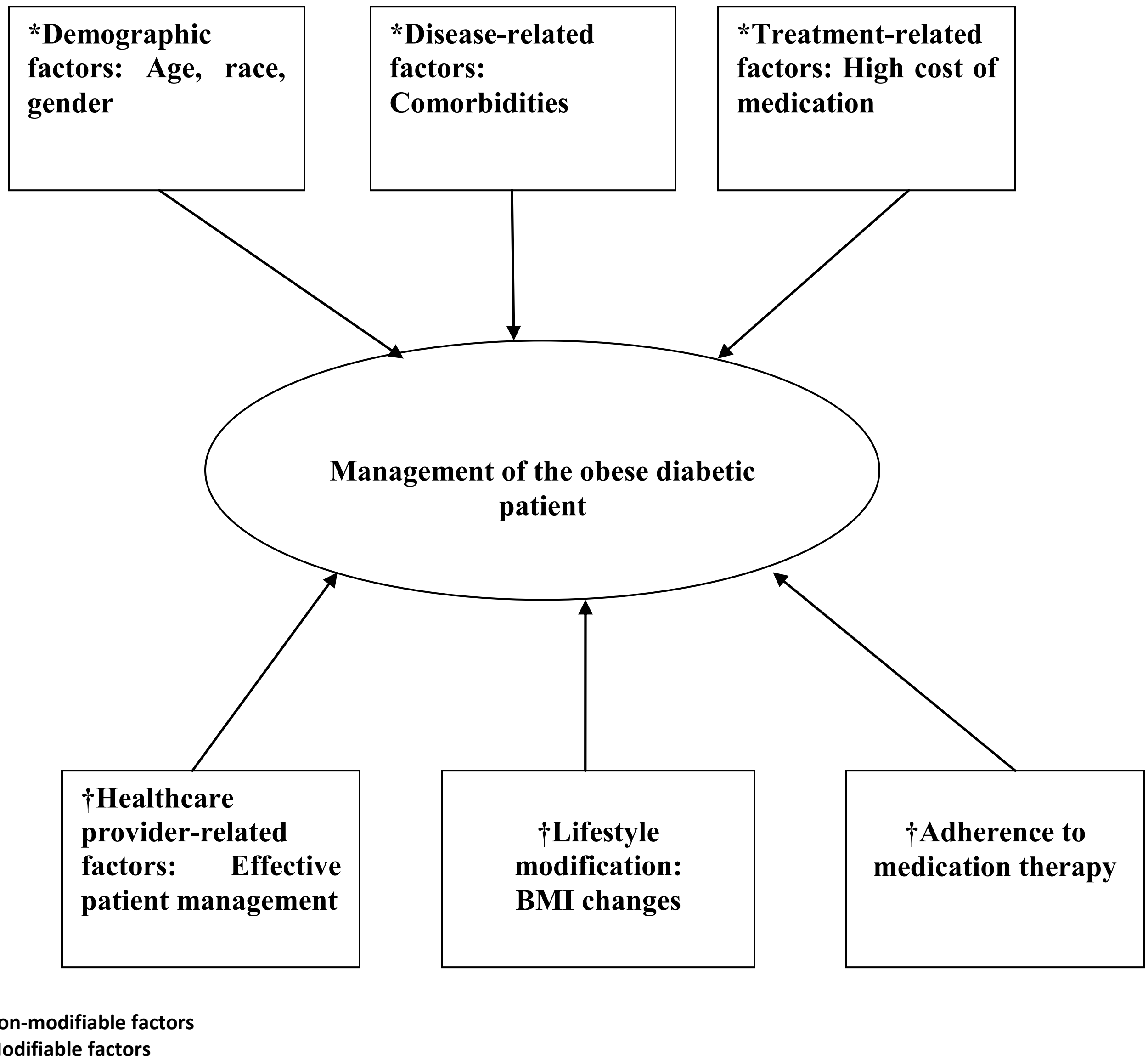
Furthermore, the patients' socioeconomic status (SES) and educational levels are important factors to consider, as poor adherence has been associated with low SES and low educational levels.[196] Also, patients who desire bariatric surgery may not have the access to such procedures if they do not meet insurance requirements for surgery unless they are ready to pay out-of-pocket. For many patients this would be a large financial burden, as insurance companies decline coverage for most bariatric surgeries.[197]

Lack of peer/social support, poor self-image, anxiety and depression are also psychosocial factors associated with obesity which may negatively influence adherence. [69, 81, 188, 195-196]

1.3.4.4d Healthcare provider-related factors

The ability of providers to competently provide patients with clear, up-to-date and adequate information about their disease, implications and the importance of adherence to disease management options has been associated with increased medication adherence.[196, 198] For optimal disease management, it is the responsibility of healthcare providers to manage patients based on clinical guidelines such that overweight and obese patients are adequately identified, evaluated and managed.[81] Poor communication between patients and their healthcare provider has also been reported to be one of the reasons for poor adherence to OAD medications in patients with type 2 diabetes.[199] Furthermore, when providers encourage active involvement by patients in the management of their health, the likelihood of improved adherence to therapy increases.[81] Another important factor is the physician's physical fitness and BMI status, as it has been observed that healthcare providers with high BMI status are less likely to counsel patients concerning weight loss compared to their peers with normal weight.[200-201] Finally, certain factors have been reported to discourage adherence to clinical guidelines by healthcare providers; hence; negatively influence disease management, these are inadequate reimbursement and complexities encountered in disease management (a typical case study is the obese diabetic patient).[81] Figure 1.3 below is a diagrammatic representation of factors that influence the management of the obese diabetic patient.

Figure 1.3: Diagrammatic representation of both the modifiable and non-modifiable factors that influence management of the obese diabetic patient



1.3.4.5 Addressing the epidemic, diabesity

As with the individual management of diabetes and obesity, the management of diabesity requires individualization depending on age, race, the presence of co-morbid disease conditions, severity and behavioral patterns.[52, 138]

It is recommended that patients who are without symptoms while presenting with HbA1c levels lower than 7 percent be placed initially on lifestyle modifications which include diet restrictions (medical nutrition therapy), reduction in sedentary lifestyle and an increase in physical exercise.[138] [10] However, in symptomatic patients, studies have shown that lifestyle intervention alone is ineffective in more than 90 percent of adults; thus, there is a need for adequate disease management involving the prompt introduction of medications, especially in obese patients with poorly controlled glucose levels (having HbA1c levels above 7 percent). [145]

Regular patient counseling which ensures that patients are adequately informed about their disease state and its management is vital. This is relevant in order to increase the chances of achieving and maintaining optimal health outcomes such as a healthy weight and glycemic control, as well as preventing or minimizing complications.[1, 138] Furthermore, providing education for self-management is recommended. Self-management includes skills required by patients to be able to self-monitor their blood glucose in conjunction with scheduling regular examinations to address complications and adverse effects.[146] Finally, emphasis on the roles of physical exercise and social support cannot be overstated due to the influence families and friends have on the patients' ability to adhere to the prescribed lifestyle and treatment interventions.[147] These non-pharmacological recommendations should also be stressed in patients presenting with prediabetes, glucose intolerance, impaired blood glucose, or asymptomatic hyperglycemia. An annual screening of adults above 30 years old, as well as at-risk patients such as patients with prediabetes, is recommended to be able to detect and manage diabetes as soon as it occurs.[52, 202] Surgery should also be recommended in patients who meet the conditions for surgery, that is, the severely obese and/or obese patients presenting with comorbid conditions.[12] Significant reductions in healthcare costs and use have been reported in at least 75 percent of type 2 diabetes patients who underwent bariatric surgery.[176,197] Because the early management of diabetes has been associated with better outcomes, after 3-6 months of ineffective non-pharmacological intervention, medication therapy is recommended, while being aware of how certain antidiabetic medications affect body weight.[135] Finally, the prevention of these diseases is of utmost importance in addressing the epidemic. With the knowledge of how diabesity impacts healthcare costs, productivity, and quality of life, significant actions are required to prevent diabesity. Effective strategies to ensure that the incidence of diabesity is reduced to the barest minimum are essential, knowing that absolute prevention may be impossible. This may involve the implementation of strict programs that will promote the availability of healthy foods and drinks with low caloric contents in restaurants and schools (especially for the pediatric population) as well as easy and safe access to facilities that will encourage exercise and active lifestyles such as sidewalks, walkways and bicycle tracks.[41]

1.3.4.6 HRQoL of diabetic patients by BMI status

The peculiarity of the management of obese type 2 diabetic patients lies in the fact that some OAD medications induce weight gain; hence, may worsen patients' comorbid disease conditions. A number of studies involving different populations outside the US and different utility measures have reported varied conclusions about the relationship between BMI status and HRQoL among patients with comorbid diseases such as diabetes and cardiovascular diseases.[28, 203-205] It is not clear as to what extent poor quality of life reported is actually due to patients' high BMI or the associated diseases.[206] Generally, obese diabetic patients stand a higher risk of presenting with other comorbid diseases as these two disease conditions independently pose as risk factors to other diseases. In fact, it has been reported that cardiovascular diseases are common complications in about 66 percent of type 2 diabetic patients and because obesity is a risk factor for several cardiovascular diseases, obese diabetic patients frequently present with cardiovascular diseases concurrently as explained in earlier sections. [207]

Logically, the quality of life of patients with these comorbid conditions is more likely to be significantly poorer, and a number of studies have supported this using several quality of life instruments.[15, 25, 28, 208] With the EQ-5D and standard gamble utility measures, Redekop et al. and Matza et al. reported that obese (≥30 BMI) diabetic patients reported significantly more symptoms and poorer health status compared to their non-obese peers.[15, 208] Svenningsson et al. also reported that compared to normal-weight (BMI:18.5-25) adults, at least 20 percent of obese diabetic (BMI:30-40) patients suffer from depression, thus translating to poorer quality of life compared to their peers.[209] Another study using the SF-36 reported significantly improved quality of life scores in obese diabetic patients who had lost weight through lifestyle intervention.[207] The influence of obesity on the quality of life of type 2 diabetic patients is apparent in the improved quality of life scores when a significant amount of weight loss is achieved. A number of other studies have also found that after intentional weight loss, for example, through bariatric surgery, the quality of life of obese diabetic patients is significantly increased.[181, 210] This is to be expected because the ease of carrying out activities of daily living is improved and several risk factors associated with obesity are greatly minimized, for example, insulin sensitivity increases with weight loss.[100, 181, 210]When the health-related quality of life of patients with diabetes and co-morbid obesity was evaluated, another study by Fu et al. using Medical Expenditure Panel Survey (MEPS) data supported earlier studies that the quality of life of diabetic patients with or without microvascular and macrovascular complications was significantly different. Diabetic patients with complications reported, on average, worse quality of life.[15, 211] Using the SF-12 and EQ-5D quality of life instruments, Sullivan et al. also reported that obesity significantly worsened the quality of life of patients with diabetes and hypertension.[212] However, a study reported no significant difference in weight-related HRQoL when diabetic patients were compared against their non-diabetic peers.[31]

In summary, most studies support that higher BMI was significantly associated with poorer HRQoL in patients irrespective of their diabetes status.

1.3.4.7 Methods used in cost of illness studies

Several studies have been carried out evaluating the cost of illness for various disease conditions, such as asthma, diabetes, obesity, and schizophrenia.[213] In the estimation of the cost of illness, the direct and indirect costs are commonly determined, and the direct cost components that are usually considered include: 1) emergency room/inpatient hospital costs; 2) outpatient physician costs; 3) drug costs; and 4) laboratory costs. Indirect costs commonly accessed are lost productivity costs. There are also 4 major methods that are commonly used in evaluating the cost of illness.

1) Sum of all medical costs: this involves the sum of all the costs incurred by a patient with the disease of interest.
2) Sum of diagnosis-specific costs: the sum of the specific medical costs incurred by a patient which are related to the diagnosis of interest.
3) Matched control: this method identifies and sums up the costs incurred by patients with a specific diagnosis and finds the incremental costs which are obtained by subtracting the costs from a matched cohort [or subtracting out the average cost for a sample].[213]
4) Regression: the incremental cost of illness estimate can be evaluated by applying the beta coefficient obtained on a binary indicator/factor for a diagnosis.

In assessing the incremental costs of a specific disease, the precision of the obtained estimate is dependent on the use of appropriate techniques to control for confounding factors. [213]

1.3.4.8 Cost of illness studies: A focus on obesity and diabetes

In a review of 2007-2010 European studies that evaluated the cost of obesity mainly from a societal perspective, high costs were associated with men, people with high socioeconomic status, with abdominal obesity and other co-morbid factors. Excess per capita costs due to obesity was up to €1,873, accounting for 0.61 percent of Europe's gross domestic product (GDP).[214] In the US, the Medical Expenditure Panel Survey (MEPS) has been used to evaluate the cost of illness for obesity and diabetes separately using different age populations. For example, Trasande et al. evaluated healthcare expenditures in children by BMI status, such that the difference in expenditures incurred from the inpatient hospitalizations, prescription drugs, outpatient visits and emergency room visits in obese children were significantly higher compared to their non-obese peers.[215] Some studies have also reported significant healthcare costs incurred by patients who were at least overweight within the MEPS database. For instance, a study reported that healthcare expenditures in whites was significantly higher compared to blacks irrespective of the BMI category compared.[216] A study found a significant interaction between age and gender when the impact of obesity was assessed in a MEPS population that included children and adults.[217]

A number of studies have also focused on diabetes. For example, Fu et al. assessed the total (direct and indirect) incremental costs associated with macrovascular comorbid conditions (MVCC) in adults with diabetes. This study concluded that MVCC in diabetic patients accounted for $7,508 ($5,120 in healthcare costs and $2,388 in lost productivity), which was found to be statistically significantly higher than for diabetic patients without MVSS.[218] Using

2000 and 2002 MEPS data, Sullivan et al. concluded that obesity significantly increased total costs in adults presenting with a number of cardio-metabolic risk factors - including diabetes.[219] In addition, Lee et al. used the 2000 MEPS data to evaluate disparities in healthcare costs by race in diabetic patients and found that whites had significantly higher costs compared to blacks and Hispanics.[220] An earlier study used MEPS 1996 data to assess the impact of depression on healthcare costs in diabetic patients and found that incremental costs due to depression in these patients was significant.[221]

1.3.4.9 Healthcare costs and expenditures in the obese diabetic patient

Not many studies have been carried out to specifically determine the effect of obesity on the healthcare costs of the type 2 diabetic patient; however, a number of studies have suggested that obesity has a significant impact on healthcare costs for the general population. In a study involving Spanish type 2 diabetic patients, Ballesta et al. suggested that obesity was one critical factor responsible for significantly higher healthcare costs in this population of diabetic patients.[222] Another study using the 2005 US Nationwide Inpatient Sample reported a significantly higher number of hospitalizations and higher costs among obese and morbidly obese type 2 diabetic patients compared to their non-obese peers.[17] Obese and morbidly obese type 2 diabetic patients spent significantly more $16,347 [$p<0.01$] and $18,360 [$p<0.01$] in hospitalization costs (median costs), respectively compared to the $16,112 spent by their non-obese peers.[17] A German study also supported this finding with the conclusion that obesity was associated with significant increases in healthcare costs in diabetic adults.[22] Another study concluded that based on healthcare costs, the population-attributable risk of diabetes was significantly associated with obesity.[24] Conversely, a number of studies have reported that being overweight or obese did not significantly increase healthcare costs or that being of normal weight actually increased healthcare costs compared to being obese. A study involving veterans above 65 years old reported that diabetic patients with normal weight had significantly higher healthcare costs ($10,470) compared to their overweight ($7,526) and obese ($6,597) peers, respectively.[21] A search of the literature produced only four US-based studies that specifically reported how obesity influences healthcare costs in adult diabetic patients, including one study which assessed the impact of obesity on cardio-metabolic risk factors, of which diabetes was included.[16] The fact that not many studies have been carried out in the US population and that mixed conclusions were reached by the few studies warrants the need to evaluate how BMI status influences healthcare utilization and costs using a recent database that is representative of the US non-institutionalized civilian population.

Provided in Tables 1.1 and 1.2 below is a summary of studies that have assessed the relationship between obesity and healthcare costs, and quality of life in adult patients with or without diabetes.

Table 1.1: Summary of studies on the association between obesity and healthcare costs

Study	**Disease of interest**	**Dataset used (Sample size [n])**	**Age range**	**Outcome Variable of interest**	**BMI (kg/m^2) category studied**	**Study conclusion**
*Sullivan et.al[16](2007)	Cardio-metabolic risk factors (diabetes, hypertension, hyperlipidemia, overweight/obesity)	MEPS 2000 & 2002 (n=43,221)	Adults ≥18 years	Healthcare costs	BMI ≥25	Significant medical costs independent of cardiovascular disease estimated at $80 billion (p-value not provided)
*Kim et al.[17] (2009)	Diabetes/obesity	Nationwide Inpatient Sample 2005 (n~8 million)	Adults	Hospital charges (costs)	Normal weight BMI: <30; obese BMI ≥30; morbidly obese BMI ≥40	Hospital charges for obese (p<0.01)/ morbidly obese (p<0.01) patients significantly higher compared to non-obese peers irrespective of diabetes status (with or without diabetes)
*Shen et al.[21] (2009)	Diabetes/obesity	Veterans Health Administration 1999 claims data (n=79,934)	Adults (≥ 65 years)	Healthcare costs	Normal weight:18.5-24.9; overweight :25-29.9; obese: 30-34.9; morbidly obese: ≥35	Significantly higher mean total costs in normal weight(p<0.0001), overweight (p<0.0001) patients compared to obese peers

Table 1.1 (cont'd): Summary of studies on the association between obesity and healthcare costs

Study	**Disease of interest**	**Dataset used (Sample size [n])**	**Age range**	**Outcome Variable of interest**	**BMI (kg/m^2) category studied**	**Study conclusion**
*Sullivan et.al[219](2008)	Cardio-metabolic risk factors (diabetes, hypertension, hyperlipidemia, overweight/obesity	MEPS 2000 & 2002 (n=43,221)	Adults (≥18 years)	Medical expenditure and productivity costs	BMI ≥25	Significant medical expenditures and productivity costs associated with obese patients compared to their non-obese peers ($p<0.05$)
Von Lengerke et al.[22] (2010)	Diabetes/obesity	German Statutory Sickness Fund claims data 2004 (n=37,570)	Adults (≥18 years)	Healthcare costs	BMI not specified (only mentioned obese vs. non-obese)	Obesity was associated with significant increases in costs ($p<0.01$)
Zhao et al.[24] (2008)	Diabetes, hypertension, coronary heart disease (CHD), stroke/obesity	China National Nutrition and Health Survey (CNHS) 2002 and 2003 The Third National Health Service Survey	Adults	Healthcare costs	Overweight:≥24 <28; obese:≥28	$2.74 billion in total medical costs was attributed to overweight and obesity. Population-attributable risk of diabetes, hypertension, CHD and stroke associated with overweight (OR: 2.31 [2.00-2.81]) /obesity (OR: 3.99 [3.28-4.84]) was also significant

Table 1.1 (cont'd): Summary of studies on the association between obesity and healthcare costs

Study	Disease of interest	Dataset used (Sample size [n])	Age range	Outcome Variable of interest	BMI (kg/m^2) category studied	Study conclusion
Ballesta et al.[222](2006)	Diabetes/obesity	Electronic Medical Records of patients within a healthcare area of Southern Spain 1999 (n=517)	Patients (≥ 15 years)	Total healthcare costs	BMI was used as a continuous variable	Obesity (BMI was continuous) was a significant independent factor responsible for increased healthcare costs ($p<0.01$)

*US-based diabetes/obesity-related studies

Table 1.2: Summary of studies on the association between obesity and Health-Related Quality of Life and health status

Health-Related Quality of Life and health status						
Author year	**Disease of Interest**	**Data source (Sample size)**	**Age range**	**Outcome Variable of Interest**	**BMI category studied**	**Study Conclusion**
*Hlatky et al.[28] (2010)	Diabetes and coronary artery disease/obesity	The Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial in US & Canada (n=1,798)	Adults (≥ 25 years)	HRQoL	Normal weight:≤25; Overweight:≥25-<30; Class 1 obesity:≥30-<35; Class II/III obesity: ≥35	Higher BMI categories were significantly related to poorer HRQoL based on 4 HRQoL measures (Duke Activity status Index, DASI; energy score, health distress score and self-rated health status [p<0.001])
Redekop et al.[223] (2002)	Diabetes/obesity	Sample of Dutch patients filled physician administered questionnaire (n=1,348)	Not specified	HRQoL	Obese:≥30	Obesity was associated with lower (poorer quality of life) EQ-5D utility scores (p=0.004)
Gough et al.[25] (2009)	Diabetes/obesity	Health Survey of England 2003 (n=12,188)	Adults (≥ 17 years)	HRQoL	Obese (≥30) vs. non-obese	Obesity had a significant and additive effect on HRQoL in diabetic patients using the EQ-5D (p<0.05)

Table 1.2 (cont'd): Summary of studies on the association between obesity and Health-Related Quality of Life and health status

Author year	**Disease of Interest**	**Data source (Sample size)**	**Age range**	**Outcome Variable of Interest**	**BMI category studied**	**Study Conclusion**
*Wexler et al.[30](2006)	Diabetes/obesity	Surveyed diagnosed diabetic patients in outpatient US clinics (n=909)	Adults	HRQoL	Normal weight<25; Overweight 25-29.9; obese ≥30	Obesity was not significantly associated with decreased HRQoL using the Health Utilities Index III
*Kolotkin et al.[31] (2003)	Diabetes/obesity	Patients enrolled in a US clinical trial (n=1,197)	Adults	HRQoL		No significant difference in weight-related HRQoL between obese diabetic and non-diabetic patients
Tuthill et al.[207] (2007)	Diabetes/obesity	Outpatient clinics in Dublin (n=68)	Adults	HRQoL	BMI > 30	HRQoL improved significantly with weight loss using the [a]SF-36 ($p<0.05$)
Matza et al.[208] (2007)	Diabetes/obesity	UK sample with diabetes (n=129)	Adults	HRQoL	Obese (≥30) vs. non-obese	Obesity significantly associated with poorer health status using the EQ-5D ($p<0.001$) in diabetic patients.

Table 1.2 (cont'd): Summary of studies on the association between obesity and Health-Related Quality of Life and health status

Author year	**Disease of Interest**	**Data source (Sample size)**	**Age range**	**Outcome Variable of Interest**	**BMI category studied**	**Study Conclusion**
*Sullivan et al.[212] (2008)	Diabetes, hypertension/obesity	MEPS (n=43,221)	Adults ≥18 years	HRQoL	BMI ≥25	Significantly poorer HRQoL associated with obese patients vs. normal weight peers using the EQ-5D and SF-12 instruments ($p<0.05$)(in patients with or without diabetes)
*Kannan et al.[27] (2008)	Diabetes, hypertension, dyslipidemia/obesity	National Health Wellness Survey (NHWS) 2006 (n=19,759)	Adults ≥18 years	HRQoL	BMI >27	Significantly poorer HRQoL in the at least overweight patients compared to normal weight peers ($p<0.001$). (Not all the patients had diabetes).
Svenningsson et al.[209] 2011	Diabetes/ obesity	Primary care centers (n=339)	Adults 30-75	HRQoL (Beck Depression Inventory II) BDI-II	Normal weight:18.5-25; Obese:30-40	Based on the BDI-II, obese patients had greater depression compared to their non-obese peers ($p=0.04$).

Table 1.2 (cont'd): Summary of studies on the association between obesity and Health-Related Quality of Life and health status

Author year	**Disease of Interest**	**Data source (Sample size)**	**Age range**	**Outcome Variable of Interest**	**BMI category studied**	**Study Conclusion**
Wong et al.[224] 2013	Diabetes/obesity	Interviewer-administered survey at government-funded general outpatient clinic (n=488)	Adults	HRQoL (SF-12)	BMI: continuous variable	Negative association between BMI and PCS-12 and positive association between BMI and MCS-12 ($p<0.05$)
*Rejeski et al.[225] 2006	Diabetes/ overweight & obesity	Look AHEAD (Action for Health in Diabetes) trial (n=5,145)	Adults 45-74 years	HRQoL (SF-36)	Overweight 25-29.9; obese class I :30-34.9; obese class II:35-39.9; obese class III:≥40	Higher BMI associated with greater depressive symptomatology
Doll et al.[226] 2000	Obesity	Postal survey data [Oxford Regional Health Authority of England] (n=8,889)	Adults ≥18 years	HRQoL (SF-36)	Under weight<18.5; Normal weight BMI 18.5-24.99; overweight 25-29.99; obese BMI 30-39.99; morbidly obese BMI ≥40	Being at least obese was associated with lower PCS and MCS scores $p<0.001$

[a]Medical Outcomes Trust Short Form-36 (SF-36).
*US-based diabetes/obesity-related studies

1.3.4.10 Summary of literature review

Evidence suggests that the simultaneous increase in the prevalence of diabetes and obesity has had a significant impact on healthcare costs and utilization which may be daunting to patients and society at large. Significant decreases in productivity, quality of life and life expectancy of these patients have also been reported due to these comorbid disease conditions. While several measures are available to help in curbing the rising incidence and prevalence of these diseases, studies suggest that a significant impact of these preventive measures is yet to be observed. The mixed conclusions obtained from the literature regarding the relationship between obesity and healthcare costs and the HRQoL of diabetics create a need to assess this relationship using a nationally representative US population.

1.3.5 Study Aim

The present study sought to specifically determine the relationship between healthcare costs and BMI among patients presenting with type 2 diabetes in the adult MEPS population. The relationship between HRQoL and BMI in the diabetic adult population was also assessed using data from the SF-12 quality of life instrument provided on each adult in the MEPS dataset eligible for the study.

1.3.6 Study Objectives and Hypotheses

Objective 1: To describe the study sample and evaluate the differences in socio-demographic characteristics (age, age category, gender, race, marital status, insurance status, socioeconomic status and geographical region), smoking status and comorbidity index of the diabetic MEPS population by BMI status.

Objective 2: To estimate the prevalence of overweight and obesity among the diabetic MEPS population.

Prevalence=number of obese diabetic patients/total number of diabetic patients in the study, for each level of overweight/obesity.

Objective 3: To estimate differences in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypothesis:

H_{01}: There is no significant difference in diabetes-related healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 4: To estimate differences in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypothesis:

H_{02}: There is no significant difference in direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 5: To estimate differences in indirect (lost productivity) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypothesis:

H_{03}: There is no significant difference in indirect (lost productivity) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 6: To estimate differences in total (direct medical and indirect) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypothesis:

H_{04}: There is no significant difference in total (direct medical and indirect) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 7:

To determine how healthcare utilization (ambulatory care [outpatient department visits and office-based medical provider visits], emergency room visits and prescribed medicines) rates of diabetic patients differ between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypotheses:

H_{05}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

H_{06}: There is no significant difference in the number of emergency room visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

H_{07}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 8:

To compare the HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypotheses:

H_{08}: There is no significant difference in PCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

H_{09}: There is no significant difference in MCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 9: To estimate differences in healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

Hypotheses:

H_{10}: There is no significant difference in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

H_{11}: There is no significant difference in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 10: To estimate differences in indirect (productivity loss) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

Hypothesis:

H_{12}: There is no significant difference in indirect costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 11: To estimate differences in total healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

Hypothesis:

H_{13}: There is no significant difference in total healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 12: To estimate the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

Hypotheses:

H_{14}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

H_{15}: There is no significant difference in the number of emergency room visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

H_{16}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 13: To estimate the differences in HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

Hypotheses:

H_{17}: There is no significant difference in PCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age, gender, race, marital status, smoking status, socioeconomic status, insurance status, geographical region and co-morbid factors.

H_{18}: There is no significant difference in MCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age, gender, race, marital status, smoking status, socioeconomic status, insurance status, geographical region and co-morbid factors.

CHAPTER TWO: MEDICAL EXPENDITURE PANEL SURVEY (MEPS) DATABASE

2.0 Overview of the Medical Expenditure Panel Survey (MEPS) database

This chapter gives detailed information about the dataset used in this study. Information concerning the files used from the MEPS dataset and the rationale for using this dataset for the study are also provided.

2.0.1 Use of the Medical Expenditure Panel Survey (MEPS)

The dataset used for this study is the Medical Expenditure Panel Survey (MEPS). This is a collection of a number of large surveys involving nationally representative samples of the non-institutionalized civilian US population. While there are several datasets which may be used in addressing the research questions of this study, these datasets may not be able to adequately address the research questions. Ideally, a dataset which is created to specifically estimate the effect of obesity on the cost and management of diabetes patients as well as evaluate how the health-related quality of life of obese diabetes patients differs from that of their non-obese peers is desired for reasons of precision and accuracy. However, monetary limitations, time constraints and practicality come into play when choosing a database. Hence, readily available datasets which might be used to address these questions were considered based on their advantages and disadvantages. For example, the Medicaid dataset possesses certain required information such as demographic characteristics, disease conditions, and the cost of medication; however, the population (patients of low socioeconomic status) covered as well as the absence of other important variables, such as HRQoL measures, are significant limitations of this dataset. The use of the Medicare, Veterans Health Administration, and private healthcare plans (such as

Marketscan, Humana and the Scott and White Healthcare plan) datasets are also limited mainly due to the challenges with the availability of data (accessibility and cost of purchasing data) and the specific populations covered, which may not be nationally representative of the US population.

The Medical Expenditure Panel Survey (MEPS) is a readily available and nationally representative database which provides information on healthcare utilization and costs on both the individual and household levels of the non-institutionalized US population. This dataset, which is a set of large survey data, contains pertinent information required to adequately address this study's questions. A brief overview of the MEPS dataset is provided below.

2.0.2 History of MEPS

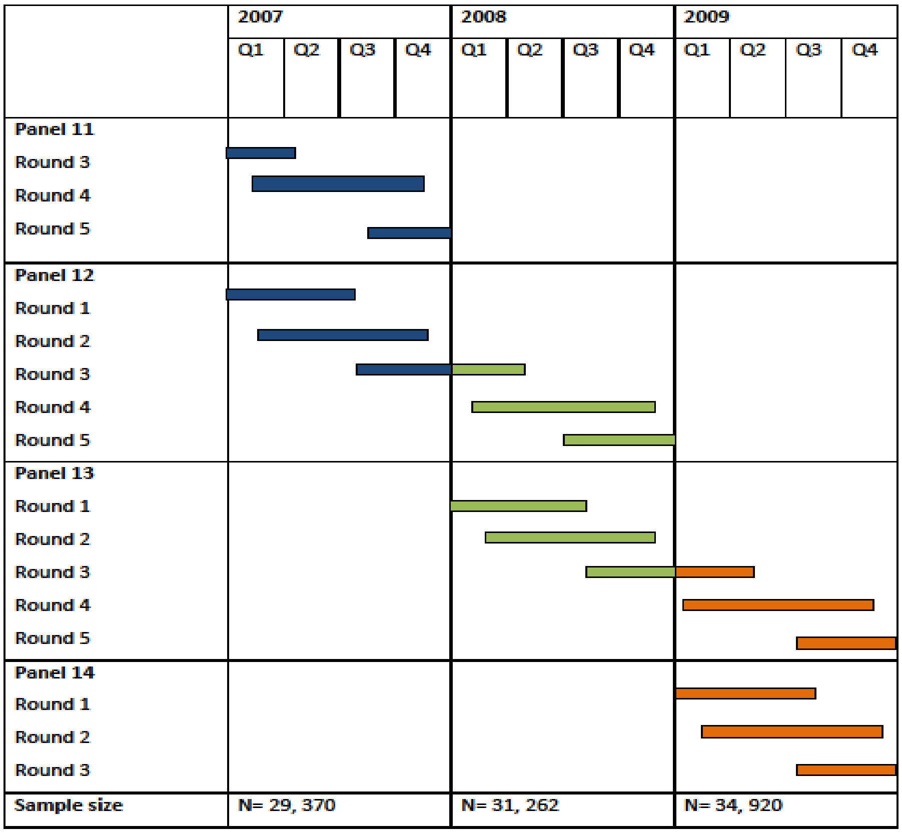
In the past, data on medical expenditures has been collected every ten years through surveys in the US since the 1970s. Starting in 1977, the National Medical Care Expenditure Survey (NMCES) was the first set of surveys established by the Agency for Healthcare Quality and Research (AHRQ) in conjunction with the National Center for Health Statistics (NCHS) and the US Department of Health and Human Services with the purpose of conducting surveys regarding healthcare costs and utilization in the US. The second set of surveys - the National Medical Expenditure Survey (NMES) – was initially conducted in 1987. However, in 1996, another set of surveys (i.e., MEPS) was designed to provide current information on a yearly basis, and its focus was broadened to better assess the dynamics of healthcare delivery, use, and costs, while incorporating the role of insurance. MEPS has since been responsible for the collection of 'real-world' data regarding healthcare utilization, costs, methods of payment and insurance coverage of nationally representative samples of the US non-institutionalized civilian population (from birth to up to 90 years) on a yearly basis.

2.0.3 Structure of MEPS

A yearly survey of about 15,000 households is carried out, and vital information is obtained from the respondents using the Computer Assisted Personal Interview (CAPI) technology, whereby 5 separate rounds of interviews are conducted with respondents over a span of 2.5 years, during which 2 years worth of information on healthcare utilization is collected. A panel is made up of a selected sample to be interviewed over 5 rounds. For example, a full sample for year 2009 is comprised of 2 overlapping panels; 2008 panel 13 (rounds 3, 4 and 5) and 2009 panel 14 (rounds 1, 2 and 3). The MEPS database is made up of three main survey components including: 1) the Household Component (HC); 2) the Medical Provider Component (MPC); and 3) the Insurance Component (IC). The Nursing Health Component (NHC) was only included in the 1996 set of surveys. These three components may be linked together in order to extract and merge necessary information required for the study.

The MEPS design is a longitudinal survey of the non-institutionalized US civilian population that provides information on healthcare utilization and costs on an individual and household level. Figure 2.1 illustrates the overlapping panel design.

Figure 2.1: MEPS panel design



N= number of people with a positive person weight on file.

2.0.4 MEPS design and sampling

Sampled subjects included in the MEPS sample are obtained from the household component. The MEPS HC sample used is a sub-sample of the NHIS sample from the previous year. For example, the 2006 MEPS sample is a sub-sample obtained from the patients included in the 2005 NHIS sample. The NHIS sample is derived based on a complex, stratified multi-stage probability design. This design involves three major sampling stages. Initially, samples for the NHIS (and sub-samples for MEPS) are picked from a primary sampling unit (PSU) which is typically a county that is grouped into homogeneous design strata. Second stage units (SSUs), which are clusters of housing units within counties, are then sampled from selected PSUs. The final stage units, which are households within the SSUs, are selected to make up the final sample, making households the sampling unit for MEPS. Different samples are selected from different households but within the same SSUs and PSUs yearly; however, every 10 years, the NHIS is redesigned and entirely new SSUs and PSUs are sampled.

In ensuring that minority populations are adequately represented in the sample, blacks, Hispanics, Asians (included between 2002-2006), functionally impaired adults, adults predicted to have high medical costs, and people of low socioeconomic status are usually oversampled. However, oversampling increases sampling weight variation and weights are used in order to correct for bias in the estimates; more information regarding the use of weights is provided in the appendix.

2.0.5 Household component (HC)

Of the 3 MEPS components, (the Household, Medical Provider and Insurance components), core interview information data are collected at every round of interviews under the HC. These include demographic factors (age, sex, race/ethnicity, marital status and education), smoking status, and socioeconomic status (SES). Information on charges and payments for each medical event in terms of total charges, co-payments, out-of-pocket and insurance payments, reimbursements, discounts, disallowed amounts, balances, and other sources of payments are also collected under the HC in order to provide national estimates. Other information collected under the HC are identified physical and mental health conditions, health status, healthcare use, and insurance, as well as respondents' employment status, type of employment (if employed), employer information and reasons for unemployment (where applicable). Under the 'Health Status' section of the HC, the physical and mental health status in terms of activities of daily living limitations (ADLs), physical and activity limitations, hearing, mental and visual impairments are all assessed for both children and adults. Childhood immunizations, special education, general health status, height and weight are additional information collected on children.

Data on health insurance status i.e., details on the type of insurance (private, public or none) in terms of members covered, name and type of plan, type and duration of coverage, and how the premiums are paid - are all collected under the HC component. Healthcare utilization and expenditure information for each person at the event level in terms of office and hospital-based care, home health care, dental, vision aids and prescription medications is also collected in this component. Also under the HC, other pieces of information are collected during specific rounds of interviews. Access to care for each member in a household is collected at rounds 2 and 4 of the interviews, information regarding the provider of usual source of care (and also reasons for lack of usual care where applicable), satisfaction with the providers as well as challenges encountered in obtaining the required healthcare service are collected. For children, additional information on general health status, special healthcare needs, potential behavioral problems, ease of access to healthcare, and preventive care are also collected in these 2 rounds.

Also in the second and fourth rounds of interviews, information regarding overall satisfaction with health plan and providers for both private and public types of insurance (Medicare managed care, Medicaid/SCHIP and TRICARE) in terms of ease of medical care access, obtaining approval for medical treatments and care and completion of paperwork is collected. Finally, in these 2 rounds, the Self-Administered Questionnaire (SAQ) i.e., a mail back survey is given to adults. This includes the Consumer Assessment of Health Plans (CAHPS), the SF-12, EQ5D, and attitude items. The adult SAQs are given to adults above 18 years for the assessment of self-reported information such as height, weight measures, and opinions concerning healthcare issues, as well as measures of quality of care.

A similar version, i.e., the Parent Administered Questionnaire (PAQ) was administered in 2000 to parents of children below 18 years, this was however included in the Child Preventive Health section of the CAPI instrument from 2001. In rounds 3 and 5, access to preventive care, frequency of physical and dental check-ups, flu shots and other preventive measures are also assessed; household income, assets (collected only in round 5) and priority conditions are also assessed. Finally, as supplemental information, the HC assesses diabetes-related and cancer-related care and their management in respondents identified to be diabetic or have cancer. Self-reported views of individual respondents regarding quality of care, physical and mental health are assessed using the MEPS-HC Supplemental Paper Questionnaires (SAQs); and once a year, the diabetes care SAQ is given to identified diabetic patients.

The HC is able to provide national estimates of healthcare utilization, costs, access to care, healthcare quality, insurance coverage and payment sources. It is also used for behavioral and policy-related research centered on factors that predict healthcare use, costs and insurance coverage. However, there are limitations with the use of the HC, including sample size limitations (in some cases), and the possibility of biased or inaccurate information provided as only one respondent reports on behalf of all the individuals in a household.

2.0.5.1 Types of MEPS-HC files

Point-in-time: this file provides preliminary information regarding patients at a particular point in time such that it provides a snapshot of the first part of the year, i.e., it provides insurance estimates for the beginning of the year to give analysts an idea of what the full year estimates may look like.

Full-year consolidated files: these contain information on costs and utilization for a year, the information contained in this file is compiled from many rounds; full-year consolidated data files, person round plan public use files, medical conditions and job files.

Event files: each medical event reported under the HC is provided in these files. Pooled linkage files provide person-level files that have variance stratum and PSU variables for 2 years which can be used with the MEPS full-year consolidated files. More information regarding individual event files is provided below.

The condition and prescription link files are also types of MEPS-HC files used for linking the appropriate files. The MEPS/ NHIS link files permit the merging of HC files with the NHIS files for longitudinal studies. The HC/IC link files provide information links for employers of HC job holders contacted through the insurance component (IC).

2.0.6 Public Use files (PUFs)

The ready availability of the MEPS data is one of the advantages of using this dataset. After data collection and necessary editing has been carried out, the collected data are made publically available at no cost on the MEPS website (http: www.meps.ahrq.gov/) as PUFs.

2.0.7 Levels of MEPS-HC public use files

In order to ensure respondents' privacy and confidentiality of the information provided, the data are de-identified by the use of special identification codes which are computer-generated; these identification codes, known as "DUPERSID", are not linked to any respondents' personal information and individual data can be accessed at different file levels with the DUPERSID. These file levels include person level, event-level, condition-level and job-level files.

2.0.7.1 Person-level files

For each person, demographic information (age, sex, race/ethnicity, marital status, education), smoking status and socioeconomic status (SES)) is collected. Information on payment for medical events in terms of total charges, co-payments, out-of-pocket and insurance payments, reimbursements, discounts, disallowed amounts, balances and other sources of payments are also provided in this file. Other information collected under this file includes physical and mental health conditions, health status as well as the respondents' employment status, type of employment (if employed), employer information and reasons for unemployment (where applicable). Data on health insurance status i.e., details on the type of insurance (private, public or none) in terms of members covered, name and type of plan, type and duration of coverage, and how the premiums are paid - are all collected under the HC component. Healthcare utilization and expenditure information for each person in terms of office and hospital-based care, home health care, dental, vision aids and prescription medications are also collected in this file.

2.0.7.2 Event files

In the acquisition of information regarding healthcare utilization and costs, respondents report all healthcare use for all individuals in the household within the specified period of time. Unique household-reported medical events in a year are reported. These include office-based medical provider visits, prescription medicines, outpatient visits, emergency room visits, hospital inpatient stays, dental visits and other medical expenses files.

1) Office-based medical provider visits: information provided regarding every healthcare provider visited include an identification code that is event-specific, date of the event, the specialty of the physician, whether or not treatment and/or x-ray was provided, condition and procedure codes, whether or not medication was prescribed, number of visits, and payment made.
2) Dental visits: information on dental visits is also provided; however, this information is not provided under the MPC and can only be accessed through the HC.
3) Outpatient department visits: information provided is similar to that provided in the office-based visits. Additional information provided includes the total expenditures, total amounts charged for the doctor, and the facility used. The actual amounts paid for the doctor's services and facility are also reported.
4) Emergency room visits: in addition to the information provided for outpatient visits, an identification number is provided for the patient if there is a hospital admission following the emergency room visit. Information is also provided if surgeries were carried out.

5) Hospital inpatient stays: other information added to the outpatient department visit information provided for all admitted patients includes an identification number if the patient was transferred from the emergency room, the date of admission, reason for admission, number of nights spent and the discharge date.
6) Prescribed medicines (including refills): an identification code (which can be linked to the corresponding event file) is provided for each medication prescribed; also included in this file are the date the medication was obtained, the NDC code, dosage, type of pharmacy used, and the amount paid.
7) Home health care: the identification number associated with each event is reported. Other information provided includes the date of the event, type of event, the type of health care provider, reason for visit, type of service received, time spent at each visit/length of time (days) spent at the facility and the amount paid.
8) Other medical expenses: finally, information concerning medical expenses such as glasses, orthopedic services, insulin, ambulance services and medical supplies, total number of other medical visits and amount paid are provided.

2.0.7.3 The medical conditions file

This file contains records for each condition or procedure an individual has. It is therefore possible that an individual is represented once, multiple times or not at all. For analytical purposes, this file can be linked to person and event files. Detailed information on respondents' medical conditions (identified by condition identification codes [CONDIDX]) is provided. These include the date the condition was first reported, whether or not a healthcare provider was seen, whether or not treatment and/or follow-up was provided, source of conditions in terms of medical events, disability, and condition/priority conditions with related ICD-9CM condition and procedure codes. Through the condition identification code (CONDIXDX), this information can be linked to the condition event link files by using corresponding event identification codes (EVENTIDX). In order to protect the confidentiality of these data, full ICD-9 codes are aggregated into 3-digit code categories; these condition codes are clearly linked to specific disease conditions and 259 mutually exclusive condition codes exist. Due to their high prevalence, burden to healthcare costs, or significance to healthcare policy, a number of disease conditions are a priority to MEPS. These include chronic, life-threatening conditions such as diabetes, hypertension, HIV/AIDS, cancer, dyslipidemia and cardiovascular conditions. Other priority conditions are arthritis, asthma, emphysema, depression and dementia. When chronic conditions such as diabetes are reported in the first round of interviews, it is assumed that the patient has the disease in the remaining rounds of the interview.

In 2000, diabetes was included as one of the priority disease conditions and specific disease-related questions were included in the survey. To better understand how the disease affects patients' health status and quality of healthcare received, a self-administered questionnaire (SAQ) was also introduced in 2000. The SF-12, EQ-5D, CAHPS are instruments used to build the SAQ. [227] The SF-12 is a quality of life instrument with 12 items which evaluates 8 main domains: physical functioning, mental functioning, role limitations as a result of physical health problems, role limitations as a result of emotional health problems, social functioning, body pain and general health and vitality.[62] These domains are collapsed into two components, that is, the physical component summary scale (PCS-12) and the mental component summary scale (MCS-12). MEPS administers an adult Self-Administered Questionnaire (SAQ) to all respondents who are at least 18 years of age in the rounds 4 and 2 of the panels 4 and 5 respectively and the completed forms are mailed back to MEPS. Since the SF-12 is administered to only adults, respondents younger than 18 years old were excluded from the present study.

2.0.8 Healthcare expenditures

Generally, healthcare expenditures are accessed from two main survey components: the HC and the Medical Provider Component (MPC). Expenditure information obtained from the MPC is used if present; however, where absent, information provided in the HC is used. Under the HC, this information is collected at the event level, representing the payments made to healthcare providers. The sources of payment are also provided, specifically how much of the expenditures are out-of-pocket for the patient, or paid by private or public insurance programs. The sum of all payments, irrespective of source, equals the total expenditures.

During interviews with the healthcare providers that have been identified by the respondents in the HC, detailed information is gathered concerning the total charges, amount paid as well as source of payment. The cost information provided under this component is used to calculate estimates for missing cost values in the HC. Thereafter, using data provided by respondents, total costs and missing expenditure values are imputed using a weighted sequential hot-deck procedure which also accounts for respondents' weighted distributions in the imputation process. Costs included in the total healthcare costs include out-of-pocket costs, payments made by private or public insurance and Medicaid/Medicare. Costs not factored into the total costs include bad debts, bonuses, payment reductions or adjustments made by third parties and the cost for free services, for example charitable care not provided by public hospitals. Other services provided that are not paid for include follow-up visits with no associated charges, and costs of services with a flat fee rate from a previous year. When healthcare costs fall under any of these costs mentioned, no healthcare costs are recorded. Imputations are made where an event does not have any expenditure data in the MPC or HC.

2.0.9 Sources of healthcare expenditure data

The costs accrued from several sources make up the total healthcare costs. These sources include: out-of-pocket costs, private insurance, Medicare/Medicaid, TRICARE, Veterans Health Administration, Indian Health Service, Military treatment facilities, and other federal, state and local government sources. Other sources include workers' compensation, unclassified or miscellaneous sources, and other insurance payment sources for respondents who were reported not having private health insurance coverage.

2.0.10 Files required for the present study

Only the household component was used for the purpose of this study since it contains the information needed to address the study objectives. The PUFs with the information required for this study include: 1) full-year consolidated file; 2) medical conditions file; 3) medical events file; and 4) two link files, that is, the condition and prescription link files.

2.0.11 Handling missing data

All data collected are edited to ensure that there are no missing values. All missing values from non-response and other missing data are handled by using imputation techniques described in Table 2.1 below.

Table 2.1: MEPS imputation techniques for certain variables[228]

Variable	Imputation method
Age	1) The mean age difference between the MEPS participants with certain family relationships. 2) The mean age value for the MEPS participants.
Gender	1) NHIS data. 2) First name. 3) Random assignment.
Race/ ethnicity	1) NHIS data. 2) Relationship to other members of the dwelling unit, giving precedence to blood relatives in the immediate family.
Hourly wage	Weighted sequential hot-deck procedure.
Expenditures	Weighted sequential hot-deck procedure.

2.0.12 Variance estimation

Unlike simple random sampling assumptions, the use of a complex sampling design in MEPS requires that the variance and standard errors are specially derived in order to avoid biased estimates. SAS 9.2 and STATA were used for this study, as these analytical software packages include programs which take into account the complex sampling design of MEPS.

2.0.13 Stratum and PSU variables

Since MEPS panels are normally selected from the same sample of PSUs, there is the possibility of correlation at both the person-level and among persons within the same PSU when creating a pooled file for analyses. To account for this correlation, MEPS recommends specifying both stratum and PSU variables while making variance estimations from pooled data. Since 2002, MEPS has included standardized stratum and PSU variables in annual data files.

Also in ensuring accurate estimates in analyses, subsetting of files is discouraged since this may leave out important information regarding variance and standard error estimations. MEPS recommends that when data is pooled across years into one analytical file, the person weights used for variance estimation be averaged over the number of years of pooled data, this is to ensure that the weights are adjusted to reflect the average yearly number of patients in the pooled period. Since this study spans over 5 years, that is, between 2006 and 2010, the pooled person weights was divided by 5.

CHAPTER THREE: METHODS

3.0 OVERVIEW OF STUDY METHODOLOGY

This chapter provides information concerning the study design and methods. Also included in this chapter are the study variables (dependent and independent variables), objectives and hypotheses, and the statistical analytical methods used in testing the hypotheses.

3.1 STUDY DESIGN

This was a retrospective cross-sectional study of the relationship between BMI status and healthcare utilization and expenditures (*diabetes-related* direct medical, and all-cause direct medical, indirect, and total healthcare costs) and the health-related quality-of-life (HRQoL) of adult patients above 18 years presenting with type 2 diabetes using a secondary database – the Household Component (HC) files of the Medical Expenditure Panel Survey (MEPS). Healthcare use, costs, and HRQoL scores of type 2 diabetes subjects were extracted and cohorts were formed based on patients' BMI.

3.2 DATA COLLECTION AND STUDY TIMEFRAME

Data were extracted from the MEPS database from January 1, 2006 to December 31, 2010 for subjects who met the inclusion/exclusion criteria provided below. Subjects were identified by their unique identification number (DUPERSID) and information regarding their demographic characteristics, anthropometric measures (BMI value), medical conditions, healthcare utilization, expenditures, and HRQoL scores were extracted from the appropriate files. These files were merged using link files. The information required to address the research questions were extracted from the following public use files (PUFs):

1. The MEPS 2006 - 2010 full-year consolidated data files

2. The MEPS 2006 - 2010 medical conditions data files

3. The MEPS 2006 - 2010 office-based provider visits data files

4. The MEPS 2006 - 2010 hospital inpatient stays data files

5. The MEPS 2006 - 2010 outpatient visits data files

6. The MEPS 2006 - 2010 emergency room visits data files

7. The MEPS 2006 - 2010 home health data files

8. The MEPS 2006 - 2010 prescribed medicines data files

9. The MEPS 2006-2010 other medical expenses files

10. Appendices to MEPS 2006 - 2010 event link files (condition and prescribed medicines event link files)

Table 3.1 shows the files extracted and linked for the purpose of this study.

Table 3.1: Household Component (HC) files required for study

Year	**Full-year consolidated file**	**Medical conditions file**	**Events file**
2006	HC-105	HC-104	HC-102A, HC-102C HC-102D, HC-102E, HC-102F, HC-102G, HC-102H
2007	HC-113	HC-112	HC-110A, HC-110C HC-110D, HC-110E, HC-110F, HC-110G, HC-110H
2008	HC-121	HC-120	HC-118A, HC-118C, HC-118D, HC-118E, HC118F, HC-118G, HC-118H
2009	HC-129	HC-128	HC-126A, HC-126C, HC-126D, HC-126E, HC-126F, HC-126G, HC-126H
2010	HC-138	HC-137	HC-135A, HC-135C, HC-135D, HC-135E, HC-135F, HC-135G, HC-135H

With the use of the condition-event link files, the full-year consolidated files were merged with their respective event-level files.

The following data from the *condition-event link files* variables were utilized:

1) Patient identifier: DUPERSID.

2) Condition identifier: identifies each condition for a person, corresponding to a unique record in the MEPS HC 2006-2010 medical condition files.

3) Event identifier: identifies each event for a person, corresponding to a unique record on one of the MEPS 2006-2010 event-level files.

4) Condition-event identifier: uniquely identifies each record in the condition-event link file. This is a combination of the condition identifier and the event identifier.

The condition-event link files were used to link all the *event-level data files* (that is, office-based provider visits files, hospital inpatient stays files, outpatient visits files, emergency room visits files, home health files, prescribed medicines files and other medical expense files). The *event-level files* contained the following variables:

1) Patient identifier: DUPERSID

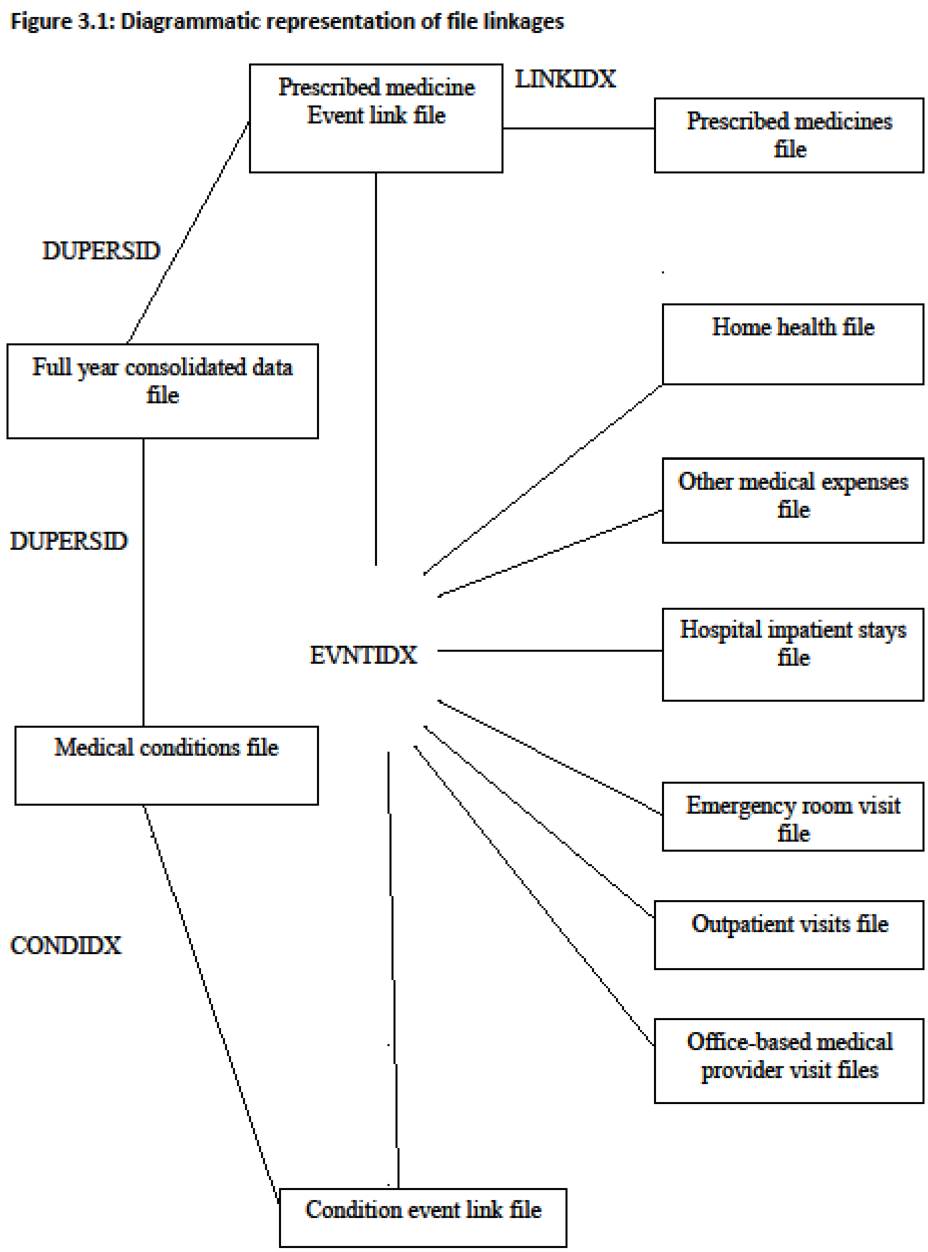
2) Event identifier: identifies each event for a person that corresponds to a unique record on one of the MEPS 2006-2010 event-level files.

3) Prescription medicine identifier: identifies the records in the prescription medicine file and can be linked to the event-level file.

4) Prescription-event identifier: uniquely identifies each record in the prescription-event link file.

Figure 3.1 provides a diagrammatic representation of how the required files were linked to arrive at the final file needed for the study.

Figure 3.1: Diagrammatic representation of file linkages



3.3 Institutional Review Board (IRB) approval

This study involved the analysis of a secondary database. Institutional Review Board (IRB) exemption was requested from and granted by the University of Texas IRB committee and the study was considered to be exempt from human studies review (IRB Study Number: 2012-07-0007).

3.4 Data cleaning and imputation

MEPS uses several techniques to ensure the completeness of data; hence, there were no missing variables; however, there was a need for imputation of wage variables and number of missed work days for caregivers and subjects below the age of 65 years who had zero values for these variables (details of this is provided below).

3.5 Inclusion/ exclusion criteria

Provided in this section are conditions that were met by subjects in the population making them qualified to be included in the study.

1) Subjects with diabetes (identified using the International Classification of Diseases – 9 (ICD-9 CM) codes for diabetes, that is, 250 [for the purpose of maintaining confidentiality, MEPS collapses ICD-9 codes into 3 digits]) and MEPS Clinical Classification Codes -049 or 050.
2) Type 2 diabetes patients who were identified as subjects with diabetes who responded "yes" to the Diabetes Care Survey question: "Is your diabetes being treated by medications taken by mouth?" Subjects were excluded if they responded "no" to this question.
3) Subjects between 18 and 85 years of age.
4) Subjects with BMI values used for BMI classification into normal weight, overweight, obese categories or morbidly obese categories.

Patients below 18 years of age were excluded from the present study because MEPS considers the diabetes diagnosis question not applicable to this group of respondents.

3.6 Target population

Based on the study objectives, the population of interest was the type 2 diabetes non-institutionalized civilian US population. This study was focused on two main age categories: 1) the adult population between 18 and 64 years and 2) the elderly adult population above 64 years. Type 2 diabetic patients were classified into weight categories based on their BMI values.

3.7 Study variables

3.7.1 Dependent variables

1) *Diabetes-related* direct medical costs: in evaluating diabetes-related medical costs, information from the event files regarding inpatient hospitalizations, outpatient visits, emergency room visits, office-based medical provider visits, prescription medicines and home healthcare visits that pertained to diabetes were extracted and total direct expenditures were summed for each patient.
2) Direct medical costs: all-cause medical costs of type 2 diabetic patients were extracted from the full-year consolidated files.
3) Indirect costs: These were evaluated through costs associated with productivity loss. Information regarding the number of missed work days due to illness was extracted from the full-year consolidated files to estimate these costs. A daily wage rate was calculated such that total annual wage rate was divided by 240 days under the assumption that in a year, working adults work for 240 days after taking into account the number of weekend days, number of sick leave days and number of vacation days in a year.[229] Productivity loss was then derived by finding the product between daily wage rate and the number of

missed work days. For all patients, the lost productivity costs for the caregivers were derived by finding a product of the daily wage rate and the number of days that work was missed as a result of providing care for the patient.

4) The human capital approach was applied for patients above 65 years not reported to earn wages. A significant proportion of the study sample (49.9%) was reported not earning wages, hence, using data from the Bureau of Labor Statistics, housekeeping income values were imputed for patients below 65 years of age who were reported not earning wages (with zero values) and for caregivers who also reported not earning wages (with zero values). Since missed work days for this group of people was by default zero, missed work days for these persons (patients below 65 years and caregivers) were derived by finding an average of missed work days of patients below 65 years and caregivers who earned wages respectively. The number of additional bed days (an indication of restricted activity) was also multiplied by wages. Total lost productivity cost was the sum of these 3 values, that is, patients' lost productivity costs, cost as a result of restricted activity and caregivers' costs.

5) Healthcare utilization: This was evaluated by assessing the frequency of use of each of these healthcare services: ambulatory care visits (sum of outpatient and office-based medical provider visits), emergency room visits and prescription medicines (including refills).

6) Health-Related Quality of Life (HRQoL): The SF-12 physical component score (PCS) and the mental component score (MCS) of the MEPS-HC were assessed to determine the relationship between BMI status and the HRQoL of diabetic patients.

The SF-12:

In evaluating the relationship between BMI status and the quality of life of diabetic patients, the scores of SF-12 version 2 instrument used in assessing quality of life in the population were evaluated. The SF-12 is a quality of life instrument with 12 items which evaluates 8 main domains: physical functioning, mental functioning, role limitations as a result of physical health problems, role limitations as a result of emotional health problems, social functioning, body pain and general health and vitality.[62] These domains are collapsed into two components, that is, the physical component summary scale (PCS-12) and the mental component summary scale (MCS-12). MEPS administers an adult Self-Administered Questionnaire (SAQ) to all respondents who are at least 18 years of age in rounds 4 and 2 of panels 4 and 5 respectively and the completed forms are mailed back to MEPS. The following 12 questions make up the SF-12 in the SAQ, these questions have a 4-week recall period.

1) General rating of health (poor to excellent).
2) Limitations to moderate physical activities such as moving a table, pushing a vacuum cleaner, bowling as a result of health problems (limited a lot to not limited at all).
3) Limitations to climbing several flights of stairs due to health problems (limited a lot to not limited at all).
4) Accomplished less work or other regular daily activities than preferred due to physical health (yes or no)
5) Limitations encountered in the kind of work or other activities. (yes or no)
6) Accomplished less work or other regular daily activities than preferred due to emotional problems.(yes/no)

7) Work or other activities were less carefully done than usual due to emotional problems (yes or no).
8) Pain interfered with normal work (including work outside and inside the home) (not at all to extremely)
9) How much of the time have you felt calm and peaceful? (all of the time to none of the time)
10) How much of the time did you have a lot of energy? (all of the time to none of the time)
11) How much of the time have you felt downhearted and depressed? (all of the time to none of the time)
12) How much of the time has your physical health or emotional problems interfered with your social activities (including visiting family and friends)? (all of the time to none of the time)

Two separate scores are obtained from the SF-12 - the physical component summary score (PCS-12) and the mental component summary score (MCS-12). The PCS-12 scores are weighted more heavily on questions 2-5 and 8 while the MCS-12 scores are weighted more heavily on questions 6, 7, 9 and 11. In the general population, SF-12 scores have a mean of 50 and a standard deviation of 10, with higher scores correlating with better quality of life.[62] The scores obtained from subjects based on this instrument were analyzed to evaluate how BMI status influences the subjects' self-reported health-related quality of life.

3.7.2 Independent variables

All the independent variables (except the variable "co-morbidity score index" which was extracted from the medical conditions file) were extracted from the full-year consolidated files.

1) BMI status: This is the main independent variable.

Table 3.2 shows how identified diabetic patients were classified into 4 main BMI categories. The underweight BMI category was initially included in the study; however, this category had a very small sample size (n=25), and hence was dropped from the study.

Table 3.2: BMI classification

BMI categories (kg/m^2)	**Weight status**
18.5 – 24.9	Normal weight
25.0 – 29.9	Overweight
30.0 – 39.9	Obese
>40.0	Morbidly obese

Covariates include the following variables:

1) Age: this is a continuous variable and patients were further classified into the following groups: 18-64 and ≥65 years.
2) Gender: this variable was dichotomized as male or female.
3) Race: this categorical variable identified subjects as white, black and others (American Indian/Alaska native, Pacific Islander/Native Hawaiian, and Asian) racial categories. MEPS considers the term 'Hispanic' an ethnicity not a race.[228]
4) Marital status: this categorical variable groups subjects into married or unmarried categories.
5) Smoking status: this categorical variable is dichotomized as yes or no.

6) Insurance coverage status: patients' insurance coverage status was classified into private insurance, public insurance only and uninsured.
7) Census region: this includes the following four regions: Northeast, Midwest, South and West. Northeast (Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, and Pennsylvania); Midwest (Ohio, Indiana, Illinois, Michigan, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, and Kansas); South (Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi, Arkansas, Louisiana, Oklahoma, and Texas) and West (Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Washington, Oregon, California, Alaska, and Hawaii) categories.
8) Socioeconomic status: this categorical variable grouped patients based on the poverty line. Poor: Less than 1.00 times poverty line; Near poor: 1.01 to 1.24 times poverty line; Low income: 1.25 to 1.99 times poverty line; Middle income: 2.00 to 3.99 times poverty line; High income: 4.0 or more times poverty line.
9) Co-morbidity score index: this information was derived from details extracted from the medical conditions files. The Charlson's Comorbidity Index (CCI)'s D'Hoore's adaptation was used for this study and the codes for this adaptation are included in Appendix B. Below is a brief description of the CCI and its adaptations.

3.8 The Charlson Comorbidity Index Score

The Charlson Comorbidity Index (CCI) is a comorbidity score which is assigned to a patient based on a score generated from the patient's diagnoses. Depending on the ICD-9 or 10 codes provided, the CCI has 4 main adaptations: the Deyo, Ghali, Dartmouth-Manitoba and D'Hoores adaptations.[230] These are used particularly when diagnoses and prescription claims data are available. As an adaptation of the CCI, the D'Hoores adaptation was derived by matching the diagnosis information from the CCI with similar ICD-9 diagnoses and procedures. To derive the CCI score, a set of predefined comorbidities (that is, major disease conditions which are present as secondary diagnoses) for which weights (1 to 6) have been assigned are summed for each patient from the required claims data information. These assigned weights were derived from claims data analyzed through a Cox proportional hazards regression model which provides estimates of the relative risk of each comorbid condition.[230-231] Although the commonly used CCI adaptations are the Deyo and Dartmouth adaptations, for the purpose of this study, the D'Hoores CCI adaptation will be used, being the only adaptation that uses only the first 3 digits of the ICD-9 to compute the comorbidity index score.[231] This is of particular importance to this study because MEPS, for the purpose of protecting data confidentiality, uses only 3-digit ICD-9 codes.

Table 3.3 provides the operational definitions of variables included in the present study.

Table 3.3: Operational definitions of variables

Variable	Operational definition
Dependent variables	
Diabetes-related direct healthcare costs	All diabetes-related direct medical costs associated with the following events: inpatient hospitalizations, outpatient visits, emergency room visits, office-based medical provider visits, prescription medicines, home healthcare visits and other medical expenses
Direct healthcare costs	All-cause direct medical costs of type 2 diabetic patients.
Indirect healthcare costs	All costs associated with productivity loss (i.e., sum of missed work days × daily wage rate, additional bed days × daily wage rate and caregivers cost)
Total healthcare costs	Sum of all direct and indirect healthcare costs
Healthcare utilization	Number of events associated with the following healthcare use: ambulatory care (sum of outpatient visits and office-based medical provider visits), emergency room visits and prescription medicines (including refills).
Health-Related Quality of life (HRQoL)	Physical Component Summary (PCS-12) scores Mental Component Summary (MCS-12) scores
Independent variables	
Body Mass Index (BMI) status (ordinal)	0=Normal weight: BMI 18.5 – 24.9 1=Overweight: BMI 25.0 – 29.9 2=Obese: BMI 30.0 – 40.0 3=Morbidly obese: BMI >40.0
Covariates	
Age	1) Age: Continuous 2) Age category 0=18-64 years 1=65 years and above
Gender	0=Male 1=Female
Race	0=White 1=Black 2=Others (American Indian/Alaska native & Pacific islander/Native Hawaiian) [MEPS considers term ‘Hispanic’ an ethnicity not a race].[228]
Marital status	0=Married 1=Not married
Smoking status	0=No 1=Yes
Insurance status	0=Private insurance 1=Public insurance only 2=Not insured

Table 3.3 (cont'd): Operational definitions of variables

Variable	Operational definition
Socio-economic status (ordinal)	This ordinal variable grouped patients based on the poverty line. 0=Poor: Less than 1.00 times poverty line 1=Near poor: 1.01 to 1.24 times poverty line 2=Low income: 1.25 to 1.99 times poverty line 3=Middle income: 2.00 to 3.99 times poverty line 4=High income: 4.0 or more times poverty line.
Geographical region	0=Northeast 1=Midwest 2=South 3=West
Charlson comorbidity index	A function of the number of comorbid diseases, using the CCI (D'Hoore's adaptation)

3.9 DATA ANALYSIS

All statistical analyses were carried out using two-tailed tests with alpha levels set at 0.05 a priori. The Statistical Analyst Software SAS 9.2 version and STATA 12 were used for all data management and analyses.

3.9.1 Objectives and hypotheses

Objective 1: To describe the study sample and evaluate the differences in socio-demographic characteristics (age, age category, gender, race, marital status, insurance status, socioeconomic status and geographical region), smoking status and comorbidity index of the diabetic MEPS population by BMI status.

This objective involved descriptive statistics and utilized the "surveymeans" (for continuous variables: age and comorbidity index) and "surveyfreq" (for categorical variables: age category, gender, race, marital status, insurance status, socioeconomic status [ordinal] and geographical region,) SAS procedures in addressing this objective. Chi-square and Regression analyses were used to evaluate the relationship/difference in the said variables by BMI.

Objective 2: To estimate the prevalence of overweight and obesity among the diabetic MEPS population.

Prevalence=number of obese diabetic patients/total number of diabetic patients in the study, for each level of overweight/obesity.

Objective 3: To estimate differences in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

A generalized linear model with a gamma distribution and a log link function was used to determine differences in diabetes-related direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. Diabetes-related events were identified by linking the medical conditions files of diabetic patients with event files based on the 3-digit ICD-9 code for diabetes. Total costs for the following diabetes-related event categories were determined: inpatient hospitalizations, outpatient visits, emergency room visits, office-based medical provider visits, prescription medicines, home healthcare visits and other medical expenses.

Hypothesis:

H_{01}: There is no significant difference in diabetes-related healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 4: To estimate differences in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. A GLM using a gamma distribution with a log link function procedure was used to determine differences in the total direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypothesis:

H_{02}: There is no significant difference in direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 5: To estimate differences in indirect (lost productivity) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

In deriving the indirect costs, the cost of productivity loss was determined by multiplying the number of missed work days by the daily wage by the person weight based on BMI status. In addition, costs as a result of restricted activity and caregivers' productivity costs were estimated in a similar manner and the 3 costs summed up to give the indirect costs per patient. A GLM with a gamma distribution and a log link function was used to determine differences in indirect costs. Table 3.4 provides detailed information regarding total cost calculations.

Hypothesis:

H_{03}: There is no significant difference in indirect (lost productivity) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 6: To estimate differences in total (direct medical and indirect) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. A GLM with a gamma distribution and a log link function was used to determine differences in total costs (sum of the total direct and total indirect costs).

Hypothesis:

H_{04}: There is no significant difference in total (direct medical and indirect) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Table 3.4: Total Cost Calculations

Costs	
Diabetes-related direct costs	**Formula**
Outpatient visits	Outpatient visits cost per person × weighted number of people having outpatient visits
Emergency room visits	Emergency room visit cost per person × weighted number of people having emergency room visits
Office-based medical provider visits	Office-based medical provider visits cost per person × weighted number of people having office-based medical provider visits
Inpatient hospitalizations	Inpatient hospitalizations cost per person × weighted number of people having inpatient hospitalizations
Home health care	Home healthcare visits cost per person × weighted number of people having home healthcare visits
Prescription medicines (including refills)	Prescription medicines cost per person × weighted number of people having prescription medicines
Other medical services	Other medical services cost per person × weighted number of people having other medical services
Direct costs	
Total medical costs associated with patient	Total medical cost per person × weighted frequency of people by BMI status
Indirect costs	
Productivity loss (missed work days)	Lost productivity cost due to missed work days per person × weighted frequency of people having missed work days
Restricted activity	Lost productivity cost due to additional bed days per person × weighted frequency of people having additional bed days

Table 3.4 (cont'd): Total Cost Calculations

Indirect costs	**Formula**
Caregivers	Lost productivity cost due to missed work days of caregiver per patient × the weighted frequency of caregivers having missed work days
Total costs	Total direct costs + total indirect costs

*****All cost data were adjusted to 2010 dollars (the current MEPS data) using the medical Consumer Price Index (CPI) for direct medical costs and average CPI for indirect costs (wages).

Objective 7:

To determine how healthcare utilization (ambulatory care [outpatient department visits and office-based medical provider visits], emergency room visits and prescribed medicines) rates of diabetic patients differ between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Negative binomial regression analysis was employed to determine mean healthcare utilization by event, i.e., ambulatory care and number of prescribed medicines by BMI status. Due to the presence of excessive zeroes, the zero-inflated negative binomial regression analysis was employed to determine the relationship between BMI status and the number of emergency room visits.

Hypotheses:

H_{05}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

H_{06}: There is no significant difference in the number of emergency room visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

H_{07}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 8:

To compare the HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. The "surveyreg" SAS procedure was used to compare mean HRQoL scores (PCS-12 and MCS-12 scores) between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Hypotheses:

H_{08}: There is no significant difference in PCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

H_{09}: There is no significant difference in MCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Objective 9: To estimate differences in healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

The differences in healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients were assessed by using a generalized linear model with a gamma distribution and a log link function controlling for covariates.

Hypotheses:

H_{10}: There is no significant difference in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

H_{11}: There is no significant difference in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 10: To estimate differences in indirect (productivity loss) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

A GLM with a gamma distribution and a log link function was used to address this objective. Lost productivity costs were determined using the wages provided for both the patient and caregivers of the patient. The daily wage rate was obtained by dividing annual wages by 240 days (this is based on the assumption that in a year, a working adult will work for 240 days: Number of days in a year (365) – number of weekend days (104) – number of vacation days (14) – number of days spent on sick leave (7).[229]

Hypothesis:

H_{12}: There is no significant difference in indirect costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 11: To estimate differences in total healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

The same analyses used in analyzing the differences in healthcare between overweight, obese or morbidly obese diabetes patients compared to normal weight patients(Objective 6) was used to address this objective.

Hypothesis:

H_{13}: There is no significant difference in total healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 12: To estimate the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

The same analyses used in analyzing the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients(Objective 7) was used to address this objective.

Hypotheses:

H_{14}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental

HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

H_{15}: There is no significant difference in the number of emergency room visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).H_{16}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age category, gender, race, marital status, smoking status, socioeconomic status, insurance status, census region, CCI score, physical and mental HRQoL scores and restricted activity (number of additional bed days a patient stays in bed excluding the missed work days spent in bed).

Objective 13: To estimate the differences in HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

Multiple regression was used to address this objective using the 2 quality of life components of the SF-12, that is, PCS-12 and MCS-12 while controlling for covariates. For both the PCS-12 and MCS-12, ordinary least squares (OLS) regression was used.

Hypotheses:

H_{17}: There is no significant difference in PCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age, gender, race, marital status, smoking status, socioeconomic status, insurance status, geographical region and co-morbid factors.

H_{18}: There is no significant difference in MCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for the following covariates: age, gender, race, marital status, smoking status, socioeconomic status, insurance status, geographical region and co-morbid factors.

Table 3.5 gives a summary of the study's objectives and hypotheses as well as the variables and the proposed statistical tests used in addressing the objectives.

Table 3.5: Summary of objectives, hypotheses and statistical analyses

Objectives/hypotheses	**Dependent variable**	**Independent variable**	**Statistical analysis**
Objective 1: To describe the study sample and evaluate the socio-demographic characteristics of the diabetic patient population by BMI status	Age (continuous variable)	BMI status (ordinal variable)	Descriptive statistics (mean, standard error) and regression
	Gender (nominal variable)		Descriptive statistics (frequency) and Chi-square
	Race (nominal variable)		Descriptive statistics (frequency) and Chi-square
	Marital status (nominal variable)		Descriptive statistics (frequency) and Chi-square
	Smoking status (nominal variable)		Descriptive statistics (frequency) and Chi-square
	Socio-economic status (ordinal		Descriptive statistics (frequency) and

Table 3.5 (cont'd): Summary of objectives, hypotheses and statistical analyses

Objectives/hypotheses	**Dependent variable**	**Independent variable**	**Statistical analysis**
	variable)		Chi-square
	Insurance status (nominal variable)		Descriptive statistics (frequency) and Chi-square
	Geographic region (nominal variable)		Descriptive statistics (frequency) and Chi-square
	Co-morbid index (continuous)		Descriptive statistics (mean, standard error) and regression
Objective 2: To estimate the prevalence of overweight/obesity among the diabetic population		BMI status (ordinal variable)	Descriptive statistics: Percentage of overweight/obese patients among the diabetic patients
Objective 3: To estimate differences in *diabetes-related* medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients			
H_{01}:There is no significant difference in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.	Total *diabetes-related* direct medical costs	BMI status (ordinal variable)	Descriptive statistics: Mean, Standard Error, GLM (with gamma distribution and log link function)
Objective 4: To estimate differences in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients			
H_{02}: There is no significant difference in direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.	Total direct medical costs	BMI status (ordinal variable)	Descriptive statistics: Mean, Standard Error, GLM (with gamma distribution and log link function)
Objective 5: To estimate differences in indirect costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients			

Table 3.5 (cont'd): Summary of objectives, hypotheses and statistical analyses

Objectives/hypotheses	**Dependent variable**	**Independent variable**	**Statistical analysis**
H_{03}: There is no significant difference in indirect (lost productivity) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.	Total indirect costs	BMI status (ordinal variable)	Descriptive statistics: Mean, Standard Error, GLM (with gamma distribution and log link function)
Objective 6: To estimate differences in total costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients			
H_{04}: There is no significant difference in total (direct medical and indirect) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.	Total (direct and indirect) costs	BMI status (ordinal variable)	Descriptive statistics: Mean, Standard Error, GLM (with gamma distribution and log link function)
Objective 7: To estimate differences in healthcare utilization rates between overweight, obese or morbidly obese diabetes patients compared to normal weight patients			
H_{05}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.	Total number of ambulatory care visits	BMI status (ordinal variable)	Descriptive statistics: Mean, Negative binomial regression
H_{06}: There is no significant difference in the number of emergency room visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.	Total number of emergency room visits		Descriptive statistics: Mean, Zero-inflated negative binomial regression.
H_{07}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.	Total number of prescribed medicines		Descriptive statistics: Mean, Negative binomial regression
Objective 8: To compare the HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients			
H_{08}: There is no significant difference in the physical component between overweight, obese or morbidly obese diabetes patients compared to normal	HRQoL (physical and mental)	BMI status (ordinal variable)	Descriptive statistics: Mean, Standard Error, Regression

Table 3.5 (cont'd): Summary of objectives, hypotheses and statistical analyses

Objectives/hypotheses	**Dependent variable**	**Independent variable**	**Statistical analysis**
weight patients H_{09}: There is no significant difference in the mental component between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.			
Objective 9: To estimate the differences in medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates			
H_{10}: There is no significant difference in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	Total *diabetes-related* direct medical costs	BMI status (ordinal variable)	Generalized linear models with gamma distribution and log link function
H_{11}: There is no significant difference in direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	Total direct medical costs	BMI status (ordinal variable)	Generalized linear models with gamma distribution and log link function
Objective 10: To estimate the differences in indirect (productivity loss) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates			
H_{12}: There is no significant difference in indirect (productivity loss) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	Indirect costs	BMI status (ordinal variable)	Generalized linear models with gamma distribution and log link function)
Objective 11: To estimate the differences in total costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates			
H_{13}: There is no significant difference in total costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	Total healthcare costs (direct and indirect) costs	BMI status (ordinal variable)	Generalized linear models with gamma distribution and log link function
Objective 12: To estimate the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates			
H_{14}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	Number of ambulatory care visits	BMI status (ordinal variable)	Negative binomial regression
H_{15}: There is no significant difference in number of emergency room visits between	Number of emergency	BMI status (ordinal	Zero-inflated negative

Table 3.5 (cont'd): Summary of objectives, hypotheses and statistical analyses

Objectives/hypotheses	**Dependent variable**	**Independent variable**	**Statistical analysis**
overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	room visits	variable)	binomial regression
H_{16}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	Number of prescribed medicines	BMI status (ordinal variable)	Negative binomial regression
Objective 13: To estimate the differences in HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates			
H_{17}: There is no significant difference in PCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	PCS-12 scores	BMI status (ordinal variable)	Ordinary Least Squares regression (Multivariate regression analysis)
H_{18}: There is no significant difference in MCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	MCS-12 scores		Ordinary Least Squares regression (Multivariate regression analysis)

3.10 DESCRIPTION OF STATISTICAL ANALYSES RELEVANT TO THE PRESENT STUDY

3.10.1 Generalized Linear Regression (GLM)

The GLM regression centers on the relationship between the dependent variable and a set of linear combinations of independent (predictor) variables. The GLM compared to the ordinary linear regression is more flexible such that the dependent variable may be of either a normal or non-normal distribution. Non-normal distributions include binomial, Poisson, geometric, negative binomial, exponential, gamma and inverse normal distributions. This model can be used to predict responses for both dependent variables with discrete distributions and dependent variables with non-linear relationships with the predictors. Basically, under the same framework, the GLM allows for both linear and non-linear models. Three main components make up the GLM: 1) the dependent variable distribution known as the exponential family; 2) the independent variables which maybe linear in their relationship with the dependent variable (usually depicted linearly mathematically but these may be non-linear transformations of the variables); and 3) a link function. The GLM permits the fit of regression models for univariate response data that have broadly general distributions known as the exponential family such as normal, binomial, Poisson, geometric, negative binomial, exponential, gamma and inverse normal distributions. The response variable may be derived from specific exponential family distributions, such as the distributions mentioned above. Usually, with count data where there is heterogeneity in the variance in relation to the mean, there is a need to transform the data to ensure normality of data and the variance homogeneity. However with the GLM, the response variable is not required to be normal, nor is the variance required to be homogeneous.

Information regarding the independent variables is incorporated into the model by the linear predictor while the link function estimates the relationship between the linear predictor and the natural mean of the response distribution function.

Provided below in Table 3.6 are some common distributions and link functions.

Table 3.6: Distribution and link functions

Predictor variable	**Distribution**	**Characteristics and examples**	**Link function**
Continuous or categorical	Normal	Symmetric with specified densities (e.g., IQ)	Identity
	Binomial	Binary response variable (e.g., had healthcare expenditure/did not have healthcare expenditure	Logit / logistic regression
	Poisson	Count data when variance=mean (e.g., number of missed work days)	Log
	Negative Binomial	Count data when variance > mean (e.g., number of missed work days)	Log
	Gamma	Right skewed (e.g., healthcare costs and utilization data)	Inverse, log

The relationships among the components of the GLM are presented in Figure 3.2.

Figure 3.2: Relationships across Components of Generalized Linear Models

$\boldsymbol{\eta=X\beta}$

$\boldsymbol{E(Y)=\mu=g-1(X\beta)=g-1(\eta)}$

$\boldsymbol{Var\ (Y)=\phi\ w-1\ V\ (\mu)=\phi\ w-1\ V\ (g-1\ (X\beta))=\phi\ w-1\ V\ (g-1(\eta))}$

- X= the independent variables
- β= the unknown parameters which can be estimated using maximum likelihood
- $X\beta$= the linear combination of unknown parameters and is equivalent to the link predictor (η)
- $E(Y)$=the expected value of the response or dependent variable (Y)
- μ= the mean of the distribution

- g= link function
- Var (Y)=the variance of the distribution (i.e., dependent variable (Y)) and this is a function (v) of the mean of the distribution and possibly, the dispersion parameter (ϕ)
- W is a prior weight that specifies the precision of Y

General assumptions of the GLM include the following:

1) statistical independence of observations; 2) correct specification of the variance function (V); 3) correct specification of the dispersion effect ϕ; 4) correct specification of the link function (g); 5) correct form for the explanatory variables (X); and 6) lack of undue influence of individual observations.[232]

3.10.2 GLM with gamma link function

Based on the table provided above, the GLM with gamma distribution and log link function is the most appropriate analyses for cost and expenditure data which are usually rightly skewed. The GLM with gamma link function is robust toward outliers and is the most appropriate since it uses raw cost data (rather than the log transformed cost variable) in its analyses; hence, there is no dispute with interpretation of results, nor is there a need to back-transform the results.

The effect of BMI status on healthcare costs of diabetic patients was assessed by using a generalized linear model with a gamma distribution and a log link function, controlling for covariates.

3.10.3 Negative binomial regression

Table 3.6 also shows that the negative binomial regression analysis is appropriate to analyze data where the variance is greater than the mean. Studies using MEPS have used this type of analysis for healthcare utilization. The following are assumptions of negative binomial regression: 1) independence of observations; 2) changes in the rate from combined effects of different exposures or risk factors are multiplicative; 3) logarithm of the event rate changes linearly with equal increment in the exposure variable; and 4) at each level of the covariates, the number of cases has variance greater than the mean.

Negative binomial regression analysis was used to evaluate the relationship between BMI status and healthcare use in the sample.

3.10.4 Multiple regression

In carrying out multiple regression analyses, there are a number of assumptions to be considered: 1) a linear relationship between the dependent and independent variables; 2) a normal distribution; 3) constant variance of the errors; and 4) independent observations.[233] Figure 3.3 shows a multiple regression model.

Figure 3.3: Multiple Regression Model

$Y=a + b_1X_1 + b_2X_2 + \ldots\ldots\ldots\ldots b_nX_n$

Y=value predicted for variable Y

a=constant of the intercept

b=regression coefficient

X=values of independent variables

Multiple regression was used to evaluate the relationship between BMI status and HRQoL scores using the 2 quality of life components of the SF-12 mentioned, (PCS-12 and MCS-12) while controlling for covariates. For both the PCS-12 and MCS-12, ordinary least squares (OLS) regression was used.

CHAPTER FOUR: RESULTS

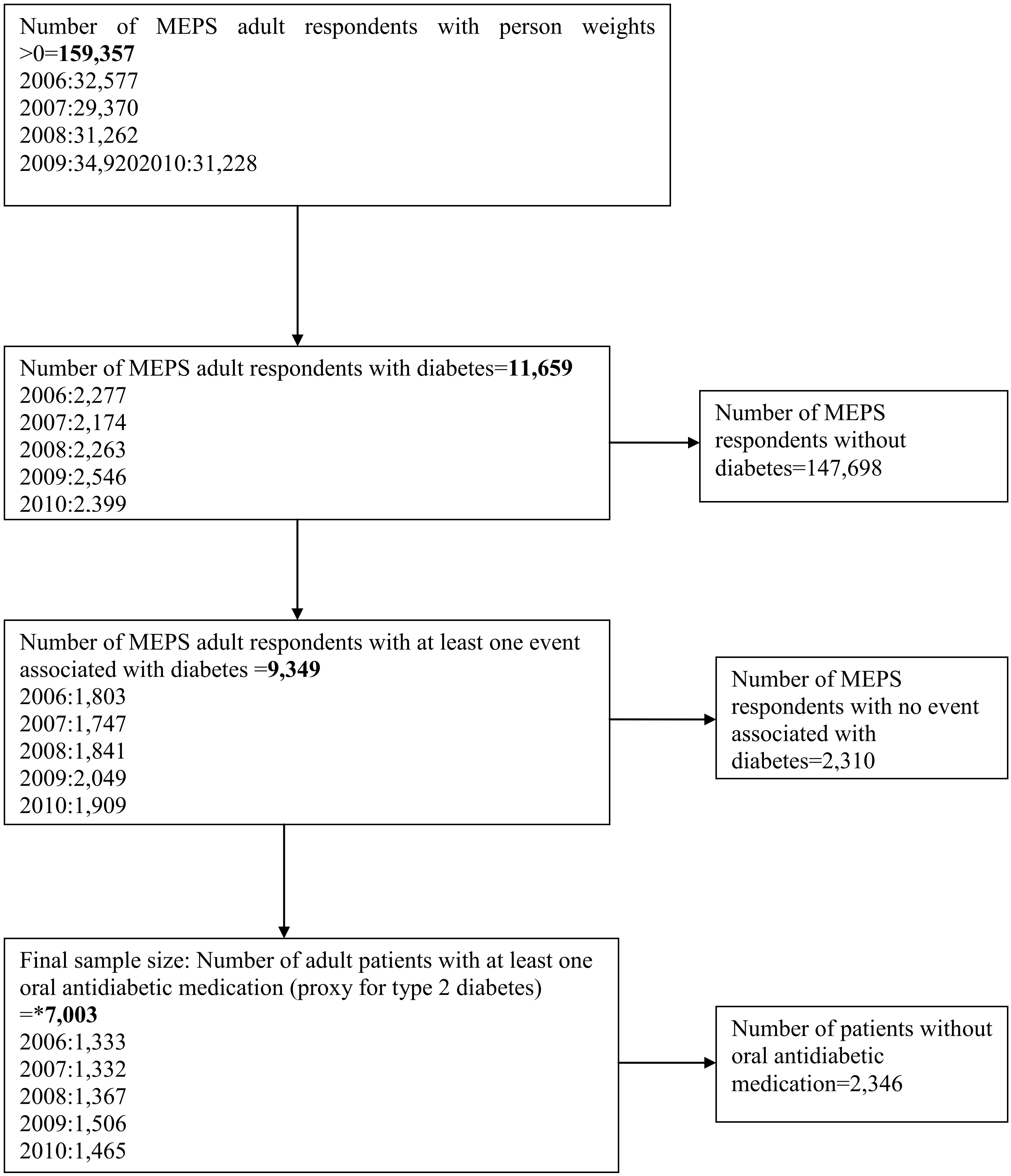
4.0 OVERVIEW OF RESULTS SECTION

This chapter provides in detail the results of the study starting with how the final study sample was derived. This is followed by the descriptive statistics of the population of interest. A comparison of demographic characteristics by body mass index (BMI) cohorts is presented followed by the results corresponding to the main objectives.

4.1 SAMPLE SIZE DERIVATION

A total of 159,357 respondents (≥18 years) were included in MEPS data between 2006 and 2010. Of these 159,357 respondents, 11,659 respondents (about 7 percent) reported a diagnosis of diabetes. When other inclusion criteria were applied, of the 11,659 diabetic patients, 9,349 patients reported having at least one event associated with diabetes. Finally, 7,003 (ranging from normal weight to morbidly obese) diabetic patients reported that they were on at least one oral antidiabetic (OAD) medication; this criterion was used as proxy to identify patients presenting with type 2 diabetes. Figure 4.1 below is a flow diagram showing the method of extraction and illustrates how the final sample size was derived. As a result of observed small cell sizes in the underweight BMI category (n=25), patients who fell in this category (underweight) were excluded from the study making a final sample size of 7,003 eligible respondents for the study. Sensitivity analysis was carried out by adjusting the BMI cut-off points of obese and morbidly obese categories from 30-39.9 for obese and ≥40 for morbidly obese to 30-34.9 and ≥35 for obese and morbidly obese categories, respectively.

Figure 4.1: Final sample size derivation



*Total sample size=7,003 (underweight patients excluded)

4.2 DESCRIPTIVE STATISTICS

The average age (±SE) of the 7,003 patients who met the inclusion criteria of the study was 61.2 (±0.24) years, mean BMI (±SE) was 32.2 (±0.12), and 50.4% were males. When age was categorized into 2 groups (18-64 and ≥65 years age categories), the majority (59.5%) of patients fell within the 18 to 64 years age category. The majority were white (77.4%), did not smoke (84.5%), and were married (60.4%). Based on census region, 39.5% of subjects resided in the South. By insurance category, 60.8% of patients were on private insurance, 31.1 and 33.7% of patients lived in middle-income and high-income households, respectively. Based on BMI status, 12.6% were normal weight; 29.2% were overweight; 45.6% of patients were considered obese, and 12.6% were morbidly obese.

Chi-square test results showed significant relationships between BMI and most socio-demographic characteristics except for smoking status: age category ($\chi 2=47.85$; df=4; $p<0.0001$), younger patients were more likely to have higher BMI compared to older patients [>64 years] in the population, gender ($\chi 2=19.81$; df=4; $p<0.0001$), higher BMI was more associated with females compared to males, race ($\chi 2=15.20$; df=8; $p<0.0001$), higher BMI was found for blacks compared to whites and other races, marital status ($\chi 2=5.98$; df=16; $p<0.0001$), higher BMI was found for patients who were unmarried compared to their married peers, poverty category ($\chi 2=2.90$; df=16; $p<0.0001$), higher BMI was found for patients in the poor SES category compared to the near poor, low, middle and high income categories; and insurance status ($\chi 2=5.53$; df=8; $p<0.0001$), the direction of insurance status in relation to BMI cohorts is not as clear. While patients on public insurance are more likely to be of normal weight than the other two insurance categories, they are also more likely to be morbidly obese. In addition, a higher percent of those with private insurance are overweight while a higher percent of those with no insurance are obese. Rather than use the regular Chi-square analysis to evaluate the relationship between BMI and SES variables which are considered ordinal variables, the Rao-Scott Chi-Square test is usually used to assess the relationship between ordinal variables with survey data.[234] MEPS also recommends that to obtain reliable national estimates, there should be at least 100 subjects per sub-category. Table 4.1 is a summary of chi-square test results of BMI status by socio-demographic characteristics.

Table 4.1: Chi-square results of socio-demographic characteristics by BMI status of type 2 diabetic patients

	Normal Weight (BMI 18 to 24.9)	**Overweight (BMI 25 to 29.9)**	**Obese (BMI 30 to 39.9)**	**Morbidly obese (BMI 40 and above)**	**Total**	
Total Un-weighted N	919	2,081	3,100	903	7,003	
[Un-weighted row %]	[13.1]	[29.7]	[44.3]	[12.9]	[100.0]	
Weighted N	1,851,952	4,279,563	6,685,904	1,842,900	14,660,318	
Weighted row %	12.6	29.2	45.6	12.6	100.0	
Socio-demographics						**Chi-Square** **χ2 df p-value**
Age category **N** **[Row %]** **(Column %)**						316.86 3 <0.0001*
18-64 years	402 [9.5] (41.2)	1,119 [26.3] (52.2)	2,031 [47.7] (64.3)	701 [16.5] (77.4)	4,253 [100.0] (59.5)	
≥65 years	517 [18.8] (58.8)	962 [35.0] (47.8)	1,069 [38.9] (35.7)	202 [7.3] (22.6)	2,750 [100.0] (40.5)	
Gender **N** **[Row %]** **(Column %)**						146.54 3 <0.0001*
Male	364 [11.6] (41.4)	1,109 [35.4] (58.5)	1,381 [44.0] (51.4)	283 [9.0] (37.0)	3,137 [100.0] (50.4)	
Female	555 [14.4] (58.6)	972 [25.1] (41.5)	1,719 [44.5] (48.6)	620 [16.0] (63.0)	3,866 [100.0] (49.6)	

Table 4.1 (cont'd): Chi-square results of socio-demographic characteristics by BMI status of type 2 diabetic patients

	Normal Weight (BMI 18 to 24.9)	**Overweight (BMI 25 to 29.9)**	**Obese (BMI 30 to 39.9)**	**Morbidly obese (BMI 40 and above)**	**Total**	
Race **N** **[Row %]** **(Column %)**						174.91 6 <0.0001*
White	544 [11.3] (69.3)	1,440 [30.0] (77.8)	2,203 [46.0] (79.4)	607 [12.7] (77.3)	4,794 [100.0] (77.4)	
Black	186 [11.3] (13.1)	455 [27.7] (14.6)	740 [45.1] (15.6)	260 [15.8] (18.1)	1,641 [100.0] (15.3)	
Others	189 [33.3] (17.6)	186 [32.8] (7.6)	157 [27.6] (5.1)	36 [6.3] (4.6)	568 [100.0] (7.4)	
Census region **N** **[Row %]** **(Column %)**						68.71 9 <0.0001*
Northeast	154 [13.9] (21.1)	337 [30.5] (19.5)	473 [42.8] (17.1)	142 [12.8] (19.2)	1,106 [100.0] (18.5)	
Midwest	141 [10.5] (15.2)	363 [26.9] (19.8)	634 [47.0] (22.6)	211 [15.6] (26.4)	1,349 [100.0] (21.3)	
South	340 [11.6] (36.8)	868 [29.6] (39.3)	1,339 [45.7] (41.1)	384 [13.1] (36.6)	2,931 [100.0] (39.5)	
West	284 [17.6] (27.0)	513 [31.7] (21.5)	654 [40.5] (19.3)	166 [10.3] (17.9)	1,617 [100.0] (20.7)	

Table 4.1 (cont'd): Chi-square results of socio-demographic characteristics by BMI status of type 2 diabetic patients

	Normal Weight (BMI 18 to 24.9)	Overweight (BMI 25 to 29.9)	Obese (BMI 30 to 39.9)	Morbidly obese (BMI 40 and above)	Total			
Smoking status **N** **[Row %]** **(Column %)**						15.58	3	0.0533
Smokes	167 [15.8] (19.2)	322 [30.4] (16.3)	450 [42.5] (14.2)	121 [11.4] (14.5)	1,060 [100.0] (15.5)			
Does not smoke	752 [12.7] (80.8)	1,759 [29.6] (83.7)	2,650 [44.6] (85.9)	782 [13.2] (85.5)	5,943 [100.0] (84.5)			
Marital status **N** **[Row %]** **(Column %)**						16.17	3	<0.0001*
Married	509 [12.8] (58.4)	1,236 [31.1] (61.8)	1,772 [44.6] (61.6)	457 [11.5] (54.9)	3,974 [100.0] (60.4)			
Not married	410 [13.5] (41.6)	845 [27.9] (38.2)	1,328 [43.8] (38.4)	446 [14.7] (45.1)	3,029 100.0] (39.6)			
Insurance status **N** **[Row %]** **(Column %)**						56.00	6	<0.0001*
Private insurance	419 [11.7] (53.3)	1,114 [31.1] (63.1)	1,635 [45.7] (62.8)	411 [11.5] (55.6)	3,579 [100.0] (60.8)			
Public insurance only	427 [15.6]	767 [28.0]	1,146 [41.9]	396 [14.5]	2,736 [100.0]			

Table 4.1 (cont'd): Chi-square results of socio-demographic characteristics by BMI status of type 2 diabetic patients

	Normal Weight (BMI 18 to 24.9)	**Overweight (BMI 25 to 29.9)**	**Obese (BMI 30 to 39.9)**	**Morbidly obese (BMI 40 and above)**	**Total**	
	(41.0)	(30.4)	(29.7)	(36.2)	(32.1)	
Not insured	73 [10.6] (5.7)	200 [29.1] (6.5)	319 [46.4] (7.5)	96 [13.9] (8.2)	688 [100.0] (7.1)	
Poverty category **N** **[Row %]** **(Column %)**						57.91 12 <0.0001*
Poor	180 [13.0] (14.1)	379 [27.4] (12.4)	599 [43.3] (13.0)	224 [16.2] (18.2)	1,382 [100.0] (13.6)	
Near poor	68 [13.5] (5.3)	127 [25.3] (4.7)	228 [45.3] (5.7)	80 [15.9] (7.7)	503 [100.0] (5.6)	
Low income	167 [13.1] (17.0)	370 [29.0] (15.1)	587 [45.9] (15.9)	154 [12.1] (17.1)	1,278 [100.0] (16.0)	
Middle income	292 [13.8] (32.3)	641 [30.4] (31.1)	908 [43.0] (30.5)	271 [12.8] (32.1)	2,112 [100.0] (31.1)	
High income	212 [12.3] (31.4)	564 [32.6] (36.8)	778 [45.0] (34.9)	174 [10.1] (25.0)	1,728 [100.0] (33.7)	

Numbers in parentheses represent the weighted column percentages, sum of which may not be 100 due to rounding;
*Significant at $p<0.05$

Objective 1 (continued): To determine if there is a difference in age and Charlson comorbidity index (CCI) score between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, an unadjusted regression analysis was conducted.

Table 4.2 shows that there is a significant difference in age by BMI status. Patients who were overweight (63.63±0.38 years), obese (59.81±0.34 years) and morbidly obese (55.06±0.53years) were significantly younger compared to patients with normal weight (66.93± 0.64years).

Table 4.2: Regression results of Age by BMI status

BMI status	**Mean Age (years)**	**Std. Error**	**t**	**p-value**	**95% Confidence Interval**	
Normal weight (comparator)	**66.93**	**0.64**				
Overweight	63.63	0.38	-4.78	<0.0001*	-4.6646	-1.9449
Obese	59.81	0.34	-9.85	<0.0001*	-8.5412	-5.6997
Morbidly obese	55.06	0.53	-14.25	<0.0001*	-13.5176	-10.2397

Reference group= Normal weight; $F(3, 387)=83.49$; $p<0.0001$ *Significant at $p<0.05$

Regression analysis also showed a significant difference in Charlson Comorbidity Index (CCI) score by BMI status. Overweight (1.72±0.04), obese (1.73±0.04) and morbidly obese (1.83±0.06) patients had significantly lower CCI scores compared to patients with normal weight (2.01±0.07), see Table 4.3.

Table 4.3: Regression results of Charlson Comorbidity Index (CCI) score by BMI status

BMI status	Mean CCI score	Std. Error	t	p-value	95% Confidence Interval	
Normal weight (comparator)	**2.01**	**0.07**				
Overweight	1.72	0.04	-3.80	<0.0001*	-0.4361	-0.1389
Obese	1.73	0.04	-3.46	0.001*	-0.4361	-0.1199
Morbidly obese	1.83	0.06	-2.02	0.044*	-0.3663	-0.0051

Reference group= Normal weight; F (3, 387)=5.20; p=0.0016 *Significant at p<0.05

4.3 Objective 2

Prevalence=number of obese diabetic patients/total number of diabetic patients in the study, for each level of overweight/obesity.

The prevalence of overweight patients in the weighted population of patients with type 2 diabetes was 29.19%, while obesity prevalence was 58.18% (that is, obesity prevalence 45.61% and prevalence of the morbidly obese 12.57%). See Table 4.1

4.4 Objective 3 (H_{01})

To estimate differences in <u>*diabetes-related* direct medical costs</u> between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Due to the highly skewed nature of healthcare costs, a generalized linear model (GLM) with a gamma distribution and a log link function was used to estimate the differences in diabetes-related direct medical costs by BMI status. The modified Park test was performed to confirm the appropriateness of the statistical analytical test used for cost data. The mean (±SE) of <u>*diabetes-related* direct medical costs</u> were as follows:

normal weight: \$1,622 (±112); overweight: \$1,955 (±118); obese: \$2,259 (±104); morbidly obese: \$2,636 (±201) respectively. The results of the test showed that there was a significant difference in diabetes-related direct medical costs of diabetes patients by BMI status. Table 4.4 shows that compared to the normal weight patients, overweight ($p=0.038$), obese ($p<0.0001$) and morbidly obese ($p<0.0001$) patients had significantly higher diabetes-related direct medical costs.

Table 4.4: GLM (gamma distribution with log link function) of diabetes-related direct medical costs of type 2 diabetes patients by BMI status

	Mean cost (\$)	**Std. Error**	**†Estimate**	**†Std. Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status								
Normal weight (comparator)	1,622	112						
Overweight	1,955	118	0.19	0.09	2.08	0.0380*	0.0104	0.3626
Obese	2,259	104	0.33	0.08	4.01	<0.0001*	0.1690	0.4936
Morbidly obese	2,636	201	0.49	0.10	4.66	<0.0001*	0.2805	0.6904

Reference group= Normal weight; *Significant at $p<0.05$
†Linearized coefficient estimates and standard errors

4.5 OBJECTIVE 4 (H_{02})

To estimate differences in direct medical (all-cause) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

The mean (±SE) of direct medical (all-cause) costs of type 2 diabetes patients by BMI status were normal weight: $11,623 (±664); overweight: $9,715 (±433); obese: $11,419 (±399); and morbidly obese: $13,043 (±841) respectively. Given the highly skewed nature of the dependent variable (direct medical [all-cause] costs), a similar analysis as objective 3 (GLM using gamma distribution with a log link function) was conducted, the results of this analysis showed a significant difference in direct medical costs of overweight type 2 diabetic patients (p=0.012) compared to patients with normal weight (Table 4.5). Overweight patients had significantly lower all-cause direct medical costs compared to their peers with normal weight. There was no significant difference in all-cause direct medical costs of obese and morbidly obese patients compared to patients with normal weight.

Table 4.5: GLM (gamma distribution with log link function) of direct medical (all-cause) costs of type 2 diabetes patients by BMI status (unadjusted analysis)

	Mean costs ($)	**Std. Error**	**†Estimate**	**†Std. Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status								
Normal weight (comparator)	11,623	664						
Overweight	9,715	433	-0.18	0.07	-2.51	0.012*	-0.3195	-0.0391
Obese	11,419	399	-0.02	0.07	-0.26	0.795	-0.1515	0.1162
Morbidly obese	13,043	841	0.12	0.08	1.42	0.157	-0.0448	0.2753

Reference group= Normal weight; *Significant at p<0.05

†Linearized coefficient estimates and standard errors

4.6 OBJECTIVE 5 (H_{03})

To estimate differences in indirect (lost productivity) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. The mean (±SE) of indirect (lost productivity) costs of type 2 diabetes patients by BMI status were normal weight: $535 (±115); overweight: $533 (±57); obese: $534 (±48) and morbidly obese: $532 (±48) respectively. Results of the GLM with a gamma distribution and a log link function showed that there was no significant difference in indirect costs by BMI status (Table 4.6).

Table 4.6: GLM (gamma distribution with log link function) of indirect medical costs of type 2 diabetes patients by BMI status [unadjusted analysis]

	Mean costs ($)	**Std. Error**	**†Estimate**	**†Std. Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status								
Normal weight (comparator)	535	115						
Overweight	533	57	-0.003	0.24	-0.01	0.989	-0.4663	0.4596
Obese	534	48	-0.002	0.23	-0.01	0.992	-0.4448	0.4405
Morbidly obese	532	48	-0.006	0.23	-0.02	0.980	-0.4656	0.4539

Reference group= Normal weight; *Significant at $p<0.05$
†Linearized coefficient estimates and standard errors

4.7 OBJECTIVE 6 (H_{04})

To estimate differences in total (all-cause direct medical and indirect) costs of diabetes patients between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

The mean (±SE) of total costs of type 2 diabetes patients by BMI status were normal weight: $12,158 (±675); overweight: $10,249 (±448); obese: $11,953 (±409) and morbidly obese: $13,575 (±846). A GLM analysis similar to the one conducted for the previous objective was conducted; the results of this analysis showed a significant difference in total healthcare costs of overweight type 2 diabetic patients (p=0.014) compared to patients with normal weight (Table 4.7). Overweight patients had significantly lower total healthcare costs compared to their peers with normal weight. There was no significant difference in total healthcare costs of obese and morbidly obese patients compared to patients with normal weight.

Table 4.7: GLM (gamma distribution with log link function) of total (indirect + direct) costs of type 2 diabetes patients by BMI status [unadjusted analysis]

	Mean costs ($)	**Std. Error**	**†Estimate**	**†Std. Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status								
Normal weight (comparator)	12,158	675						
Overweight	10,249	448	-0.17	0.07	-2.46	0.014*	-0.3076	-0.0341
Obese	11,953	409	-0.02	0.07	-0.26	0.797	-0.1467	0.1128
Morbidly obese	13,575	847	0.11	0.08	1.39	0.166	-0.0458	0.2663

Reference group= Normal weight; *Significant at p<0.05
†Linearized coefficient estimates and standard errors

4.8 OBJECTIVE 7 (H_{05})

To determine if healthcare utilization rates (that is, number of ambulatory care visits [sum of outpatient department visits and office-based medical provider visits]) between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. Negative binomial regression was used to address this objective given that the outcome variable (number of ambulatory care visits) is a count variable with a variance that is greater than the mean.

The mean (±SE) number of ambulatory care visits of type 2 diabetes patients by BMI status were normal weight: 10.73 (±0.46); overweight: 10.59 (±0.37); obese: 12.53 (±0.40) and morbidly obese: 13.00 (±0.78) respectively.

The results in Table 4.8 show that there was a significant difference in the number of ambulatory care visits of obese (p=0.004) and morbidly obese (p=0.008) patients compared to their peers who were of normal weight. Obese and morbidly obese patients had significantly higher number of ambulatory care visits compared to their peers with normal weight. There was no significant difference in the number of ambulatory care visits between overweight patients compared to their peers with normal weight.

Table 4.8: Negative binomial regression analysis of number of ambulatory care visits by BMI status (unadjusted analysis)

	Mean ambulatory visits	Std. Error	†Estimate	†Std. Error	t	p-value	95% Confidence interval	
BMI status								
Normal weight (comparator)	10.73	0.46						
Overweight	10.59	0.37	-0.01	0.06	-0.22	0.822	-0.1224	0.0973
Obese	12.53	0.40	0.16	0.05	2.93	0.004*	0.0511	0.2601
Morbidly obese	13.00	0.78	0.19	0.07	2.67	0.008*	0.0509	0.3344

Reference groups= Normal weight; F (4, 387)=6.46; p=0.0003 *Significant at p<0.05
†Linearized coefficient estimates and standard errors

4.9 OBJECTIVE 7 (H_{06})

To determine if the number of emergency room visits of diabetic patients differ between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Due to the nature of the dependent variable (number of emergency room visits), a count variable with excess zeroes, the Vuong test was conducted to determine whether the zero-inflated negative binomial regression analysis was a better fit compared to the normal negative binomial regression.[235] The Vuong test recommended that the zero-inflated binomial regression model was the better fit so the zero-inflated negative binomial regression analysis was conducted. The mean (±SE) of the number of emergency room visits of type 2 diabetes patients by BMI status were normal weight: 0.36 (0.03); overweight: 0.25 (0.02); obese: 0.30 (0.02) and morbidly obese: 0.37 (0.04) respectively.

The results however showed that there was no significant difference in the number of emergency room visits by BMI status [F (1, 389)=0.01; p=0.9341].

4.10 OBJECTIVE 7 (H_{07})

To determine if the number of prescribed medicines (this is the total number of prescriptions including refills in a year) differ between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

The mean (±SE) of the number of prescribed medicines for these type 2 diabetic patients by BMI status were normal weight: 40.79 (±1.51); overweight: 37.96 (±0.91); obese: 47.40 (±1.04) and morbidly obese: 53.90 (±2.06) respectively. Negative binomial regression was used to address this objective given that the outcome variable (number of prescribed medicines) is a count variable with a variance that is greater than the means. The results in Table 4.9 show that there is a significant difference in the number of prescribed medicines of obese (p<0.0001) and morbidly obese (p<0.0001) patients compared to their peers who were of normal weight. Obese and morbidly obese patients had a significantly higher number of prescribed medicines compared to their peers with normal weight. There was no significant difference in the number of prescribed medicines between overweight patients compared to their peers with normal weight.

Table 4.9: Negative binomial regression analysis of number of prescribed medicines by BMI status (unadjusted analysis)

	Mean # of prescribed medicines	Std. Error	†Estimate	†Std. Error	t	p-value	95% Confidence interval	
BMI status								
Normal weight (comparator)	40.79	1.51						
Overweight	37.96	0.91	-0.07	0.04	-1.82	0.0690	-0.1497	0.0056
Obese	47.40	1.04	0.15	0.04	3.54	<0.0001*	0.0668	0.2333
Morbidly obese	53.90	2.06	0.28	0.05	5.46	<0.0001*	0.1783	0.3787

Reference groups= Normal weight; F (4, 387)=32.88; p<0.0001 *Significant at p<0.05
†Linearized coefficient estimates and standard errors

4.11 Objective 8 (H_{08})

To compare the HRQoL (physical component) scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

The mean (±SE) scores of the physical component of the HRQoL by BMI status of the type 2 diabetes patients were normal weight: 40.99 (±0.51); overweight: 42.69 (±0.34); obese: 40.13 (±0.31) and morbidly obese: 35.64 (±0.62) respectively. Linear regression analysis was conducted to address this objective given the normally distributed nature of the outcome variable (physical component of HRQoL). There was a significant difference in the physical component summary (PCS-12) scores of patients' HRQoL by BMI status. Overweight (p=0.005) patients had significantly better health-related quality of life (HRQoL) PCS scores compared to their peers with normal weight while morbidly obese (p<0.0001) patients had significantly poorer PCS scores) compared to their peers with normal weight, (Table 4.10).

Table 4.10: Linear regression analysis of the physical component – PCS-12 Health-Related Quality of Life (HRQoL) scores by BMI status (unadjusted analysis)

	Mean PCS-SF-12 HRQoL scores	**Std. Error**	**†Estimate**	**†Std. Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status								
Normal weight (comparator)	40.99	0.51						
Overweight	42.69	0.51	1.70	0.60	2.82	0.005*	0.5161	2.8911
Obese	40.13	0.31	-0.86	0.58	-1.47	0.1410	-1.9960	0.2858
Morbidly obese	35.64	0.62	-5.35	0.79	-6.74	<0.0001*	-6.9103	-3.7878

Reference groups= Normal weight; F (4, 389)=38.51; p<0.0001 *Significant at p<0.05
†Linearized coefficient estimates and standard errors
PCS-12=Physical Component Summary scores of the SF-12 – Higher scores indicate better HRQoL

4.12 Objective 8 (H_{09})

To compare the HRQoL (mental component) scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

The mean (±SE) scores of the mental component of the SF-12 (MCS-12) by BMI status of the type 2 diabetes patients were normal weight: 48.88 (±0.46); overweight: 50.86 (±0.33); obese: 49.67 (±0.29) and morbidly obese: 46.92 (±0.56) respectively. Linear regression analysis was conducted to address this objective given the normally distributed nature of the outcome variable. Table 4.11 showed that there was a significant difference in the MCS-12 scores of patients by BMI. Overweight (p<0.0001) patients had significantly higher MCS-12 health-related quality of life (HRQoL) scores compared to their peers with normal weight while morbidly obese (p=0.005) patients had significantly poorer MCS-12 scores compared to their normal weight peers. There was no significant difference in the

HRQoL mental component between obese patients compared to their peers with normal weight.

Table 4.11: Linear regression analysis of the mental component – MCS-12 Health-Related Quality of Life (HRQoL) scores by BMI status (unadjusted analysis)

	Mean MCS-SF-12 HRQoL scores	**Std. Error**	**†Estimate**	**†Std. Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status								
Normal weight (comparator)	48.88	0.46						
Overweight	50.86	0.46	1.98	0.52	3.78	<0.0001*	0.9468	3.0035
Obese	49.67	0.29	0.78	0.54	1.45	0.1470	-0.2753	1.8391
Morbidly obese	46.92	0.56	-1.96	0.70	-2.81	0.005*	-3.3313	-0.5899

Reference groups= Normal weight; F (4, 387)=14.57; p<0.0001 *Significant at p<0.05
†Linearized coefficient estimates and standard errors
MCS-12=Mental Component Summary scores of the SF-12 – Higher scores indicate better HRQoL

4.13 OBJECTIVE 9 (H_{10})

To estimate the differences in direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

Diabetes-related direct medical costs.

A GLM with a gamma distribution and a log link function was used to address this objective and covariates controlled for include age category, gender, race, census region, insurance status, smoking status, marital status, poverty category, CCI score, number of additional bed days, physical and mental HRQoL scores. There was a significant difference in diabetes-related direct medical costs of overweight (p=0.031), obese (p=0.001) and morbidly obese (p=0.003) patients compared to their peers with normal weight while controlling for covariates. Being overweight, obese or morbidly obese were significantly associated with higher diabetes-related medical costs. With respect to the covariates, insurance status (not being insured: p<0.0001), number of additional bed days (p=0.001), physical (p<0.0001) and mental (p=0.001) HRQoL scores and CCI score (p=0.001) were significantly associated with diabetes-related healthcare costs, controlling for other covariates. Having a higher CCI score, and having more additional bed days were associated with an increase in diabetes-related direct medical costs; while having no insurance, and having higher mental and physical HRQoL scores were associated with lower diabetes-related direct medical costs while controlling for covariates, Table 4.12 provides detailed information regarding these results.

Table 4.12: GLM (gamma distribution with log link function) analysis comparing diabetes-related direct medical costs by BMI status controlling for covariates

	Estimate	**Std. Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status						
Overweight	0.19	0.09	2.17	0.0310*	0.0173	0.3582
Obese	0.27	0.08	3.33	0.0010*	0.1115	0.4322
Morbidly obese	0.31	0.10	3.01	0.0030*	0.1091	0.5197
Covariates						
Age category						
≥ 65 years	-0.10	0.06	-1.62	0.1060	-0.2277	0.0221
Gender						
Female	-0.06	0.06	-1.04	0.2980	-0.1687	0.0519
Race						
Black	0.13	0.07	1.82	0.0700	-0.0104	0.2666
Other races	-0.12	0.10	-1.24	0.2170	-0.3089	0.0704
Geographical region						
Midwest	-0.06	0.09	-0.65	0.5150	-0.2358	0.1183
South	-0.12	0.07	-1.73	0.0850	-0.2450	0.0160
West	-0.05	0.09	-0.57	0.56710	-0.2185	0.1199
Insurance status						
Public insurance only	-0.03	0.08	-0.34	0.7360	-0.1845	0.1304
Not insured	-0.60	0.10	-6.03	<0.0001*	-0.7900	-0.4015
CCI score	0.06	0.02	3.26	0.0010*	0.0227	0.0914
Poverty category						
Near poor	0.18	0.14	1.35	0.1780	-0.0832	0.4463
Low income	0.08	0.10	0.82	0.4100	-0.1142	0.2791
Middle income	0.01	0.08	0.14	0.8920	-0.1427	0.1639
High income	0.10	0.09	1.22	0.2220	-0.0630	0.2698
Smoking status						
Does not smoke	0.08	0.08	1.05	0.2950	-0.0734	0.2411
Marital status						
Not married	0.13	0.07	1.90	0.0590	-0.0046	0.2552
PCS-12 score	-0.02	0.002	-6.67	<0.0001*	-0.0204	-0.0111
MCS-12 score	-0.01	0.002	-3.25	0.0010*	-0.0123	-0.0030

Table 4.12 (cont'd): GLM (gamma distribution with log link function) analysis comparing diabetes-related direct medical costs by BMI status controlling for covariates

	Estimate	Std. Error	t	p-value	95% Confidence interval	
†Additional bed days	0.003	0.001	3.50	<0.0001*	0.0011	0.0040

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; poverty category: poor; census region: Northeast
†Additional bed days: additional days spent in bed due to restricted activity
*Significant at p<0.05
PCS-12 [Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

4.14 OBJECTIVE 9 (H_{11})

To estimate differences in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

A GLM with a gamma distribution and a log link function analysis was used to address this objective controlling for previously specified covariates. There was a significant difference in all-cause direct medical costs of overweight (p=0.021) patients compared to their peers with normal weight while controlling for covariates (Table 4.13). Being overweight was significantly associated with lower direct medical costs compared to patients with normal weight. With respect to the covariates, race (other races besides white and blacks: p<0.0001), insurance status (public insurance only; p<0.0001, no insurance; p<0.0001), census region of residence (West; p=0.019), marital status (p=0.027), physical (p<0.0001) and mental (p<0.0001) HRQoL scores, CCI score (p<0.0001) and additional bed days (p<0.0001) were significantly associated with direct medical costs, controlling for other covariates. Belonging to other races apart from white and black, not being insured or having public insurance only, residing in the West and having higher physical and mental HRQoL scores were associated with a decrease in direct medical costs. Being unmarried, having an increase in CCI score and additional bed days were significantly associated with an increase in direct medical costs, controlling for other covariates.

Table 4.13: GLM (gamma distribution with log link function) analysis comparing all-cause direct medical costs by BMI status controlling for covariates

	Estimate	**Std. error**	**t**	**p-value**	**95% Confidence interval**	
BMI status						
Overweight	-0.15	0.07	-2.32	0.0210*	-0.2763	-0.0228
Obese	-0.01	0.07	-0.20	0.8390	-0.1402	0.1140
Morbidly obese	-0.05	0.08	-0.62	0.5380	-0.2079	0.1087
Covariates						
Age category						
≥ 65 years	0.05	0.04	1.08	0.2820	-0.0383	0.1311
Gender						
Female	-0.04	0.04	-0.94	0.3500	-0.1257	0.0446
Race						
Black	-0.01	0.05	-0.19	0.8530	-0.1104	0.0914
Other races	-0.29	0.08	-3.75	<0.0001*	-0.4407	-0.1377
Geographical region						
Midwest	0.01	0.06	0.08	0.9340	-0.1158	0.1261
South	-0.07	0.05	-1.35	0.1770	-0.1799	0.0333
West	-0.14	0.06	-2.37	0.0190*	-0.2630	-0.0243
Insurance status						
Public insurance only	-0.24	0.05	-4.85	<0.0001*	-0.3332	-0.1410
Not insured	-0.72	0.11	-6.33	<0.0001*	-0.9425	-0.4959
CCI score	0.20	0.01	14.02	<0.0001*	0.1708	0.2264
Poverty category						
Near poor	0.20	0.10	1.94	0.0530	-0.0025	0.3914
Low income	-0.04	0.06	-0.62	0.5350	-0.1647	0.0856
Middle income	0.04	0.06	0.49	0.6230	-0.0897	0.1495

Table 4.13 (cont'd): GLM (gamma distribution with log link function) analysis comparing all-cause direct medical costs by BMI status controlling for covariates

	Estimate	Std. error	t	p-value	95% Confidence interval	
High income	0.12	0.07	1.75	0.0810	-0.0147	0.2508
Smoking status						
Does not smoke	0.08	0.06	1.28	0.2000	-0.03995	0.1904
Marital status						
Not married	0.09	0.04	2.22	0.027*	0.0103	0.1689
PCS-12 score	-0.03	0.002	-14.82	<0.0001*	-0.0317	-0.0229
MCS-12 score	-0.01	0.002	-5.07	<0.0001*	-0.0129	-0.0057
†Additional bed days	0.01	0.001	6.11	<0.0001*	0.0032	0.0063

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; poverty category: poor; census region: Northeast
†Additional bed days: additional days spent in bed due to restricted activity
*Significant at p<0.05
PCS-12 [Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

4.15 Objective 10 (H_{12})

To estimate the differences in costs of productivity loss (indirect costs) between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

A GLM with a gamma distribution and a log link function analysis was used to address this objective. There was no significant relationship between indirect costs and BMI while controlling for covariates. However, age (p<0.0001), gender (p=0.0400), insurance status (public insurance only, p<0.0001; no insurance, p<0.0001), smoking status (p=0.012), CCI score (p=0.001), poverty category (low income; p<0.0001, middle income; p<0.0001, high income; p<0.0001), marital status (p=0.001) and number of additional bed days (p<0.0001) were significantly associated with indirect costs. Being older (≥65 years), female, having public insurance only or not having insurance, not smoking and having a higher number of additional bed days were significantly associated with lower indirect costs while being unmarried, having a higher CCI score and belonging to households with low, middle and high income were significantly associated with higher indirect costs(Table 4.14). A sensitivity analysis was conducted using 260 days (assuming an adult worked 5 days a week for 52 weeks in a year), and results obtained were robust.

Table 4.14: GLM (gamma distribution with log link function) analysis comparing indirect healthcare costs by BMI status controlling for covariates

	Estimate	**Std. error**	**t**	**p-value**	**95% Confidence interval**	
BMI status						
Overweight	-0.14	0.13	-1.11	0.2670	-0.3893	0.1080
Obese	-0.02	0.13	-0.15	0.8780	-0.2682	0.2292
Morbidly obese	0.07	0.15	0.46	0.6470	-0.2326	0.3739
Covariates						
Age category						
≥ 65 years	-0.91	0.11	-8.24	<0.0001*	-1.1243	-0.6913
Gender						
Female	-0.16	0.08	-2.06	0.0400*	-0.3109	-0.0073
Race						
Black	0.09	0.07	1.21	0.2280	-0.0554	0.2315
Other races	0.25	0.19	1.28	0.2020	-0.1316	0.6212
Geographical region						
Midwest	-0.15	0.13	-1.22	0.2240	-0.4029	0.0948
South	0.10	0.12	0.81	0.4190	-0.1363	0.3267
West	0.07	0.12	0.58	0.5660	-0.1687	0.3081
Insurance status						
Public insurance only	-0.77	0.10	-8.01	<0.0001*	-0.9614	-0.5824
Not insured	-0.63	0.12	-5.04	<0.0001*	-0.8687	0.3813
CCI score	0.08	0.02	3.41	0.001*	0.0345	0.1287

Table 4.14 (cont'd): GLM (gamma distribution with log link function) analysis comparing indirect healthcare costs by BMI status controlling for covariates

	Estimate	Std. error	t	p-value	95% Confidence interval	
Poverty category						
Near poor	0.19	0.10	1.89	0.0590	-0.0077	0.3923
Low income	0.39	0.10	4.04	<0.0001*	0.2011	0.5821
Middle income	0.83	0.11	7.79	<0.0001*	0.6182	1.0353
High income	1.47	0.13	11.66	<0.0001*	1.2190	1.7134
Smoking status						
Does not smoke	-0.30	0.12	-2.53	0.0120*	-0.5410	-0.0677
Marital status						
Not married	0.26	0.08	3.37	0.0010*	0.1096	0.4174
PCS-12 score	-0.01	0.004	-1.33	0.1840	-0.0133	0.0026
MCS-12 score	-0.004	0.004	-1.01	0.3140	-0.0107	-0.0034
†Additional bed days	-0.004	0.001	-6.06	<0.0001*	-0.0054	-0.0027

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; poverty category: poor; census region: Northeast

†Additional bed days: additional days spent in bed due to restricted activity

*Significant at p<0.05

PCS-12 [Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

4.16 OBJECTIVE 11 (H_{13})

To estimate the differences in total costs (direct plus indirect) between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates.

A GLM with a gamma distribution and a log link function analysis was used to address this objective. There was a significant relationship between total healthcare costs and being overweight (p=0.011) while controlling for covariates; compared to patients with normal weight, overweight patients had significantly lower total healthcare costs. With respect to covariates, race (other races besides whites and blacks; p=0.001), census region of residence (West; $p=0.0180$), insurance status (public insurance only, $p<0.0001$; no insurance, $p<0.0001$), CCI score ($p<0.0001$), poverty category (near poor, $p=0.039$; high income, $p=0.006$), marital status ($p=0.005$), both physical ($p<0.0001$) and mental ($p<0.0001$) HRQoL, and additional bed days ($p<0.0001$) were significantly associated with total healthcare costs, while controlling for covariates. Being of another race besides white and black, residing in the West, having public insurance only or being uninsured, having higher physical and mental HRQoL scores were significantly associated with lower total healthcare costs. However, being unmarried, belonging to the near poor and high income households, having a higher CCI score and having higher number of additional bed days were significantly associated with higher total healthcare costs. Table 4.15 provides detailed information regarding these results.

Table 4.15: GLM (gamma distribution with log link function) analysis comparing total healthcare costs by BMI status controlling for covariates

	Estimate	**Standard Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status						
Overweight	-0.16	0.06	-2.55	0.0110*	-0.2909	-0.0375
Obese	-0.03	0.06	-0.51	0.6110	-0.1592	0.0937
Morbidly obese	-0.06	0.08	-0.77	0.4410	-0.2161	0.0944
Covariates						
Age category						
≥ 65 years	-0.002	0.04	-0.04	0.9660	-0.0863	0.0827
Gender						
Female	-0.05	0.04	-1.11	0.2680	-0.1311	0.0365
Race						
Black	0.004	0.05	0.08	0.9340	-0.0934	0.1016
Other races	-0.26	0.08	-3.33	0.0010*	-0.4060	-0.1045
Geographical region						
Midwest	-0.01	0.06	-0.11	0.9100	-0.1270	0.1132
South	-0.07	0.05	-1.34	0.1810	-0.1793	0.0339
West	-0.14	0.06	-2.37	0.0180*	-0.2559	-0.0237
Insurance status						
Public insurance only	-0.27	0.05	-5.59	<0.0001*	-0.3580	-0.1718
Not insured	-0.73	0.10	-6.93	<0.0001*	-0.9332	-0.5205
CCI score	0.20	0.01	14.06	<0.0001*	0.1682	0.2228
Poverty category						
Near poor	0.20	0.10	2.07	0.0390*	0.0099	0.3900
Low income	-0.02	0.06	-0.30	0.7620	-0.1413	0.1036
Middle income	0.06	0.06	1.06	0.2890	-0.0534	0.1786
High income	0.18	0.07	2.78	0.0060*	0.0535	0.3107
Smoking status						
Does not smoke	0.05	0.06	0.93	0.3530	-0.0603	0.1688
Marital status						
Not married	0.11	0.04	2.83	0.0050*	0.0338	0.1874
PCS-12 score	-0.03	0.002	-14.77	<0.0001*	-0.0310	-0.0238

Table 4.15 (cont'd): GLM (gamma distribution with log link function) analysis comparing total healthcare costs by BMI status controlling for covariates

	Estimate	Standard Error	t	p-value	95% Confidence interval	
MCS-12 score	-0.01	0.002	-5.04	<0.0001*	-0.0124	-0.0054
†Additional bed days	0.01	0.001	6.01	<0.0001*	-.0030	0.0059

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; SES: poor; census region: Northeast
*Significant at p<0.05
†Additional bed days: additional days spent in bed due to restricted activity
PCS-12 [Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

4.17 Objective 12 (H_{14})

To estimate the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates. Specifically to determine if the number of ambulatory care visits differ between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Negative binomial regression was used to address this objective given that the outcome variable (number of ambulatory care visits) is a count variable with a variance that is greater than the means. There was a significant difference in the number of ambulatory care visits of obese (p=0.009) patients compared to their peers with normal weight, while controlling for covariates. Obese patients had a significantly higher number of ambulatory care visits compared to their peers with normal weight. With respect to the covariates, female gender (p=0.043), race (being black, p=0.025; being of other race besides whites and blacks, p<0.0001), Census region (residing in the South, p<0.0001;West, p=0.027), being uninsured (p<0.0001), physical (p<0.0001) and mental (p<0.0001) HRQoL scores, CCI score (p<0.0001), additional bed days (p=0.043), poverty category (belonging to middle, p=0.042; high, p<0.0001) income households and smoking status (p<0.0001) were significantly related to the number of ambulatory care visits. Being female, belonging to middle or high income households, having a higher CCI score, having a higher number of additional bed days and not smoking were significantly associated with a higher number of ambulatory care visits. While being non-white, residing in the South or West, being uninsured and having high physical and mental HRQoL scores were significantly associated with a lower number of ambulatory care visits. Table 4.16 provides detailed information regarding these results.

Table 4.16: Negative binomial regression analysis comparing number of ambulatory visits by BMI status controlling for covariates

	Estimate	**Standard Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status						
Overweight	0.03	0.05	0.52	0.6060	-0.0744	0.1275
Obese	0.12	0.05	2.61	0.009*	-0.0305	0.2172
Morbidly obese	0.04	0.07	0.61	0.5400	-0.0895	0.1707
Covariates						
Age category						
≥ 65 years	0.09	0.04	1.94	0.0530	-0.0010	0.1700
Gender						
Female	0.09	0.04	2.03	0.0430*	0.0026	0.1681
Race						
Black	-0.11	0.05	-2.24	0.0250*	-0.21155	-0.0139
Other races	-0.21	0.05	-3.85	<0.0001*	-0.3100	-0.1005
Geographical region						
Midwest	-0.06	0.05	-1.05	0.2960	-0.1631	0.04975
South	-0.22	0.05	-4.78	<0.0001*	-0.3162	-0.1319
West	-0.13	0.06	-2.22	0.0270*	-0.2406	-0.0145
Insurance status						
Public insurance	-0.05	0.05	-1.00	0.3190	-0.1364	0.0445

Table 4.16 (cont'd): Negative binomial regression analysis comparing number of ambulatory visits by BMI status controlling for covariates

	Estimate	**Standard Error**	**t**	**p-value**	**95% Confidence interval**	
only						
Not insured	-0.48	0.08	-6.05	<0.0001*	-0.6289	-0.3203
CCI score	0.14	0.01	10.51	<0.0001*	0.1164	0.1701
Poverty category						
Near poor	0.09	0.10	0.90	0.3670	-0.1005	0.2715
Low income	-0.04	0.06	-0.64	0.5220	-0.1511	0.0768
Middle income	0.11	0.06	2.04	0.0420*	0.0043	0.2206
High income	0.23	0.06	4.27	<0.0001*	0.1255	0.3408
Smoking status						
Does not smoke	0.26	0.05	5.56	<0.0001*	0.1682	0.3523
Marital status						
Not married	0.05	0.04	1.18	0.2370	-0.0327	0.1315
PCS-12 score	-0.03	0.002	-16.60	<0.0001*	-0.0291	-0.0229
MCS-12 score	-0.01	0.002	-3.86	<0.0001*	-0.0090	-0.0029
†Additional bed days	0.001	0.001	2.03	0.0430*	0.00004	0.0023

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: not smoking; insurance status: private insurance; SES: poor; census region: Northeast

†Additional bed days: additional days spent in bed due to restricted activity

$F(22, 368)=41.89$; $p<0.0001$ *Significant at $p<0.05$

PCS-12 [Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

4.18 OBJECTIVE 12(H_{15})

To estimate the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates. Specifically to estimate –if the number of emergency room visits differ between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

A zero-inflated negative binomial regression was used to address this objective due to a number of reasons.

1) The outcome variable (number of emergency room visits) is a count variable with a variance that is greater than the means.
2) The Vuong test was carried out due to the presence of zeroes in a significant proportion (78.4%) of the sample. Based on the Vuong test, instead of the normal negative binomial regression analysis, a zero-inflated negative binomial regression analysis was recommended.

The zero-inflated negative binomial regression analysis showed that there was a significant difference in the number of emergency room visits of overweight patients (p=0.035) compared to their peers with normal weight controlling for covariates. Being overweight was associated with a significantly lower number of ER visits compared to that of patients with normal weight. Among the covariates, smoking status (p=0.005), both physical (p=0.016) and mental (p=0.024) HRQoL scores, CCI score (p=0.009) and additional bed days (p=0.006) were significantly associated with the number of ER visits. Not smoking, having high physical and mental HRQoL scores were significantly associated with having a lower number of ER visits. While a higher CCI score and higher number of additional bed days were significantly associated with a higher number of ER visits. Race (being black; p=0.006) and number of additional bed days (p<0.0001), which were included in the part of the logit model, were significant in predicting excessive zeroes. The log odds of being an excessive zero would decrease by 0.63 if the patient were black and decrease by 0.73

for each additional bed day. Hence, a patient is more likely to have an ER visit if the patient is black (compared to being white) or has a higher number of additional bed days. Table 4.17 provides detailed information regarding these results.

Table 4.17: Zero-inflated Negative Binomial Regression analysis comparing number of emergency room visits by BMI status controlling for covariates

	Estimate	**Standard Error**	**t**	**p-value**	**95% Confidence interval**	
BMI status						
Overweight	-0.24	0.11	-2.12	0.0350*	-0.4675	-0.0176
Obese	-0.10	0.12	-0.81	0.4210	-0.3263	0.1365
Morbidly obese	-0.19	0.16	-1.14	0.2540	-0.5082	0.1349
Covariates						
Age category						
≥ 65 years	-0.03	0.09	-0.34	0.7330	-0.2047	0.1442
Gender						
Female	0.015	0.09	0.17	0.8650	-0.1594	0.1896
Race						
Black	0.04	0.10	0.36	0.7220	-0.1561	0.2250
Other races	-0.12	0.15	-0.83	0.4090	-0.4049	0.1653
Geographical region						
Midwest	0.15	0.13	1.22	0.2200	-0.0928	0.3981
South	-0.02	0.10	-0.16	0.8720	-0.2187	0.1855
West	-0.16	0.15	-1.05	0.2940	-0.4613	0.1402
Insurance status						
Public insurance only	0.09	0.10	0.92	0.3580	-0.0967	0.2753
Not insured	-0.02	0.15	-0.14	0.8870	-0.3095	0.2678
CCI score	0.08	0.03	2.64	0.0090*	0.0220	0.1340
Poverty category						
Near poor	-0.26	0.16	-1.57	0.1180	-0.5776	0.0651
Low income	-0.02	0.11	-0.14	0.8900	-0.2308	0.2004
Middle income	-0.13	0.10	-1.28	0.2030	-0.3233	0.0689

Table 4.17 (cont'd): Zero-inflated Negative Binomial Regression analysis comparing number of emergency room visits by BMI status controlling for covariates

	Estimate	**Standard Error**	**t**	**p-value**	**95% Confidence interval**	
High income	-0.15	0.12	-1.23	0.2180	-0.3980	0.0911
Smoking status						
Does not smoke	-0.27	0.10	-2.80	0.0050*	-0.4529	-0.0793
Marital status						
Not married	-0.06	0.09	-0.73	0.4680	-0.2368	0.1090
PCS-12 score	-0.01	0.004	-2.41	0.0160*	-0.0194	-0.0020
MCS-12 score	-0.01	0.004	-2.27	0.0240*	-0.0154	-0.0011
†Additional bed days	0.002	0.001	2.78	0.0060*	0.001	0.0028
Inflate						
BMI status						
Overweight	-0.12	0.33	-0.36	0.7170	-0.7718	0.5317
Obese	0.23	0.30	0.74	0.4600	-0.3736	0.8234
Morbidly obese	-0.07	0.39	-0.17	0.8630	-0.8433	0.7073
Age category						
≥ 65 years	-0.09	0.23	-0.41	0.6830	-0.5468	0.3585
Gender						
Female	-0.12	0.21	-0.57	0.5680	-0.5325	0.2927
Race						
Black	-0.63	0.23	-2.77	0.0060*	-1.0696	-0.1821
Other races	0.04	0.34	0.11	0.9100	-0.6282	0.7048
Geographical region						
Midwest	-0.16	0.31	-0.50	0.6190	-0.7823	0.4661
South	-0.29	0.27	-1.09	0.2750	-0.8125	0.2322
West	-0.20	0.36	-0.56	0.5750	-0.9008	0.5008
Insurance status						
Public insurance only	0.18	0.23	0.77	0.4440	-0.2780	0.6334
Not insured	-0.56	0.40	-1.39	0.1650	-1.3386	0.2293
CCI score	-0.15	0.11	-1.39	0.1660	-0.3585	0.0620
Poverty category						
Near poor	0.41	0.45	0.91	0.3630	-0.4772	1.3000
Low income	0.44	0.31	1.42	0.1580	-0.1708	1.0484

Table 4.17 (cont'd): Zero-inflated Negative Binomial Regression analysis comparing number of emergency room visits by BMI status controlling for covariates

	Estimate	Standard Error	t	p-value	95% Confidence interval	
Middle income	0.17	0.31	0.54	0.5880	-0.4453	0.7841
High income	-0.26	0.30	-0.86	0.3900	-0.8568	0.3354
Smoking status						
Does not smoke	-0.11	0.26	-0.42	0.6720	-0.6270	0.4048
Marital status						
Not married	-0.34	0.22	-1.54	0.1240	-0.7780	0.0937
PCS-12 score	0.01	0.01	0.87	0.3840	-0.0115	0.0298
MCS-12 score	0.02	0.01	1.78	0.0760	-0.0018	0.0364
†Additional bed days	-0.73	0.15	-4.96	<0.0001*	-1.0213	-0.4415

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; poverty category: poor; census region: Northeast
†Additional bed days: additional days spent in bed due to restricted activity
$F (22, 368) = 5.96$; $p<0.0001$*Significant at $p<0.05$
PCS-12 [Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

4.19 OBJECTIVE 12 (H_{16})

To estimate the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates. Specifically to determine –if the number of prescribed medicines (including refills) differ between overweight, obese or morbidly obese diabetes patients compared to normal weight patients.

Negative binomial regression was used to address this objective given that the outcome variable (number of prescribed medicines) is a count variable with a variance that is greater than the means. There was a significant difference in the number of prescribed medicines of obese ($p<0.0001$) and morbidly obese ($p<0.0001$) patients compared to their peers with normal weight, while controlling for covariates. Being obese or morbidly obese was significantly associated with a higher number of prescribed medicines while controlling for covariates. With respect to the covariates, age (p=0.005), female gender (p=0.004), insurance status (having public insurance only, p<0.0001; being uninsured, p<0.0001), physical (p<0.0001) and mental (p<0.0001) HRQoL scores, CCI score (p<0.0001), being unmarried (p=0.013) and additional bed days (p<0.0001) were significantly related to the number of prescribed medicines. Being female, older than 64 years of age, having public insurance only, having a higher CCI score, additional bed days and being unmarried were significantly associated with a higher number of prescribed medicines; however, being uninsured and having high physical and mental HRQoL scores were significantly associated with a lower number of prescribed medicines. Table 4.18 provides detailed information regarding these results.

Table 4.18: Negative Binomial Regression analysis comparing number of prescribed medicines by BMI status controlling for covariates

	Estimate	Standard Error	t	p-value	95% Confidence interval	
BMI status						
Overweight	0.01	0.04	0.22	0.8300	-0.0683	0.0851
Obese	0.18	0.04	4.36	<0.0001*	0.0969	0.2564
Morbidly obese	0.18	0.05	3.66	<0.0001*	0.0840	0.2794
Covariates						
Age category						
≥ 65 years	0.07	0.03	2.83	0.0050*	0.0225	0.1252
Gender						
Female	0.08	0.03	2.93	0.0040*	0.0251	0.1272
Race						
Black	-0.05	0.03	-1.62	0.1070	-0.1132	0.0110
Other races	-0.10	0.05	-1.79	0.0740	-0.1961	0.0090

Table 4.18 (cont'd): Negative Binomial Regression analysis comparing number of prescribed medicines by BMI status controlling for covariates

	Estimate	Standard Error	t	p-value	95% Confidence interval	
Geographical region						
Midwest	0.07	0.05	1.49	0.1370	-0.0214	0.1552
South	0.01	0.04	0.18	0.8550	-0.0720	0.0868
West	-0.06	0.05	-1.31	0.1900	-0.1477	0.0294
Insurance status						
Public insurance only	0.12	0.03	4.46	<0.0001*	0.0684	0.1765
Not insured	-0.27	0.05	-5.61	<0.0001*	-0.3650	-0.1755
CCI score	0.09	0.01	9.30	<0.0001*	0.0714	0.1100
Poverty category						
Near poor	0.08	0.06	1.43	0.1530	-0.0301	0.1916
Low income	0.03	0.04	0.88	0.3790	-0.0384	0.1008
Middle income	0.03	0.04	0.84	0.4030	-0.0398	0.0990
High income	0.03	0.04	0.71	0.4760	-0.0467	0.0998
Smoking status						
Does not smoke	-0.06	0.03	-1.82	0.0690	-0.1263	0.0047
Marital status						
Not married	0.07	0.03	2.49	0.0130*	0.0144	0.1235
PCS-12 score	-0.02	0.001	-16.35	<0.0001*	-0.0189	-0.0149
MCS-12 score	-0.01	0.001	-5.19	<0.0001*	-0.0072	-0.0032
†Additional bed days	0.001	0.0003	4.13	<0.0001*	0.0007	0.0020

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; poverty category: poor; census region: Northeast

†Additional bed days: additional days spent in bed due to restricted activity

F (22, 368)=55.84; p<0.0001 *Significant at p<0.05

PCS-12 [Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

4.20 OBJECTIVE 13 (H_{17})

To estimate the differences in HRQoL scores: physical component between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.

An ordinary least squares multivariate regression analysis was used to address this objective due to the normally distributed nature of the dependent variables (physical HRQoL scores). There was a significant difference in the physical component (PCS-12) HRQoL scores of patients by BMI status, controlling for covariates. Being obese ($p<0.0001$) or morbidly obese ($p<0.0001$) were significantly associated with lower PCS-12 scores compared to patients with normal weight. With regard to the covariates, age ($p=0.0001$), gender ($p=0.001$), race (black; $p<0.0001$, other races beside white and black; $p=0.009$), census region (South; $p=0.001$), insurance status (public insurance only; $p<0.0001$), CCI score ($p<0.0001$), poverty category (middle income; $p<0.0001$, high income; $p<0.0001$), smoking status ($p=0.016$) and number of additional bed days ($p<0.0001$) were significantly associated with the physical component HRQoL scores. Being female, older than 64 years of age, residing in the South, having public insurance only, having a higher CCI score and additional bed days were significantly associated with lower PCS-12 scores; however, being non-white, belonging to middle or high income households and not smoking were significantly associated with higher PCS-12 scores.. Table 4.19 provides detailed information regarding these results.

Table 4.19: Multivariate Regression analysis comparing Physical Component Summary (PCS-12) HRQoL Scores by BMI status controlling for covariates

	Estimate	Standard Error	t	p-value	95% Confidence interval	
BMI status						
Overweight	-0.10	0.55	-0.18	0.8610	-1.1688	0.9775
Obese	-2.86	0.53	-5.37	<0.0001*	-3.9052	-1.8115
Morbidly obese	-6.72	0.69	-9.73	<0.0001*	-8.0707	-5.3583
Covariates						
Age category						
≥ 65 years	-4.03	0.41	-9.81	<0.0001*	-4.8379	-3.2218
Gender						
Female	-1.24	0.37	-3.32	0.0010*	-1.9705	-0.5037
Race						
Black	1.68	0.40	4.21	<0.0001*	0.8980	2.4696
Other races	1.49	0.57	2.63	0.0090*	0.3775	2.6100
Geographical region						
Midwest	0.05	0.56	0.10	0.9220	-1.0371	1.1452
South	-1.48	0.46	-3.24	0.0010*	-2.3839	-0.5833
West	0.06	0.51	0.12	0.9070	-0.9360	1.0546
Insurance status						
Public insurance only	-3.35	0.44	-7.63	<0.0001*	-4.2134	-2.4861
Not insured	-0.34	0.64	-0.53	0.5990	-1.6056	0.9275
CCI score	-1.7083	0.1442	-11.85	<0.0001*	-1.9918	-1.4248
Poverty category						
Near poor	0.34	0.72	0.48	0.6310	-1.0618	1.7502
Low income	0.70	0.60	1.16	0.2460	-0.4829	1.8770
Middle income	2.16	0.52	4.14	<0.0001*	1.1338	3.1863
High income	3.75	0.61	6.14	<0.0001*	2.5487	4.9503
Smoking status						
Does not smoke	1.10	0.45	2.42	0.0160*	0.2047	1.9910
Marital status						
Not married	0.16	0.42	0.38	0.7010	-0.6565	0.9758
†Additional bed days	-0.07	0.004	-16.32	<0.0001*	-0.0786	-0.0617

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; poverty category: poor; census region: Northeast
†Additional bed days: additional days spent in bed due to restricted activity
F (20, 370)=95.16; p<0.0001 *Significant at p<0.05

4.21 OBJECTIVE 13 (H_{18})

To estimate the differences in HRQoL: mental component between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.

An ordinary least squares multivariate regression analysis was used to address this objective due to the normally distributed nature of the continuous dependent variables (mental HRQoL scores). There was a significant difference in the mental component (MCS-12) HRQoL scores of patients by BMI status, controlling for covariates. Being overweight (p=0.038) was significantly associated with higher MCS-12 scores compared to being of normal weight. With regards to the covariates, age (p<0.0001), female gender (p=0.045), black race (p=0.006), insurance status (public insurance only; p<0.0001, no insurance; p=0.002), CCI score (p=0.001), poverty category (belonging to middle; p<0.0001, high income; p<0.0001) households, smoking status (p<0.0001) and number of additional bed days (p<0.0001) were significantly associated with the mental component HRQoL scores. Being black, at least 65 years of age, belonging to middle- or high-income households and not smoking were significantly associated with higher MCS-12 scores; however, being female, having public insurance only or no insurance at all, having a higher CCI score and additional bed days were significantly associated with lower MCS-12 scores. Table 4.20 provides detailed information regarding these results.

Table 4.20: Multivariate Regression analysis comparing Mental Component Summary (MCS-12) HRQoL Scores by BMI status controlling for covariates

	Estimate	Standard Error	t	p-value	95% Confidence interval	
BMI status						
Overweight	1.03	0.50	2.08	0.0380*	0.0555	2.0058
Obese	0.30	0.52	0.57	0.5680	-0.7228	1.3150
Morbidly obese	-1.00	0.64	-1.57	0.1170	-2.2465	0.2511
Covariates						
Age category						
≥ 65 years	2.66	0.37	7.19	<0.0001*	1.9331	3.3884
Gender						
Female	-0.73	0.36	-2.01	0.0450*	-1.4451	-0.0173
Race						
Black	1.20	0.43	2.76	0.0060*	0.3435	2.0421
Other races	-0.61	0.63	-0.98	0.3270	-1.8462	0.6172
Geographical region						
Midwest	0.77	0.61	1.26	0.2090	-0.4314	1.9698
South	0.34	0.54	0.63	0.5290	-0.7261	1.4116
West	-0.07	0.63	-0.11	0.9120	-1.3151	1.1752
Insurance status						
Public insurance only	-3.33	0.43	-7.78	<0.0001*	-4.1698	-2.4876
Not insured	-2.00	0.64	-3.12	0.0020*	-3.2555	-0.7372
CCI score	-0.50	0.15	-3.30	0.0010*	-0.7953	-0.2012
Poverty category						
Near poor	1.18	0.73	1.61	0.1070	-0.2580	2.6208
Low income	0.63	0.62	1.02	0.3100	-0.5855	1.8391
Middle income	2.51	0.56	4.44	<0.0001*	1.3956	3.6148
High income	3.84	0.59	6.46	<0.0001*	2.6729	5.0010
Smoking status						
Does not smoke	1.62	.46	3.54	<0.0001*	0 .7199	2.5196
Marital status						
Not married	-0.48	0.39	-1.24	0.2160	-1.2499	0.2837
†Additional bed days	-0.07	0.01	-12.12	<0.0001*	-0.0845	-0.0609

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: smoking; insurance status: private insurance; poverty category: poor; census region: Northeast
†Additional bed days: additional days spent in bed due to restricted activity
F (20, 370)=34.11; p<0.0001 *Significant at p<0.05

Table 4.21 provides a summary of the study's objectives, hypotheses and the findings.

4.22 SENSITIVITY ANALYSES

Results of sensitivity analyses that involved adjusting BMI cut-off points of obese and morbidly obese categories from 30-39.9 for obese and ≥40 for morbidly obese to 30-34.9 and ≥35 for obese and morbidly obese categories respectively were robust. Obese patients had significantly higher (p=0.006) number of ambulatory care visits compared to their normal weight peers while there was no significant difference between overweight and morbidly obese patients compared to their normal weight peers. Also, by Mental Component Summary (MCS) scores, overweight patients were significantly higher MCS scores (p=0.0390) compared to their normal weight peers while no significant difference was observed with the at least obese patients compared to their normal weight peers. There was no need for further sensitivity analyses regarding other dependent variables as there was no difference between the obese and morbidly obese categories in the original analysis. That is, varying the BMI cut-off points would not have made a difference in the analyses. See Appendices C and D for results of sensitivity analyses.

Table 4.21: Summary of Objectives, Hypotheses and Findings

Objectives	**Hypotheses**	**Findings**
Objective 1: To describe the study sample and compare the socio-demographic characteristics of the diabetic patient population by BMI status		
Objective 2: To estimate the prevalence of overweight/obesity among the diabetic population		About 87 percent of the type 2 diabetes MEPS population were at least overweight
Objective 3: To estimate differences in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	H_{01}: There is no significant difference in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was a significant difference in diabetes-related direct medical costs of diabetes patients by BMI status. Compared to the normal weight patients, overweight (p=0.038), obese (p<0.0001) and morbidly obese (p<0.0001) patients had significantly higher diabetes-related direct medical costs.
Objective 4: To estimate differences in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	H_{02}: There is no significant difference in direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was a significant difference in direct medical costs of overweight type 2 diabetic patients (p=0.012) compared to patients with normal weight. Overweight patients had significantly lower all-cause direct medical costs compared to their peers with normal weight.
Objective 5: To estimate differences in indirect costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	H_{03}: There is no significant difference in indirect (lost productivity) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was no significant difference in indirect costs by BMI status
Objective 6: To estimate differences in total costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	H_{04}: There is no significant difference in total (direct medical and indirect) costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was a significant difference in total healthcare costs of overweight type 2 diabetic patients (p=0.014) compared to patients with normal weight. Overweight patients had significantly lower total healthcare costs compared to their peers with normal weight.
Objective 7: To estimate differences in healthcare utilization rates between overweight, obese or	H_{05}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly	There was a significant difference in the number of ambulatory care visits of obese (p=0.004) and morbidly obese (p=0.008)

Table 4.21 (cont'd): Summary of Objectives, Hypotheses and Findings

Objectives	**Hypotheses**	**Findings**
morbidly obese diabetes patients compared to normal weight patients	obese diabetes patients compared to normal weight patients	patients compared to their peers who were of normal weight. Obese and morbidly obese patients had a significantly higher number of ambulatory care visits compared to their peers with normal weight.
	H_{06}: There is no significant difference in the number of emergency room visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was no significant difference in the number of emergency room visits by BMI status
	H_{07}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was a significant difference in the number of prescribed medicines of obese ($p<0.0001$) and morbidly obese ($p<0.0001$) patients compared to their peers who were of normal weight. Obese and morbidly obese patients had significantly higher number of prescribed medicines compared to their peers with normal weight.
Objective 8: To compare the HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	H_{08}: There is no significant difference in the physical component scores of the HRQoL between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was a significant difference in the physical component summary (PCS-12) scores of patients' HRQoL by BMI status. Overweight ($p=0.005$) patients had significantly better health-related quality of life (HRQoL) PCS scores compared to their peers with normal weight while morbidly obese ($p<0.0001$) patients had significantly poorer PCS scores compared to their peers with normal weight
	H_{09}: There is no significant difference in the mental component scores of the HRQoL between overweight, obese or morbidly obese diabetes patients compared to normal weight patients	There was a significant difference in the MCS-12 scores of patients by BMI. Overweight ($p<0.0001$) patients had significantly higher MCS-12 health-related quality of life (HRQoL) scores compared to their peers with normal weight while morbidly obese ($p=0.005$) patients had significantly poorer MCS-12 scores compared to their normal weight peers.

Table 4.21 (cont'd): Summary of Objectives, Hypotheses and Findings

Objectives	**Hypotheses**	**Findings**
Objective 9: To estimate the differences in healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates	H_{10}: There is no significant difference in *diabetes-related* direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was a significant difference in diabetes-related direct medical costs of overweight (p=0.031), obese (p=0.001) and morbidly obese (p=0.003) patients compared to their peers with normal weight while controlling for covariates. Being overweight, obese or morbidly obese were significantly associated with higher diabetes-related medical costs.
	H_{11}: There is no significant difference in all-cause direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was a significant difference in all-cause direct medical costs of overweight (p=0.021) patients compared to their peers with normal weight while controlling for covariates, Being overweight was significantly associated with lower direct medical costs compared to patients with normal weight.
Objective 10: To estimate the differences in productivity loss costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates	H_{12}: There is no significant difference in productivity loss (indirect costs) between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was no significant difference in productivity loss by BMI status, controlling for covariates.
Objective 11: To estimate the differences in total healthcare costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates	H_{13}: There is no significant difference in total costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was a significant relationship between total healthcare costs and being overweight (p=0.011) while controlling for covariates. Compared to patients with normal weight, overweight patients had significantly lower total healthcare costs.
Objective 12: To estimate the differences in healthcare utilization between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates	H_{14}: There is no significant difference in the number of ambulatory care visits between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was a significant difference in the number of ambulatory care visits of obese (p=0.009) patients compared to their peers with normal weight, while controlling for covariates. Obese patients had a significantly higher number of ambulatory care visits compared to their peers with normal weight.
	H_{15}: There is no significant difference in number of	There was a significant difference in the number of emergency room

Table 4.21 (cont'd): Summary of Objectives, Hypotheses and Findings

Objectives	Hypotheses	Findings
	emergency room between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	visits of overweight patients ($p=0.035$) compared to their peers with normal weight controlling for covariates. Being overweight was associated with a significantly lower number of ER visits compared to that of patients with normal weight.
	H_{16}: There is no significant difference in the number of prescribed medicines between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was a significant difference in the number of prescribed medicines of obese ($p<0.0001$) and morbidly obese ($p<0.0001$) patients compared to their peers with normal weight, while controlling for covariates. Being obese or morbidly obese was significantly associated with a higher number of prescribed medicines while controlling for covariates.
Objective 13: To estimate the differences in HRQoL scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients controlling for covariates	H_{17}: There is no significant difference in PCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was a significant difference in the physical component (PCS-12) HRQoL scores of patients by BMI status, controlling for covariates. Being obese ($p<0.0001$) or morbidly obese ($p<0.0001$) were significantly associated with lower PCS-12 scores compared to patients with normal weight.
	H_{18}: There is no significant difference in MCS-12 scores between overweight, obese or morbidly obese diabetes patients compared to normal weight patients, controlling for covariates.	There was a significant difference in the mental component (MCS-12) HRQoL scores of patients by BMI status, controlling for covariates. Being overweight ($p=0.038$) was significantly associated with higher MCS-12 scores compared to being of normal weight.

CHAPTER FIVE: DISCUSSION

5.0 Overview of Discussion section

This chapter provides a more in-depth explanation of the study findings and limitations encountered in the course of carrying out the study, and how these findings relate to previous findings in the literature. The chapter concludes with the significance of the study, as well as suggestions for future research. The chapter begins with an overview of the aims of the study.

5.1 Study overview

This study was focused on evaluating the relationship between BMI status and healthcare costs, utilization and the Health Related Quality of Life (HRQoL) of type 2 diabetes patients using the MEPS database (a database representative of the non-institutionalized civilian US population). Although a number of studies assessing the association between BMI status and several disease conditions have been conducted, the literature is sparse concerning the relationship between BMI status and specifically, healthcare costs, utilization and HRQoL in adults presenting with type 2 diabetes. The use of the MEPS database provides this study with the ability to answer the study questions using a nationally representative sample of the US non-institutionalized civilian population.

5.2 Limitations

Provided below are limitations encountered in the course of carrying out this study.

1) MEPS assumes that respondents below the age of 18 do not present with diabetes; hence, respondents with type 2 diabetes below the age of 18 years could not be studied with this database.
2) Due to the small sample size of underweight patients in the present study, this sub-category of patients was excluded from the study.
3) Although assumptions were made that patients who were on oral antidiabetic medications were type 2 diabetic patients, this could not be definitively ascertained.
4) There was a need to impute income values and number of missed work days for patients (49.9%) and caregivers who did not report income and missed work days due to the significant number of missing values.
5) Because BMI values were obtained based on self-reported values provided by respondents, there is the possibility that some reported BMI values were inaccurate.
6) When the inclusion/exclusion criteria regarding having at least one event associated with diabetes and using at least an oral antidiabetic medication, 40% of patients diagnosed with diabetes (~4,000 diabetes patients) were lost. It is possible that these patients did not meet these criteria because they were on lifestyle modification only (diet and exercise), on insulin only or could not afford the costs associated with an event. Hence, the possibility that they differ

significantly from the study sample cannot be overlooked, thus the study findings cannot be generalized to the entire MEPS type 2 diabetes population.

5.3 Study objectives and hypotheses

Thirteen objectives and eighteen hypotheses were addressed in this study.

5.3.1 Objective 1

The purpose of objective 1 was to describe the study sample and compare socio-demographic characteristics of the type 2 diabetes non-institutionalized civilian population by BMI status. The average age (±SE) of the population was 61.2 (±0.24) years, with almost 6 out of 10 patients below 65 years of age. The mean BMI (±SE) was 32.2 (±0.12) and almost 90 percent of the study sample were considered at least overweight when BMI was categorized into the normal, overweight**,** obese and morbidly obese categories. This may not be surprising as the literature reports that about 85 percent of type 2 diabetes patients are at least overweight. The mean Charlson Comorbidity Index (CCI) score (±SE) of the study sample was 1.8 (±0.03) and by gender, there was a fairly equal distribution of the patients as males made up 50.4 percent of the population. More than 77 percent of the study sample was white, the majority (84.5 percent) did not smoke, 6 out of 10 patients were married and 4 out of 10 patients resided in the South (this includes the following states: Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi, Arkansas, Louisiana, Oklahoma, and Texas). Six out of 10 patients had private insurance, while 31.1 and 33.7 percent of patients lived in middle-income and high-income households respectively.

Significant relationships between BMI and most socio-demographic characteristics were observed except for smoking status: by age category, younger patients were more likely to have higher BMI compared to older patients [>64 years] in the population, the literature reports that compared to adults above 60 years, younger peers (between 40 and 59 years) were more likely to be obese.[48] By age, patients who were overweight (64±0.69; p<0.0001)), obese (60 ±0.72; p<0.0001), and morbidly obese (55±0.83; p<0.0001) were significantly younger than their peers with normal weight (67±0.64). Ogden et al. reported that people between 40 and 59 years were more likely to be obese than their older peers.[5] It is also possible that the older patients were more likely to be of normal weight due to the associated loss in muscle mass as a result of age. In fact studies have reported significant loss in muscle mass in older adults with type 2 diabetes.[236-238] By gender, higher BMI was more associated with females compared to males, Ogden et al. reported that in the general US population, there was no significant difference in the prevalence of obesity by gender, the present study's finding may be different as a result of the narrowed population studied (that is the type 2 diabetic population).[47]

When considering race, higher BMI was found for Blacks compared to whites and other races; this finding is supported by the CDC with reports that compared to whites, blacks are more likely to present with higher BMI.[34] Our study shows that by marital status, higher BMI was found for patients who were unmarried compared to their married peers, this s supported by Dixon et al. who concluded that severely obese ($\geq$35 kg/m^2) type 2 diabetes patients were more likely to live alone compared to their peers with normal weight.[239] By poverty category, higher BMI was found for patients in the poor SES category compared to the near poor, low, middle and high income categories, this is supported by literature that maintains that low income earners are more likely to be obese compared to their non-obese peers.[239-240] The direction of insurance status in relation to BMI cohorts is not as clear. While patients on public insurance are more likely to be of normal weight than the other two insurance categories, they are also more likely to be morbidly obese. In addition, a higher percent of those with private insurance are overweight while a higher percent of those with no insurance are obese, a study reported that severely obese type 2 diabetes patients were more likely to be without insurance compared to their peers with normal weight.[239] By CCI score, overweight (1.72±0.08), obese (1.73±0.08) and morbidly obese (1.83±0.09) patients had significantly fewer comorbid conditions compared to their peers with normal weight (2.01±0.07). This finding was surprising as the literature has reported an increase in the number of comorbid conditions with an increase in BMI.[64, 240] However, given that the normal weight patients in this study sample were older, it is plausible that they present with more comorbid conditions compared to their younger peers despite their being more of normal weight.

5.3.2 Objective 2

The second objective was to determine the prevalence rates of both overweight and obesity in the study sample. Results showed that almost 3 out of 10 of the study sample were overweight and 58 percent of the population was obese of which almost 13 percent were morbidly obese. Overall, 87 percent of the study sample was at least overweight and this is in line with the literature that has reported that at least 85 percent of type 2 diabetes patients are either overweight or obese.[25, 28, 31, 241]

5.3.3 Objectives 3 & 9

The purpose of objective 3 and objective 9 was to assess the differences in diabetes-related direct medical costs between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. In both the unadjusted and adjusted analyses, results show that with an increase in BMI, there was a corresponding increase in diabetes-related direct medical costs. A number of studies have concluded that type 2 diabetes-related direct medical costs increased as BMI increased.[222, 242] Ballesta et al. and Dilla et al., in studies involving Spanish patients with type 2 diabetes, reported a significant relationship between higher healthcare costs associated with type 2 diabetes in the obese compared to their non-obese peers.[222, 242] This finding is also supported by an earlier study that concluded that higher BMI generally results in an increase in healthcare costs;[243] however, the present study finding is unique as it relates to type 2 diabetes-related direct medical costs specifically in the US civilian non-institutionalized population. This implies that patients with higher BMI are more likely to utilize more diabetes-related healthcare resources (e.g., medications and diabetic supplies), leading to a corresponding increase in direct medical costs compared to their peers with lower BMI. Moreover, Apovian reported that obesity is associated with a dramatic rise (more than 13 times) in the cost of anti-diabetic medications used.[54]

Among the covariates controlled for, it was also logical to observe that higher Charlson Comorbidity Index CCI scores and additional bed days were significantly associated with higher diabetes-related medical costs as this indicates the positive association between higher medical costs and severity of disease (assessed by the higher number of comorbid diseases and tendency to spend more time in bed due to illness). Raebel et al. reported that the number of comorbid conditions which was assessed using a chronic disease score index was one of the factors that predicted higher healthcare costs in patients when obese patients were compared against their non-obese peers.[53]

Also, being uninsured and having higher physical and mental HRQoL scores (indicating better health status) were significantly associated with lower medical costs. These results logically suggest that an uninsured patient is less likely to have higher medical costs since such patients are less likely to seek medical help even when ill as a result of the financial implications of seeking medical attention.[244-245] Furthermore, higher physical and mental HRQoL scores represent better health status compared to lower scores; hence, a patient with higher physical and mental scores may have less need for healthcare services.

5.3.4 Objectives 4 &10

When all-cause direct medical costs of the diabetic patient was assessed in both the unadjusted (objective 4) and adjusted (objective 10) analyses, it was unexpected to observe that there was no significant difference in mean (±SE) direct medical (all-cause) costs of type 2 diabetes patients who were of normal weight: $11,623 (664) compared to their obese: $11,419 (399) and morbidly obese: $13,043 (841) peers respectively. It was even more surprising to observe that overweight patients had significantly lower all-cause direct medical costs $9,715 (433) compared to their peers with normal weight $11,623 (664). This finding is contrary to some studies such as that by Sullivan et al. who (using the MEPS database) reported that obesity has a significant influence on patients presenting with diabetes and comorbid dyslipidemia and hypertension,[219] and another study by Kim et al. (using a Nationwide Inpatient Sample) who reported significantly higher hospital costs in obese and morbidly obese diabetic patients compared to their non-obese peers.[246] However, it is important to note that Sullivan et al. reported the effect of obesity on the cost of cardiometabolic risk factors (that is, diabetes, dyslipidemia and hypertension) while the study by Kim et al. classified BMI into two major categories that is, obese vs. non-obese categories as opposed to the present study which assessed the influence of BMI using 4 categories (that is normal weight, overweight, obese and morbidly obese categories) on all-cause direct medical costs of type 2 diabetic patients. The present study shows that there was no significant difference in all-cause direct medical costs of type 2 diabetes patients when costs of normal weight patients were compared against their peers who were either obese or morbidly obese. However, a significant difference was observed with overweight patients having significantly lower costs compared to their peers with normal weight. It is possible that having some level of fat like that present in the overweight patient may actually promote better health outcomes in some disease conditions compared to being normal weight, hence resulting in lower all-cause direct medical costs. In what was termed the "overweight paradox," Diehr et al. reported that compared to normal weight older adults (≥65 years), their overweight peers had significantly better non-mortality outcomes.[247] Oreopoulos et al. also agreed that a u-shaped relationship has been found between BMI (less than 35kg/m^2) and mortality in adults, with overweight patients having the lowest mortality.[248] Another study concluded that mortality risks decrease as BMI increases up to the point when people become obese (BMI ≥35kg/m^2).[64]

In a systematic review and meta-analysis, another study suggested that elderly adults who were overweight did not have a higher all-cause mortality risk compared to their normal weight peers while this risk was found to increase in obese elderly adults.[249] Reduced mortality rates have been reported in patients with cardiovascular events who were at least overweight compared to their peers with normal weight.[250-252] It has also been reported that patients who were at least overweight had fewer chemotherapy-related toxicities compared to their peers with normal weight, while better outcomes were reported in schizophrenic patients on antipsychotics who intentionally gained weight.[253-254] However, it cannot be ascertained whether the overweight patients in this study had cancer or schizophrenia resulting in incurring less expenses as a result of fewer chemotherapy-related toxicities or as a result of better health outcomes relating to the management of schizophrenia. It is also possible that the insignificant association observed in healthcare costs between normal weight and obese patients was as a result of the demise of obese and morbidly obese patients who were more at risk of the harmful consequences of obesity and as such were not included in the study sample.

Among the covariates controlled for, the study results show that not having private insurance (having public insurance only or being uninsured), residing in the West belonging to other races apart from being white or black (mostly Asians), and having high physical and mental HRQoL scores were all associated with lower all-cause direct medical costs. It is logical that having public insurance or being uninsured is associated with lower medical costs as there is a stricter restriction in the amount and quality of healthcare received (if at all received) compared to having private insurance. The amount and quality of healthcare received may also be jeopardized as a result of the inability of patients to pay their share of the healthcare costs (co-pay or deductible) due to financial constraints.[244-245] Residing in the West has also been associated with lower costs. This is in line with reports from the CDC that stated that in 2012, Montana, Wyoming, Utah and Colorado (i.e., states in the West) had obesity prevalence rates between 20 and 25 percent (one of the lowest prevalence rate brackets in the US), while the rest of the West generally fell within the 25 to 30 percent prevalence rate bracket (a relatively low prevalence rate compared to the other regions).[255] There is a possibility that people who reside in the West are more health conscious and live more active lifestyles compared to other regions, hence spend less on medical expenses. Being Asian (this racial group is generally less likely to be obese) as compared to being white or black has been associated with lower medical costs. Plausibly, better health status (as reflected by higher physical and mental HRQoL scores) was associated with lower direct medical costs. Furthermore, higher CCI score and additional bed days were logically associated with higher medical costs, and being unmarried was also associated with lower costs. It is possible that spousal support improves health status which, in turn, is reflected by lower healthcare costs.[256-258]

5.3.5 Objectives 5 & 10 (hypothesis 12)

When the cost of productivity loss was assessed in both unadjusted (objective 5) and adjusted analyses (objective 10), it was observed that there was no significant difference between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. Not many studies have assessed the influence of BMI on indirect costs of diabetic patients; however, the influence of obesity was found significant in a few studies. Kannan et al. reported that obesity (defined as BMI> 27) was significantly associated with greater indirect costs when patients with comorbid hypertension, type 2 diabetes and high cholesterol were studied.[27] Sullivan et al. also reported significant indirect costs when lost productivity costs were assessed in patients with diabetes, dyslipidemia and hypertension;[219] however, these studies differ from the present study because of the definition of obesity in the former study and due to the fact that only costs for employed patients were assessed in the later (the present study utilized productivity costs that were lost as a result of restricted activity, caregivers costs, in addition to imputing housekeeping costs for unemployed patients below 65 years and caregivers).

Among covariates that were controlled for, it was observed that being older, female, having public insurance or not being insured, and not smoking were all associated with lower indirect costs. It is plausible that patients who are older than 64 years and their caregivers (often spouses) have lower productivity loss costs because more often than not, a significant proportion of this group of patients are retired and hence do not earn an income and have no loss in productivity (based on the human capital approach). It is also reasonable that non-smokers have significantly lower indirect costs since they are more likely to be healthier compared to their peers who smoke.[259-260] It is also possible that most patients with public insurance (for example Medicaid/ Medicare) or who are uninsured do not work or have low-income earning jobs and hence were assumed to earn little or nothing, hence reflecting on indirect costs.

Being unmarried and having higher CCI scores were significantly associated with higher indirect costs, being unmarried and being sicker (indicated by higher CCI scores) have been reported to result in higher costs.[256-258] Not being in the poor income category was also associated with higher indirect costs; a rational explanation for this finding may be that not belonging to poor income earning family suggests that more money is earned and this will translate to higher indirect costs when income, missed work days and additional bed days are taken into account for assessing productivity loss.

5.3.6 Objectives 6 (hypothesis 4) and 11 (hypothesis 13)

The results obtained from both the unadjusted (objective 6) and adjusted (objective 11) analyses when assessing the differences in total healthcare costs (all-cause direct medical costs plus indirect costs) between overweight, obese or morbidly obese diabetes patients compared to normal weight patients were similar to the all-cause direct medical costs. Overweight patients had significantly lower total healthcare costs compared to their peers who were of normal weight, while there were no significant differences in total healthcare costs between obese and morbidly obese patients compared to their peers with normal weight. Compared to the all-cause direct medical costs, it was observed that costs as a result of productivity loss were minimal (ranging between 3.9 and 5.2 % of total costs by BMI). Wolf and Colditz reported that productivity loss due to missed work days in the US population accounted for 3.9% of total (direct and indirect costs).[261] Hence, the observed results (similar to the all-cause direct medical costs) are logical since almost 95 percent of total healthcare costs in the present study were accounted for by the direct medical costs (all-cause).

As previously explained in the all-cause direct medical costs, it is possible that the presence of some amount of fat in overweight patients provides some level of benefit in regard to health outcomes in the treatment of some disease conditions. Meyerhardt et al. reported significantly fewer toxicity-related events in colon cancer patients who were at least overweight during chemotherapy.[253] Significantly better outcomes (in terms of survival) were reported in patients who were at least overweight who underwent coronary artery bypass grafting (CABG) compared to their peers with normal weight.[250-253] Poorer clinical outcomes were however reported in obese patients compared to their non-obese peers who underwent total knee arthroplasty.[262] Although these studies were focused on obese patients compared to their non-obese peers, it is also plausible that the obese and morbidly obese patients who could have had a significant influence on healthcare costs were already dead before the study sample was identified and could not be included in the analysis. It is also possible that these patients are muscular not overweight, even though their BMI may suggest that they are overweight.

With respect to covariates, similar to the results of objective 9, being of another race besides white and black, residing in the West, having public insurance only or being uninsured, having higher physical and mental HRQoL scores were significantly associated with lower total healthcare costs. Studies have suggested that the financial burden placed on patients with either public insurance or no insurance significantly influences whether or not they seek healthcare services; hence, resulting in lower total healthcare costs.[244-245] In addition, being unmarried, belonging to the near poor and high income households, having a higher CCI score and having higher number of additional bed days were significantly associated with higher total healthcare costs.[257-258] It is logical to consider that patients from high-income households are better able to afford healthcare services and are more likely to spend more on healthcare compared to their low income-earning peers. It is also reasonable that such patients have higher indirect costs when they miss work as a result of illness or restricted activity,[214] it is also possible that patients who are near poor are more often than not unable to pay for their healthcare and eventually spend more public funds when their health problems are addressed in the emergency room. Logically, sicker patients (indicated by higher comorbidity score and restricted activity) will have higher total healthcare costs compared to their healthier peers.[53]

5.3.7 Objectives 7(hypothesis 5) and 12 (hypothesis 14)

The results of the unadjusted analysis (objective 7) that assessed the differences in the number of ambulatory care visits made between overweight, obese or morbidly obese diabetes patients compared to normal weight patients showed that obese and morbidly obese patients made a significantly higher number of ambulatory care visits compared to their patients with normal weight, while there was no significant difference in the number of ambulatory care visits made between overweight patients and their peers with normal weight. Keating et al. reported that severely obese patients (BMI >35) had a significantly higher number of visits to general practitioners, psychiatrists and specialists compared to the general population.[263] Another study reported that obese patients (BMI≥27.9) had a significantly higher number of outpatient visits compared to their non-obese peers (BMI 18.5-24.9).[53]

However, it was surprising that the results of the adjusted analysis (objective 12) showed no significant difference in the number of ambulatory care visits made by morbidly obese patients compared to their peers with normal weight, while a significant difference was still observed with obese patients when compared with their peers with normal weight. However, it was observed that the sample size for the morbidly obese category was lower and the standard error was also distinctly higher compared to other BMI categories. It is also possible that other factors not included in the study may play a moderating role in the relationship between BMI status and the number of ambulatory care visits made. For instance, it is possible that morbidly obese patients had significant restrictions with mobility such that they were unable to make the required ambulatory care visits.

Among variables controlled for, being female, belonging to middle- or high-income households, having a higher CCI score, having a higher number of additional bed days and not smoking were significantly associated with a higher number of ambulatory care visits. It is possible that patients who belong to middle- or high-income households are both better educated (and informed about their health conditions) and also better able to afford the costs associated with ambulatory care visits compared to their poorer peers; hence, have higher number of ambulatory care visits.[214] Furthermore, it is logical that a higher CCI score and a higher number of additional bed days (usually used as proxy for disease severity) result in more ambulatory care visits;[53] hence, a patient with a higher CCI score and additional bed days is more likely to make more ambulatory care visits compared to peers with lower scores on these two variables. It was surprising that non-smoking patients had significantly higher number of ambulatory care visits. However, being non-white, residing in the South or West, being uninsured and having high physical and mental HRQoL scores were significantly associated with a lower number of ambulatory care visits. Being non-white (especially being Black) has been associated with the lower likelihood of making ambulatory care (office-based and hospital outpatient) visits even when there is a need for it.[216] Furthermore, it is logical to assume that patients who are uninsured and patients with good health status (indicated by higher physical and mental HRQoL scores) are less likely to make as many ambulatory care visits.[245]

5.3.8 Objectives 7 (hypothesis 6) and 12 (hypothesis 15)

The mean (±SE) number of ER visits made by the study sample was less than 1, that is, 0.3(0.01), and the unadjusted analysis (objective 7) showed no significant difference in the number of ER visits made between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. However, in the adjusted analysis (objective 12), overweight patients had a significantly lower number of ER visits compared to their peers with normal weight; there was no significant difference in the obese and morbidly obese patients compared to their peers with normal weight in the number of ER visits made. Although, Platts-Mills et al. reported that there was no significant difference in ER resource use between obese patients compared to their non-obese peers with abdominal pain, this study only focused on how obese patients differed compared to their non-obese peers.[264]

Plausibly, not smoking, and having better health status (in terms of high physical and mental HRQoL scores) were significantly associated with having a lower number of ER visits,[259-260] while a higher CCI score and higher number of additional bed days (indicators of disease severity) were significantly associated with a higher number of ER visits.

5.3.9 Objectives 8 (hypothesis 7) and 12 (hypothesis 16)

Objectives 8 and 12 addressed how healthcare use differed between overweight, obese or morbidly obese diabetes patients compared to normal weight patients in terms of the number of prescribed medicines obtained by the study sample. In both the unadjusted (objective 8) and adjusted (objective 12) analyses, the results showed that obese and morbidly obese patients had a significantly higher number of prescribed medicines compared to their peers with normal weight. This finding is supported by Keating et al. who reported a significantly higher number of prescribed medicines in the severely obese (BMI > 35) compared to the general population.[263] Raebel et al. also reported that obese patients (BMI ≥27.9) had a significantly higher number of prescribed medicines compared to their non-obese peers (BMI 18.5-24.9).[53] A study by Thompson et al. also concluded that the number of prescription medications of obese subjects were 84% more compared to their non-obese peers.[265] However, Ii is crucial to note that not only was their obesity classification different, these studies also did not focus on type 2 diabetes patients. Overall, a number of studies have reported a significantly higher risk of mortality and fewer years of healthy life in obese elderly adults compared to their non-obese peers and this conclusion implies that obese patients are more likely to use more healthcare resources (e.g., prescribed medicines and hospital visits) compared to their non-obese peers.[247-249, 266]

Being female, older than 64 years of age, having public insurance only, having a higher CCI score, additional bed days and being unmarried were significantly associated with a higher number of prescribed medicines. It is reasonable that older age (being at least 65 years of age), having a higher CCI score and additional bed days are associated with a higher number of prescribed medicines. Being uninsured and having high physical and mental HRQoL scores were significantly associated with a lower number of prescribed medicines. This finding suggests that uninsured patients are less likely to seek medical attention even when the need arises, while patients with better health status are less likely to consume more healthcare resources such as prescribed medicines.

5.3.10 Objectives 8 (hypotheses 8 & 9) and 13 (hypotheses 17 & 18)

Objectives 8 and 13 and their corresponding hypotheses addressed how the HRQoL scores (physical and mental component) differed between overweight, obese or morbidly obese diabetes patients compared to normal weight patients. In the unadjusted analysis (objective 8) of the physical component scores of the HRQoL, overweight patients had significantly higher scores compared to their peers with normal weight (PCS score difference=1.7[~2]) while morbidly obese patients had significantly lower scores (PCS score difference=5.4) compared to patients with normal weight. However, in the adjusted analysis (objective 13), it was observed that being at least obese was associated with significantly lower scores of the physical component of the HRQoL compared to normal weight patients. There was no significant difference in scores between overweight patients and their normal weight peers. These results suggest that being obese is significantly associated with poorer physical HRQoL and this finding is in line with the conclusion by Wong et al. who used the SF-12 to assess the impact of obesity on the HRQoL of type 2 diabetes patients in a Chinese population.[224] Doll et al. also reported that both moderately obese and morbidly obese patients had significantly poorer physical component scores on the SF-36 compared to patients who were at most overweight. In the European Male Ageing Study (EMAS), Han et al. reported that obese (BMI $\geq 30 kg/m^2$) men had significantly poorer physical, psychological and sexual functioning compared to their non-obese peers.[267] Furthermore, in their study involving type 2 diabetes patients who were either overweight or obese, using the SF-36, Rejeski et al. also found that the physical component scores of the HRQoL decreased with an increase in BMI; however, Rejeski et al. mentioned that due to the effect of other factors, this observed relationship may be highly inconsistent.[225] Rejeski at al. concluded that exercise tolerance (measured as Metabolic Equivalent [MET]) capacity and disease burden are important factors that moderate the relationship between the HRQoL physical component scores and BMI status. The present study observed that being female, older than 64 years of age, having a higher CCI score and additional bed days were significantly associated with lower scores for the HRQoL physical component. Plausibly a sicker patient (based on a higher comorbidity score and restricted activity) is more likely to have poorer health status as reflected in lower PCS scores compared to healthier peers. Rejeski et al. also reported that lower PCS scores were associated with being older and having several comorbidities in the LOOK AHEAD (Action for Health in Diabetes) trial study involving type 2 diabetic patients.[225] Also being non-white, belonging to middle- or high-income households and not smoking were significantly associated with higher physical scores in the present study.

For the mental component scores, both unadjusted (Objective 8) and adjusted (objective 13) analyses showed that overweight patients had significantly higher mental HRQoL scores compared to their normal weight peers (MCS score difference=1.98 [~2]) and significantly lower scores were observed for the morbidly obese compared to their normal weight patients (MCS score difference=1.96 [~2]) in the unadjusted analysis.

However, the significant difference in HRQoL mental scores observed between the morbidly obese and normal weight patients was no longer seen in the adjusted analysis. While a study reported high mental health scores in patients who were either overweight or of normal weight compared to their obese peers, another maintains that overweight persons are not more emotionally disturbed than their peers with normal weight. A number of studies have also suggested that there is no difference in psychological instabilities between obese and non-obese individuals.[177, 226, 268] However, a study by Le Pen et al. contends that obesity negatively affects patients' quality of life - specifically the physical well-being more than the mental state,[269] other studies suggest that the effect of obesity on mental health has been found to be significant in specific groups of obese people such as those who are binge-eaters or have other disease conditions like those that result in chronic pain.[226, 270] In line with the finding of the present study, a study by Diehr et al. concluded that overweight patients have significantly better mental health and quality of life compared to their peers with normal weight.[247] However, it should be noted that most studies were focused on assessing the difference in the HRQoL of patients who were obese compared to their non-obese peers, while the present study considered 4 BMI categories: normal weight, overweight, obese and morbidly obese categories.

Among the covariates controlled for, the present study observed that being black, being older (at least 65 years of age), belonging to middle- or high-income households and not smoking were significantly associated with higher mental HRQoL scores; while being female, having public insurance only or no insurance at all, having a higher CCI score and additional bed days were significantly associated with lower scores of the mental HRQoL scores. An earlier study concluded that poorer mental well-being is observed in females compared to men.[240] It is possible that there is a greater social pressure to be “slim” placed on females as compared to males; hence, negatively affecting their mental health.[268, 271-272] Rejeski et al. also agreed that lower mental scores were associated with younger age, and a lower income.[225]

Overall, a number of studies have associated significantly poorer HRQoL of patients with higher BMI, being older, female, single, without insurance or with public insurance such as Medicaid, higher number of comorbidities and lower income or lower education. [12, 15, 63, 70, 273-274]Using the Duke Activity Status Index (DASI), Hlatky et al. also concluded that there was a significant difference in the quality of life of obese type 2 diabetes patients (BMI ≥30) compared to their non-obese peers (BMI<30).[28]

Although statistical significance was widely reported in these studies, the importance of the study findings is dependent on its clinical significance. Based on the PCS and MCS scores of the SF-36 which has been reported to translate well into the PCS and MCS scores of the SF-12 version 2 used in the present study, a minimum clinically important difference of 2 points has been reported in the literature.[275-276] With the physical component scores of the HRQoL of overweight patients being 1.7 (~2) points higher and that of the morbidly obese patients being 5.4 points lower than normal weight patients respectively, it is appropriate to suggest that these differences are clinically significant.[275] Furthermore, the results of the study suggest that the difference in the mental component scores is clinically significant given that overweight patients had MCS scores that were 1.98 (~2) points higher and morbidly obese patients had 1.96 (~2) points lower for the morbidly obese patients compared to their peers with normal weight respectively. [276]

5.4 CONCLUSION

In summary, with respect to the management of type 2 diabetes, BMI status significantly relates with direct medical costs, it is possible that increased insulin resistance which has been associated with an increase in BMI and the corresponding increase in insulin sensitivity associated with weight loss suggests that obesity significantly increases the cost of managing the chronic disease. While the present study suggests that being overweight is associated with lower all-cause direct medical costs and total costs associated with type 2 diabetic patients, it is possible that other factors such as exercise tolerance and diet may moderate the relationship between BMI and healthcare costs. It terms of healthcare utilization, the present study agrees with a number of studies that obese patients have a significantly higher number of outpatient, inpatient visits and number of prescribed medicines compared to their non-obese peers. Hence, obesity is an important factor that needs be addressed in patients with type 2 diabetes if healthcare costs incurred due to increased healthcare resource utilization are to be curbed. With respect to HRQoL, it was observed that on average, overweight patients had significantly better mental health compared to their peers with normal weight while being at least obese was significantly associated with poorer physical health compared to non-obese patients.

Overall, the study suggests that among type 2 diabetes patients, being overweight (but not obese) may not necessarily have negative consequences but rather may be beneficial. The present study goes on to suggest that being obese is more associated with deleterious consequences compared to being at least normal weight. However, it is important to consider that while being overweight may not result in worse outcomes compared to those at normal weight, caution is required by the overweight not to cross the boundary set between the obese and non-obese. Hence, there is a need to address obesity in patients presenting with type 2 diabetes in order to improve health outcomes and significantly reduce healthcare costs and resource utilization in the management of the chronic disease- type 2 diabetes.

5.5 STUDY SIGNIFICANCE

To our knowledge, this is one of the few studies that assessed the relationship between BMI and medical costs (specific to type 2 diabetes and all-cause direct costs), indirect costs, total healthcare costs, healthcare resource utilization and the Health-Related Quality of Life of patients presenting with type 2 diabetes using a database that is representative of the non-institutionalized US civilian population.

5.6 SUGGESTIONS FOR FUTURE RESEARCH

1) The literature suggests that there may be other significant factors that influence the relationship between healthcare use, expenditures and the Health Related Quality of Life of patients with type 2 diabetes. It would be interesting to see how variables such as diet, lifestyle, and presence of diabetic complications influence this relationship using recent datasets that are representative of the US population.
2) Although the MEPS database could not be used to assess the relationship between BMI and healthcare use, expenditure and the Health Related Quality of Life of

pediatric patients (below 18 years) with type 2 diabetes, it may also be important to study this relationship using more appropriate databases for the pediatric population.

3) A longitudinal study may also be able to better explain particularly why overweight patients had significantly lower healthcare costs and utilization and HRQoL compared to their normal weight peers.

Appendices

APPENDIX A

The use of weights:

In order to ensure that estimates and standard errors obtained from the MEPS datasets are unbiased, weights are used. MEPS provides year-specific personal weight and variance estimates of variables for each subject.

Person weights

The person weights are derived after adjusting for the household selection probability, non-response from selected households and post-stratification to related estimates from the Current Population Survey (CPS). CPS estimates made by age, gender, race, census region, poverty status and Metropolitan Statistical Area (MSA) status are all controlled for in each panel. The resulting weights then form a composite after the individual panel weights have been multiplied by factors that correspond to their relative sample sizes. Finally, the population total is post-stratified on the composite weight variables: age, gender, race, census region, poverty status and MSA status.

The estimated sampling weights are obtained from weights derived from the NHIS sample weights after consideration has been given to the complex sampling design, including the disproportionate sampling that arises as a result of oversampling certain populations. MEPS has two types of weights, personal and household level weights; hence, national estimates can be calculated for both levels.

Job level files:

This provides a continuous timeline for each adult's employment history as full-year calendar information is required on their employer-provided health insurance. Demographic data as it relates to income are also obtained. Income data are also collected to determine a person's family socioeconomic status. Respondents are usually asked to use the previous year's federal income tax forms in obtaining this information to improve accuracy; however, income information is still obtained for those who did not file federal income taxes. Depending on the Current Population Survey (CPS), respondents' family income is placed in a poverty category after the family size and number of children has been factored in.

Disability Days Condition Questions

Other inquiries made include health problems that resulted in missed work or school days as well as health problems that caused a person to spend time in bed (this may be half a day or more).

The Medical Provider Component (MPC):

The MPC involves a survey of medical providers linked to the HC respondents. The information collected from the medical providers is usually information that could not be accurately confirmed from respondents, thus information obtained from the MPC supplements and validates the information in the HC. This includes hospital visitation dates, codes for both diagnoses and procedures carried out, as well as charges and payments. A pharmacy sub-component of the MPC contains information associated with drug details (National Drug Codes [NDC]), drug name, dosage, strength, dosage forms, date filled and the sources and amounts of payments to the pharmacy. Information on certain events may not be available in the MPC, especially in cases where participants do not grant consent to their medical providers or when providers simply refuse to participate in the surveys.

Insurance Component:

Since 1996, the Insurance Component, a yearly survey involving private and public sector employers, has been carried out nationally by the Census Bureau for the Agency for Healthcare Quality and Research (AHRQ). About 38,000 establishments are sampled from the private sector and are usually drawn from the Census's Business Register. The design used makes it possible to make state and national estimates. Information obtained from the private sectors are the company-level characteristics, its establishment-level features (such as the active staff size, whether health insurance is offered, the number of plans offered and number of employees who are eligible for health insurance (whether enrollment for full-time and part-time employees are separate)) and health insurance characteristics. Company characteristics that are considered include employment size, industry, age of company and provisions for retiree health insurance.

Nursing home component (NHC):

This component was included in the 1996 MEPS only and it provided nursing home information in terms of the residents, facilities, services provided, healthcare utilization and costs.

APPENDIX B: CHARLSON COMORBIDITY INDEX COMPONENTS, WEIGHTS AND THE D'HOORE ADAPTATION

Comorbid Conditions	**Weights**	**D'Hoore et al. codes**
Myocardial infarction	1	410, 411
Congestive heart failure	1	398, 402, 428
Peripheral vascular disease	1	440-447
Cerebrovascular disease	1	430-433, 435
Dementia	1	290, 291, 294
Chronic pulmonary disease	1	491-493
Connective tissue disease	1	710, 714, 725
Ulcer disease	1	531-534
Mild liver disease	1	571, 573
Diabetes	1	250
Diabetes with end organ damage		
Hemiplegia	2	342, 434, 436, 437
Moderate or severe renal disease	2	403, 404, 580-586
Any tumor	2	140-195
Leukemia	2	204-208
Lymphoma	2	200, 202, 203
Moderate or severe liver disease	3	070, 570, 572
Metastatic solid tumor	6	196-199
AIDS	6	

Adapted from:
Needham DM, Scales DC, Laupacis A, Pronovost PJ. A systematic review of the Charlson comorbidity index using Canadian administrative databases: a perspective on risk adjustment in critical care research. *J Crit Care*. 2005; 20(1):12-19
D'Hoore W, Bouckaert A, Tilquin C. Practical considerations on the use of the Charlson comorbidity index with administrative data bases. J Clin Epidemiol. 1996; 49(12):1429-1433

APPENDIX C: NEGATIVE BINOMIAL REGRESSION ANALYSIS OF NUMBER OF AMBULATORY VISITS BY BMI STATUS CONTROLLING FOR COVARIATES (SENSITIVITY ANALYSIS)

	Estimate	Standard Error	t	p-value	95% Confidence interval	
BMI status						
Overweight	0.03	0.05	0.52	0.6020	-0.0742	0.1277
Obese (30-34.9 kg/m^2)	0.14	0.05	2.77	0.006	0.0412	0.2418
Morbidly obese (≥35kg/m^2)	0.07	0.05	1.35	0.177	-0.0322	0.1744
Covariates						
Age category						
≥ 65 years	0.08	0.04	1.94	0.054	-0.0013	0.1668
Gender						
Female	0.09	0.04	2.18	0.030	0.0086	0.1701
Race						
Black	-0.15	0.05	-2.29	0.022	-0.2125	-0.0164
Other races	-0.21	0.05	-3.87	<0.0001	-0.3122	-0.1019
Geographical region						
Midwest	-0.06	0.05	-1.01	0.313	-0.1607	0.0517
South	-0.22	0.05	-4.74	<0.0001	-0.3115	-0.1290
West	-0.13	0.06	-2.16	0.031	-0.2383	-0.0113
Insurance status						
Public insurance only	-0.05	0.05	-0.98	0.326	-0.1354	0.0452
Not insured	-0.47	0.08	-6.00	<0.0001	-0.6284	-0.3184
CCI score	0.14	0.01	10.45	<0.0001	0.1162	0.1700
Poverty category						
Near poor	0.09	0.09	0.90	0.369	-0.1004	0.2698
Low income	-0.04	0.06	-0.61	0.540	-0.1487	0.0781
Middle income	0.12	0.06	2.14	0.033	0.0096	0.2248
High income	0.24	0.05	4.36	<0.0001	0.1301	0.3433

Appendix C (cont'd): Negative Binomial Regression analysis of number of ambulatory visits by BMI status controlling for covariates (sensitivity analysis)

Smoking status						
Does not smoke	0.26	0.05	5.53	<0.0001	0.1680	0.3531
Marital status						
Not married	0.05	0.04	1.15	0.251	-0.0341	0.1301
PCS-12 score	-0.03	0.002	-16.51	<0.0001	-0.0291	-0.0229
MCS-12 score	-0.01	0.002	-3.91	<0.0001	-0.0090	-0.0030
Additional bed days	0.001	0.001	2.07	0.039	0.0001	0.0023

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status: no smoking; insurance status: private insurance; SES: poor; census region: Northeast

F (22, 368)=41.91; p<0.0001 *Significant at p<0.05

PCS-12[Physical Component Summary] and MCS-12 [Mental Component Summary] scores reflect on subjects' health status and higher scores indicate better HRQoL

APPENDIX D: MULTIVARIATE REGRESSION ANALYSIS OF MENTAL COMPONENT SUMMARY (MCS-12) HRQOL SCORES BY BMI STATUS CONTROLLING FOR COVARIATES (SENSITIVITY ANALYSIS)

	Estimate	Standard Error	t	p-value	95% Confidence interval	
BMI status						
Overweight	1.03	0.50	2.07	0.0390*	0.0523	2.0038
Obese (30-34.9 kg/m^2)	0.55	0.55	0.99	0.3220	-0.5361	1.6294
Morbidly obese (≥35kg/m^2)	-1.00	0.64	-1.96	0.0510	-1.4194	0.0033
Covariates						
Age category						
≥ 65 years	2.66	0.37	7.13	<0.0001*	1.9241	3.3887
Gender						
Female	-0.71	0.36	-1.96	0.0510	-1.4194	0.0033
Race						
Black	1.20	0.43	2.75	0.0060*	0.3400	2.0341
Other races	-0.64	0.63	-1.03	0.3040	-1.8744	0.5857
Geographical region						
Midwest	0.76	0.61	1.24	0.2140	-0.4427	1.9664
South	0.38	0.54	0.69	0.4910	-0.6947	1.4460
West	-0.07	0.64	-0.12	0.9080	-1.3222	1.1747
Insurance status						
Public insurance only	-3.33	0.43	-7.81	<0.0001*	-4.1728	-2.4945
Not insured	-2.01	0.64	-3.12	0.0020*	-3.2750	-0.7453
CCI score	-0.50	0.15	-3.34	0.0010*	-0.7994	-0.2068
Poverty category						
Near poor	1.15	0.73	1.57	0.1180	-0.2903	2.5825
Low income	0.65	0.62	1.06	0.2920	-0.5604	1.8592
Middle income	2.53	0.57	4.47	<0.0001*	1.4189	3.6431
High income	3.87	0.60	6.50	<0.0001*	2.6978	5.040

Appendix D (cont'd): Multivariate Regression analysis of Mental Component Summary (MCS-12) HRQoL scores by BMI status controlling for covariates (sensitivity analysis)

Smoking status						
Does not smoke	1.63	.46	3.55	<0.0001*	0 .7252	2.5287
Marital status						
Not married	-0.50	0.39	-1.29	0.1990	-1.2699	0.2653
Additional bed days	-0.07	0.01	-12.19	<0.0001*	-0.0841	-0.0607

Reference groups= BMI status: normal weight; age category: 18-64 years; gender: male; race: white; marital status: married; smoking status smoking; insurance status: private insurance; poverty category: poor; census region: Northeast

F (20, 370)=34.35; p<0.0001 *Significant at p<0.05

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Vita

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