ANALYSIS OF GEOGRAPHIC PATTERNS IN MODIFIABLE RISK FACTORS IN PEOPLE WITH DIABETES

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Diabetes is a complex chronic disease with many causes, complications and management needs. It affects a large proportion of people of varying ages, income levels, races/ethnicities and geographic areas. Approximately 7.0% of Pennsylvanians have been diagnosed with diabetes. Diabetes is a major public health challenge due to the enormous impact on the affected individual, their families and the health care system. However, recent research has shown that diabetes related mortality and morbidity can be prevented or delayed by controlling risk factors. Certain environmental aspects play an important role in the prevention and treatment of chronic diseases such as diabetes. In order to provide the public health community with another tool to enhance our understanding of the factors that affect the numbers and types of diabetes cases in Pennsylvania, it is important that we undertake a project that will support the analysis of geographic distribution in terms of associated risk factors.

This study proposes to investigate geographical patterns of diabetes hospitalizations, risk factors for diabetes complications and glycemic control among individuals with type 2 diabetes in predominantly rural regions. Residents of more rural counties are 11% more likely to be hospitalized for uncontrolled diabetes compared to those living in areas that are less rural for every increase in rurality ranking after adjusting for individual and community level factors. Furthermore, we demonstrated that there is a clear association between the presence of food stores, food service places, and health care locations with risk factors for diabetes complications

among individuals with diabetes. Our findings also indicated that those who live more than ten miles from their diabetes management center are 88% more likely to have an HbA1c level greater than 7.0% compared to those who live less than ten miles from their center, adjusted for individual-level and community level factors. Results demonstrated that for every mile the subjects live from their diabetes management center, they are 2% more likely to have an HbA1c level greater than 7.0%. This dissertation was able to demostrate a clear association between the built environment and diabetes hospitalizations, risk factors for diabetes complications and glycemic control among individuals with type 2 diabetes in rural regions.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PREFACE

I would like to take this opportunity to acknowledge the many individuals who have contributed to both this work and my development as an epidemiologist. I would like to thank everyone at the University of Pittsburgh Diabetes Institute for all of their help and support over the past four years.

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1.0 INTRODUCTION

Diabetes is a group of diseases marked by high levels of blood glucose resulting from defects in insulin production, insulin action, or both. Diabetes can lead to serious complications and premature death, but people with diabetes can take steps to control the disease and lower the risk of complications (1). Pre-diabetes is a term used to describe people who are at increased risk of developing diabetes. People with pre-diabetes have impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). Some people may have both IFG and IGT. IFG is a condition in which the fasting blood sugar level is elevated after an overnight fast but is not high enough to be classified as diabetes (5). IGT is a condition in which the blood sugar level is elevated after a two hour oral glucose tolerance test, but is not high enough to be classified as diabetes. Progression to diabetes among those with prediabetes is not certain. Studies suggest that weight loss and increased physical activity among people with prediabetes prevent or delay diabetes (5).

Diabetes is becoming more common in the United States. From 1980 through 2007, the number of Americans with diabetes increased from 5.6 million to 17.9 million (2). It is estimated that another 5.7 million Americans are undiagnosed (2). Approximately 762,000 or 7.3% (age-adjusted) of Pennsylvanians have been diagnosed with diabetes and is responsible for nearly 4,000 deaths in Pennsylvania (6).

Diabetes is a major public health challenge due to the enormous impact on the affected individual, their families and the health care system. However, recent research has shown that diabetes related mortality and morbidity can be prevented or delayed by controlling risk factors (7).

Certain environmental aspects play an important role in the prevention and treatment of chronic diseases such as diabetes. Studies have shown that access to health care, diet, physical

activity, housing, income, and environmental exposures contribute to diabetes, which are all part an individual's environment or community (4). While there are many ways to define community, geographic location is one important way to understand the context in which people live. Until recently, there has not been a valid method for defining and analyzing geographic areas that make up a community where these risk factors and chronic diseases may cluster. Geographical modeling may allow for better identification of the geographic area of communities that provide risk for diabetes. There is great variability in the health and well being of residents depending upon where they live. Health-promotion interventions may need to be designed to target the geographic areas that represent clusters of health problems and unhealthy lifestyles.

Geographical Information Systems (GIS) may allow investigators to conduct spatial analysis that can to be used to increase comprehension of chronic disease pathogenesis. First, geographical studies may suggest possible causal factors based on geography and play an important role in the understanding of the development and control of diabetes (3). Associations between disease and place imply that the population living there possesses inherent traits that make it more susceptible to disease. However, it has been shown that there are certain risk factors that cluster in these areas that cause increased risk for disease. Second, spatial analysis can help identify how populations adapt and relate to their environment (3).

Type 2 diabetes is preventable and can be controlled with intervention. However, some areas may not have resources that would enable its residents to lead a healthy lifestyle. Geospatial mapping techniques can be used to show areas with higher prevalence of diabetes and where funds need to be targeted. Geospatial analysis tools can be used to discover and analyze cause and affect relationships based on geographic proximities. These maps can provide

important clues about the geographic variability of risk factors, disease states and clinical services utilization.

The objective of this thesis is to investigate geographical patterns of diabetes prevalence and to identify risk factors for diabetes and its complications among rural regions. Geographic data will be used to find the geographic distribution of diabetes prevalence in rural Southwestern Pennsylvania. More specfically, this geographic representation will then be juxtaposed with a variety of potentially related geographic, economic, and health risk factors. Geospatial analysis tools can be used to discover and analyze cause and effect relationships based on geographic proximities. This thesis will assess geographic variation and prevalence of diabetes in this area, assess physical accessibility to healthcare, fitness and nutritional facilities as well as access barriers of economic, social, and cultural nature for diabetic residents of rural western Pennsylvania. Finally this thesis will determine areas that are underserved and potential locations for health care facilities.

2.0 DIABETES MELLITUS

Diabetes Mellitus is a group of disorders described by abnormally high blood glucose levels due to either insulin deficieny or resistance of the body's cells to the action of insulin (7). There are two central types of diabetes. Type 1 diabetes is the third most prevalent chronic disease of childhood and is an autoimmune disease that develops when the body's immune system destroys pancreatic beta cells responsible for making insulin (2). In contrast, type 2 diabetes is characterized by the failure of the pancrease to secrete an adequate amount of insulin (2).

2.1 TYPE 1 DIABETES

2.1.1 Epidemiology

Type 1 develops predominantly in children and young adults, but may appear in all age groups (8). Type 1 diabetes accounts for roughly 5% to 10% of all diagnosed cases of diabetes (2). About one in every 400 to 600 children and adolescents has type 1 diabetes. Recently, considerable research has focused on determining the incidence of type 1 diabetes in children. It has been estimated that the yearly incidence of Type 1 diabetes ranges from 0.6 per 1,000 to 2.5 per 1,000. Using this estimate, there are nearly 123,000 individuals under 19 years old in the United States with Type 1 diabetes. The incidence of type 1 diabetes among children under 19 years old in Allegheny County, PA is 18.2 per 100,000/year (9). There is less information of the prevalence of this disease, but it is estimated that approximately 400,000 Americans have this type of diabetes (1).

2.1.1.1 Race/Ethnicity and Gender Variation

There are clear differences in race/ethnicity and gender in the incidence of type 1 diabetes. When examined nationally, the highest incidence of type 1 diabetes was among non-Hispanic Caucasians and Hispanic individuals, followed by African American and Mexican-American children (10). Incidence rates for females and males are comparable, although females have a slight excess in low-risk populations such as the Japanese (11). However, in areas such as Finland, where there is a high-risk, an excess risk for males was detected.

Gender does not appear to be a significant determinant of type 1 diabetes, since incidence rates are similar for males and females (26). The age distribution at onset for type 1 diabetes is also generally consistent across populations, with a slight peak occurring at roughly 5 years old in males and a larger peak is seen in both sexes occurring near puberty (26). This age pattern may be due to exposure to infectious agents during childhood, growth spurts, or hormonal changes that occur in adolescence. The risk of type 1 diabetes increases with age during childhood and adolescence.

2.1.1.2 Temporal and Seasonal Trends

It has been revealed that the onset of type 1 diabetes occurs in seasonal and temporal patterns (10). Type 1 diabetes is a worldwide disease but occurs with considerable geographical and ethnic variations. The incidence of type 1 diabetes shows a steady increase in its frequency during the last few decades, corresponding in some instances to an estimated doubling in incidence per generation (8). The incidence of Type 1 diabetes is characterized by extensive differences between populations, from 0.7/100,000/year in Peru to 45/100,000/year in Finland in 1996. The incidence is increasing in many populations; in Finland, England, Norway, Israel, Austria, and several other countries. In Finland, the incidence has more than tripled from 1953,

when it was 12/100,000/year, with an average increase of 2.4 percent per year (8). The greatest incidence is identified in Nordic countries, particularly in Finland, as compared to the rest of Europe. The geographical pattern is not a simple north to south incidence gradient but in fact there are sharp differences between neighboring regions. Despite its ethnic and cultural similarities with Finland, Estonia has an incidence of only one-third that in Finland (8). Conversely, the Russian population residing in Estonia presents a disease risk less than that of the native Estonians. So far, the reasons for the wide variation in the risk of Type 1 diabetes in Europe are unknown, and the power of genetic variation and environmental factors has yet to be established (8). Some researchers have tried to explain the changing incidence of environmental factors, such as breast-feeding habits, but no obvious explanations have yet been identified (8). On the other hand, the increasing frequency cannot be attributed to improved survival and reproductiveness among type 1 diabetes patients. Some studies found a correlation between apparent leveling off in the increase in incidence with a decline in the occurrence of mumps antibodies in newly diagnosed type 1 diabetes children due to the introduction of the mumps, measles, rubella vaccine. This suggests that the temporal variations in the incidence of type 1 diabetes can be modified, and that the geographical distribution of the disease may change in the future due to the implementation of health promotion programs (8).

Additionally, there is a seasonality of type 1 diabetes onset, and it is diagnosed more often during the winter and fall months, particularly during puberty (11). Since type 1 diabetes is an autoimmune disease and the destruction of the beta cells starts several years before the clinical onset, the seasonality probably reflects the importance of certain environmental precipitating factors, such as viral infections (8). However, there is not evident explanation for why this pattern exists. More research dedicated to identifying non-genetic determinants of type

1 diabetes is of great importance as these are potentially modifiable with the aim of disease prevention.

2.1.1.3 Geographic Variation

Type 1 diabetes is a world-wide disease but occurs with considerable geographical variations. The geographical variation demonstrated in the incidence of type 1 diabetes makes is one the largest observed for a noncommunicable disease (10). The greatest incidence is identified in Nordic countries, particularly in Finland, as compared with the rest of Europe (8). Overall, Europe encompasses a less than 10-fold difference in incidence annually, ranging from roughly 35 new cases in Finland (12) to two to three new cases in Macedonia (13) per 100,000 children aged 0-14 years. The geographical pattern is not a simple north to south incidence gradient but in fact there are sharp differences between neighboring areas. For example, Sardinia has an incidence of diabetes approaching that of Finland and which is several times greater than the rest of Italy (13). Another region of contrast is Estonia; despite its ethnic and cultural similarities with Finland, it has an incidence of only one-third that in Finland. Conversely, the Russian population residing in Estonia presents a disease risk less than that of the native Estonians (8). In the majority of other Caucasian populations in Europe and North and South America, incidence rates are moderate. Much of this variation can be due to the genetically heterogeneous population in the United States, compare to a very homogenous population in many of the Asian countries (10). The lowest incidence rates are seen in the Asian countries such as Japan, China and Korea. The Native American, Chilean, Cuban and Mexican populations have very low rates of type 1 diabetes (10). The reasons for this variation in the risk of type 1 diabetes in Europe are unknown, and the strength of genetic variation and of environmental factors has yet to be discovered.

2.1.2 Etiology

There are many hypotheses regarding the etiology of type 1 diabetes. In addition to the geographical variation in the incidence of childhood type 1 diabetes, there are also well-documented secular trends over time, which may also differ from country to country and from region to region within a country. Potential risk factors which may initiate the autoimmune process include early fetal events such as blood group incompatibility (12), maternal viral infections during pregnancy, (13,14) and early exposure to cow's milk components and other nutritional factors such as nitrosamines (15). Population-based case-control studies have identified some protective factors, including a long duration of breast feeding (15), early vitamin D supplementation (16), pre-school day care (as a proxy measure of infections) (17) and atopic diseases (18).

Since type 1 diabetes in childhood is associated with estimates of general wealth such as gross domestic product (19) it has been suggested that lifestyle habits related to welfare might be responsible for the changes in trend. Wealth is a well-known determinant of birth weight and childhood growth.

Different estimates of child growth such as high birth weight, an increased height, weight, weight for height and body mass index (BMI) have repeatedly been shown to be risk factors for childhood onset diabetes (20). Rapid growth is associated with high growth hormone levels and an increased number of fat cells both leading to insulin resistance and thereby an overloading of the beta cell. Although autoimmune mechanisms are responsible for the beta cell destruction leading to type 1 diabetes, overload factors may accelerate this process (21,22). Overload through accelerated child growth and body fat accumulation in association with a lifestyle with a low physical activity are potentially preventable risk factors. These are examples

of the substantial evidence that both genetic and environmental factors are major factors in the etiology of type 1 diabetes.

2.1.2.1 Genetics

Islet cell antibodies, insulin and glutamic acid decarboxylase antibodies, markers of autoimmune disease, may be detected in the circulation some years before the clinical onset of type 1 diabetes, providing a tool for individual assessment of subsequent risk of overt disease (8). Type 1 diabetes clusters within families; it is estimated that the risk of developing the disease in siblings and children of type 1 diabetes patients is approximately 5-10%, compared with about 0.5% in the general population (23). More than 80% of cases of type 1 diabetes occur in individuals without a family history of the disease. However, in the remaining 20%, type 1 diabetes runs in families (26). The risk is smaller for the children of women with diabetes than the children of men with diabetes, and the risk of type 1 diabetes in children seems to be increased with advancing maternal age (23). Such differential risk patterns probably reflect selection due to particular features in the reproductive capacity of type 1 diabetes women rather than genetic mechanisms.

Much of the data on risk of type 1 diabetes in family members are from Caucasian populations that have similar incidence rates (26). In Allegheny County, PA, there was a lower risk for developing type 1 diabetes in siblings of African-American type 1 diabetes patients compared to Caucasians (2.8% versus 6.5% through age 30 years) (27). In Caucasian populations, strong type 1 diabetes associations are found in the serologically determined HLA markers DR3 and DR4, the heterozygous state DR3/DR4 and the genes which encode them at the HLA-DQ loci on chromosome 6 (24). The HLA is a set of genes referred to as the Major Histocompatability Complex (MHC), and it controls many aspects of immune system functions.

In recent studies of data from three previous genome-wide scans (United States, United Kingdom, and Scandinavia) as well as new families collected for Type 1 Diabetes Genetics Consortium, 1435 multiplex families provided evidence for linkage of type 1 diabetes to the MHC, insulin, a region that contains several genes, including CTLA4 and seven other chromosome regions (25).

HLA studies of type 1 diabetes are focusing on the DNA level in populations across the world. Analyses in a variety of racial and ethnic groups have revealed that DNA sequences in the DQB1 gene coding fro the presence of an amino acid other than aspartic acid in the 57^{th} position (non-Asp-57) is highly associated with developing type 1 diabetes (26). This association is much stronger than the association between type 1 diabetes and HLA-DR3 and DR4.

Immunogenetic studies have been conducted in areas where the incidence rates are geographically diverse including China, Norway, Sardinia, Italy; and African Americans and Caucasians in Allegheny County, PA (26). These studies showed that the prevalence of the DQB1 *non-Asp-57 genotypes vary significantly in individuals with type 1 diabetes from these five areas (from 6% in China to 100% in Sardinia), as well in non-diabetic individuals (from 0% in China to 38% in Sardinia), with an increase in non-Asp-57 homozygosity in regions with a high incidence of type 1 diabetes (26). For Allegheny County Caucasians, the incidence rate for type 1 diabetes was highest for non-Asp-57 homozygotes (47.6 per 100,000 per year), intermediate for heterozygous individuals (13.0 per 100,000/year), and lowest for Asp-57 homozygotes (0.45 per 100,000/year), suggesting a does-response relationship between susceptibility and type 1 diabetes risk (26).

If the geographic differences in risk of type 1 diabetes are due to variation in genetic susceptibility to the disease, then incidence rates for diabetes should be similar in individuals with the same genotype across populations. One study applied the genotype-specific incidence rates for Allegheny County Caucasians to the other four populations to predict the overall type 1 diabetes incidence rate for each area. Each predicted rate fell within the 95% confidence intervals for the rates established through type 1 diabetes registries (26).

The DQA1 and DQB1 genes are important in deciding susceptibility to type 1 diabetes (28). The risk of developing this type of diabetes seems to be increased for people who are homozygous for both DQB1 *non-Asp-57 and DQA * Arg-52 alleles. In addition, at least two-thirds of the incidence of type 1 diabetes can be explained by the contribution of these high-risk genes in most populations (26). Conversely, people wiho are heterozygous at one of the genetic loci have a risk for type 1 diabetes that is similar to that for the general population.

2.1.2.2 Environmental Triggers

Several lines of evidence support a critical role of exogenous factors in the pathogenesis of type 1 diabetes. Studies in monozygotic twins indicate that only 13-33% are pairwise concordant for type 1 diabetes (29), suggesting that there is either acquired post-conceptional genetic discordance or differential exposure to the putative environmental factor (30). Migrant studies have been used sparingly in epidemiological studies of type 1 diabetes. However, available data demonstrates that the incidence of type 1 diabetes has increased in population groups who have moved from a low-incidence area to a high-incidence region, emphasizing the influence of environmental conditions (31). Accumulating evidence suggests that the proportion of individuals with high-risk HLA genotypes has decreased over the last decades among patients

with newly diagnosed type 1 diabetes, whereas the proportion of individuals with low-risk genotypes has increased (30).

In order to define the characteristics of the trigger(s) of beta-cell autoimmunity, many researchers have observed patients with increased HLA-conferred susceptibility to type 1 diabetes prospectively from birth, with frequent follow-up visits (30). These studies have demonstrated that there is an unequivocal temporal variation in the appearance of the first diabetes-associated autoantibodies reflecting the initiation of the disease process and paralleling the seasonal variation previously noted in the presentation of clinical diabetes (30). The pattern of the autoantibody appearance strongly points to the role of infectious agents with conspicuous seasonal variation as triggers of beta-cell autoimmunity. Such variations are typical for viral infections (30). Strong arguments have been made for the role of exposure to the Coxsackie B virus. Coxsackie viruses have been isolated from the sera of persons with newly diagnosed type 1 diabetes. Although it is unknown whether the virus may initiate or accelerate beta-cell destruction (26).

Persistent viral infections as possible triggers of autoimmune disease have recently gained more attention (26). The incorporation of human cytomegalovirus (CMV) gene segments into genomic DNA has been significantly associated with type 1 diabetes in recently diagnosed individuals (37), and a relationship between CMV genome positivity and islet cell antibodies has also been reported (38,39). Further research is needed to confirm these findings.

Congenital rubella syndrome (CRS), which results from maternal exposure to the virus causing measles during pregnancy, has been associated with the development of type 1 diabetes. Nearly 20% of CRS patients in the United States also have type 1 diabetes (38). It has been

hypothesized that exposure to rubella infection *in utero* triggers an autoimmune mechanism in genetically susceptible people, resulting in type 1 diabetes (38).

Several studies have found a temporal relationship between mumps virus infection and the development of type 1 diabetes (40). However, studies attempting to validate this observation have met limited success. The incidence of type 1 diabetes parallels that of mumps, after allowing for a four-year lag period in Erie County, NY, and approximately 50% of children with type 1 diabetes in this population had mumps or exposure to mumps roughly four years prior to onset of diabetes (40). As with the Coxsackie virus, it has been hypothesized that a particular variant of the mumps virus along with genetic susceptibility is necessary for diabetes onset. However, if mumps is a determinant of type 1 diabetes, it is likely to only be a small proportion of cases (26).

In addition to viral infectious, one should also consider other environmental variables with seasonal variation. There is seasonal variation in the amount of daylight hours, especially in Northern Europe, which the highest incidence of type 1 diabetes in the world. The sunlight-dependent synthesis of vitamin D in the skin is the most important source of this immunologically active hormone. Some studies have indicated that the lack of oral vitamin D substitution in infancy increases the subsequent risk of type 1 diabetes (31). However, there is a general recommendation that all young children should take daily vitamin D drops in Northern Europe, and this recommendation is implemented by more than 95% of parents, at least in children up to two years in age (30); and there are regions with a low type 1 diabetes incidence rate in Northern Europe such as Russian Karelia, having an annual incidence rate of 7.8/100,000 children under 15 years (1990-1999) (30).

Various nutritional practices have been associated with the development of type 1 diabetes. Data from three population-based case-control studies on cow's milk intake before diagnosis of type1 diabetes are conflicting. Verge et al. (32) reported that the cow's milk intake had been higher in pre-diabetic children than in control children in New South Wales, Australia. In a nationwide Childhood Diabetes in Finland (DiMe) study, a high consumption of cow's milk in childhood was associated with a more frequent appearance of diabetes-associated autoantibodies and type1 diabetes in a prospective cohort of initially unaffected siblings of children with type 1 diabetes (33). On the other hand, a Swedish retrospective survey showed that the frequency of milk intake had been lower among children who developed type 1 diabetes than among unaffected children (34). The evidence in favor of the role of bovine insulin as a driving antigen in the disease etiology is relatively fragmentary, and further research is clearly needed to confirm or exclude this hypothesis. Bovine insulin is definitely present in cow's milk, although the structural components of immunoreactive insulin are poorly characterized in milk (30).

Gluten proteins have been implicated as potential driving antigens in type 1 diabetes. Type 1 diabetes and celiac disease are both HLA associated autoimmune diseases. Two small intervention studies have been performed in family members testing positive for diabetes-associated autoantibodies to assess whether gluten elimination modifies the natural course of beta-cell autoimmunity (30). In one trial, seven autoantibody-positive first-degree relatives were placed on a gluten-free diet for 12 months followed by gluten re-exposure over the next 12 months. The autoantibody titers did not change significantly during the gluten-free intervention period or during the re-exposure period (35). Seventeen family members testing positive for at least two diabetes-associated autoantibodies were put on a gluten-free diet for another six months

in the Italian trial (36) and again on a normal diet for six months. This trial indicated that a gluten-free diet has no effect on the signs of beta-cell autoimmunity in first-degree relatives of affected individuals, but such a diet may increase the endogenous insulin secretion in family members at increased risk of type 1 diabetes (36).

Theoretically, a dietary antigen would fit well into the role as the factor driving the disease process toward clinical type 1 diabetes, since the exposure to most dietary factors tends to be frequent, and still there is some variation in the exposure both within and across populations. Bovine insulin is an attractive candidate, since an immune response initially induced by bovine insulin will cross-react and may target human insulin in the beta-cell (30).

2.1.2.3 Other Potential Risk Factors

Other potential risk factors for type 1 diabetes include maternal age, birth order, stress, and socioeconomic status. Some studies of stress and type 1 diabetes have reported positive associations, although most studies have been retrospective and suffered from methodological difficulties in assessing stress and measuring its frequency and duration (41, 42). Factors such as maternal age at birth and higher birth order have also been associated with increased type 1 diabetes risk. Several investigations have reported a higher prevalence of diabetes in children born to older mothers and in children with a higher birth order (43, 44). These studies concluded that of the two related potential determinants of type 1 diabetes risk, higher maternal age (age greater than 35 years at child's birth) was the more significant risk factor. An explanation for this association is unclear, but it has been suggested that it may be related to the intrauterine environment.

There have been a few studies on socioeconomic status (SES) as a risk factor for type 1 diabetes. In northern England, type 1 diabetes incidence rates were highest in the lower SES

areas and the lowest in the areas with a higher SES (46). However, another study reported conflicting results, with higher incidence rates in affluent areas (45).

This evidence demonstrates that there are numerous potential factors involved in the etiology and epidemiology of type 1 diabetes. This also proves that there is a need for future studies on the etiology for greater advances in the prevention of type 1 diabetes.

2.2 TYPE 2 DIABETES

2.2.1 Epidemiology

Type 2 diabetes mellitus (T2D) is the most common form of diabetes. Population studies based on standardized methods and diagnosis have shown great variation in the frequency of the disease, and prospective studies have provided new insights into its associated risk factors and its pattern of development (8). T2D, previously called non-insulin-dependent diabetes mellitus or adult-onset diabetes, usually begins as insulin resistance, in which target tissues do not use insulin properly. T2D is distinguished by the body's inability to efficiently use insulin that is produced by the pancreas. It is characterized by chronic hyperglycemia, reduced insulin response, insulin resistance, and an increase in hepatic glucose output. It accounts for approximately 90% to 95% of all diagnosed cases of diabetes (40). Uniform diagnostic criteria for diabetes were first recommended by the American Diabetes Association and the World Health Organization in 1979 and 1980 and were updated in the late 1990s (41). Currently, when typical symptoms of diabetes are present (for example, polyuria, polydipsia, or unexplained weight loss), a casual plasma glucose level of 11.1 mmol/L (200mg/dL) or greater confirms the diagnosis. Furthermore, the diagnosis can be made with a fasting plasma glucose level of 7.0

mmol/L (126 mg/dL) or greater or an oral glucose tolerance test with a 2-hour value of 11.0 mmol/L or greater (41). For epidemiologic studies, a single fasting plasma glucose or 2-hour oral glucose tolerance test measurement is used to estimate the prevalence of diabetes in a population.

The symptoms of T2D may develop gradually over time. Some individuals could be asymptomatic, while others suffer from one or a combination of symptoms such as nausea, fatigue, weight loss, blurred vision, frequent infections and slow healing of wounds (12). Harris, et al. argues that the onset of T2D may occur between nine and twelve years before its clinical diagnosis. This was demonstrated in their research by the fact that the onset of detectable retinopathy occurred four to seven years before diagnosis of type 2 diabetes in two population-based groups of Caucasian patients with type 2 diabetes in the U.S. and Australia (89). Harris and his colleagues concluded that significant morbidity was present at diagnosis and for years before diagnosis of T2D.

Currently, three national surveys track diabetes prevalence in the United States. The National Health Interview Survey and National Health and Nutrition Examination Survey (NHANES) use national population-based samples and query persons in face-to-face interviews about whether they have been told by their health care provider that they have diabetes. The third survey, the Behavioral Risk Factors Surveillance System (BRFSS), asks a similar question of state-based population samples during telephone interviews of residents. NHANES includes a laboratory-based examination that measures glucose levels and identifies persons with undiagnosed diabetes (40). All three surveys provided national estimates of prevalence of diagnosed diabetes.

In 2002, an estimated 6.3% of the U.S. population (about 18.2 million people) had diabetes (40). There are also nearly 800,000 new cases of type 2 diabetes diagnosed each year. In addition, for every two diagnosed cases of type 2 diabetes, there is one undiagnosed case (41). According to data from the National Health Interview Survey, persons 65 years of age or older make up almost 40% of all persons with diagnosed diabetes, and the prevalence in this age group is more than ten times that in individuals younger than 45 years of age (40). Minority race and ethnic groups, including Black, Hispanic, and Native American persons, are disproportionately affected; the prevalence of diagnosed diabetes is generally two to four times higher in these groups than in the majority population (40). Because of changing demographic factors, by the year 2010, it was been projected that the number of people with T2D will double (42). The prevalence of T2D varies enormously from population to population throughout the world (8). The highest rates are recorded in Pima Indians, but also in the Micronesian population living on Nauru Island in the Central Pacific. Proportions in different ethnic groups living in the same country may vary considerably (8). Rates differ in migrants as compared with natives remaining in their own country. Moreover, the ratio in migrants is greater than in the indigenous population, and these increases appear to be related to rapidly changing lifestyles (8). The prevalence is parallel with rapidly developing countries and among underprivileged individuals in developed nations.

The National Health Interview Survey found a four to eight-fold increase over the last half-century in the number of persons who received a diagnosis of diabetes (1.6 million in 1958 and 12.1 million in 2000) and the prevalence of diagnosed diabetes in the United States (40). Increases occurred across all demographic categories, including sex, race or ethnicity, and age. Between 1990 to 2001, data from the Behavioral Risk Factors Surveillance System indicate that

the largest relative increases in diagnosed diabetes occurred in persons 30 to 39 and 40 to 49 years of age (95% and 83%, respectively); increases in other age groups were 40% in persons 18 to 29 years of age, 49% in persons 50 to 59 years of age, 42% in persons 60 to 69 years of age, and 33% in persons 70 years of age or older (41). These increases can be seen in the incidence rates described below in Table 2.0 (213). In the 1990s incidence began to increase in all age groups. During the 2000s, incidence continued to increase among those aged 18-44 years but in the tow older age groups, the rate of increase in incidence appeared to have slowed (213).

Table 2.0 Incidence of Diagnosed Diabetes per 1,000 Population Aged 18-79 Years, by Age, United States, 1990-2007

Year	18-44 Years Old	45-64 Years Old	65-79 Years Old
	Incidence/1,000	Incidence/1,000	Incidence/1,000
1990	2.0	6.0	6.0
2001	2.9	11.4	11.8
2007	4.4	11.7	12.5

The NHANES found that diabetes is undiagnosed in approximately one third of all persons with diabetes and that this fraction has changed little over time. Many factors have affected these increases in the prevalence of diabetes, including changes in diagnostic criteria, improved or enhanced detection, decreasing mortality, changes in demographic characteristics of the population and growth in minority populations in whom the prevalence and incidence of diabetes are increasing (40).

2.2.2 Etiology

Type 2 diabetes is a heterogeneous disease considered to be the result of a combination of genetic factors and external/environmental exposures. External exposures may include reduced

physical activities or increased fat consumption. The result of reduced physical activity and increased caloric intake is the basis for obesity and the rise of type 2 diabetes (30).

Insulin resistance is a characteristic that precedes the development of impaired glucose tolerance (IGT) and T2D. Hyperinsulinaemia, especially in the fasting state, represents an index of insulin resistance (8). Insulin resistance show familial aggregation and is associated with obesity and physical inactivity. The development of IGT is predicted by the presence of hyperinsulinaemia, and IGT is a strong risk factor for T2D and can be considered as a stage in the development of the disease (8).

Longitudinal epidemiological studies have demonstrated the hyperinsulinaemia, even at a stage when glucose tolerance is within the normal range, is an important predictor of T2D (95). The increase in insulin concentration appears to be a compensatory response to increased intracellular insulin resistance, which leads to small increases in circulating glucose, and as a result an increase in insulin secretion, as well as subsequent increases in both fasting and stimulated insulin levels (95). As insulin resistance degenerates, the glucose tolerance deteriorates and IGT eventually occurs. After IGT develops, when insulin responsiveness diminishes, hyperglycemia worsens and diabetes appears.

2.2.2.1 Genetics

Obesity is a major determinant in the incidence of T2D, but only a small proportion of obese individuals develop the disease. Data from the Framingham Heart Cohort Study (214), indicated that as their population gained weight, a number of atherogenic traits worsened in proportion to the weight gained. Although this was true on the average, weight gain did not explain more than a small fraction of the variation in the atherogenic traits, and some persons are able to gain weight without much change in their cardiovascular risk attributes such as glucose

tolerance (214). The relation of obesity to glucose intolerance is well documented and weight control is a standard feature in the treatment of diabetes. However, the mechanism by which obesity is related to glucose intolerance is by no means clear, particularly the genetic implications of obesity and diabetes (214). Longitudinal studies among the Pima Indians have demonstrated that the likelihood of developing T2D results from an interaction between the effect of obesity in the offspring and a parental history of diabetes, which presumably reflects inherited susceptibility (90). Therefore, even when genetic susceptibility is present, the expression of the disease is largely dependent on other factors. The disease shows familial aggregation, but there is no evidence on the mode of inheritance or on whether it is caused by one or several genes.

Family history of type 2 diabetes is reported much more frequently in individuals with a medical history of T2D than in all other groups. For example, a study conducted using NHANES data from 1999-2002 demonstrated that the diabetes prevalence for individuals with a family history was more than four times higher than the prevalence for individuals without a family history ($P < .001$) (92). Among adults with a family history, diabetes prevalence increased significantly with a corresponding increase in number of family members with diabetes ($P < .001$) (92). The diabetes prevalence for individuals with three or more first-degree relatives with diabetes (44.4%) was higher than the prevalence associated with any other demographic or risk factor the researchers examined (92).

In this same study, diabetes prevalence associated with parental history significantly increased with the number of affected parents ($P < .001$). The diabetes prevalence for individuals with a mother with T2D (16.5%) was higher than for individuals with a father with T2D (12.4%). In addition, having a sibling with diabetes conferred a diabetes prevalence

approximately 4.5 times higher than the prevalence for individuals without a diabetic sibling (92).

There have been several twin studies that suggest that T2D is highly concordant among monozygous (MZ) twins and less among dizygous (DZ) twins. Newman et al. found that there were concordance rates of 58% for MZ twins and 17% for DZ twins among U.S. veterans (55). Similar results were found in a Danish study (56), where the MZ concordance was approximately twofold higher than for the DZ twins.

There is no clear relationship between HLA genes and T2D, unlike autoimmune type 1 diabetes (93). Although there have been numerous linkage studies comparing the prevalence of the genetic markers in people with T2D, this research has yet to find major associations between the genes for insulin, insulin receptors, glucose transporters and T2D in the general population (93). Type 2 diabetes is genetically complex and involves multiple genes, which may be involved with causal mechanisms, and multiple gene-environment interactions (93). There are also several limitations in understanding the genetics of T2D. This limitations cause the mode of inheritance of T2D to remain uncertain. These limitations include the misclassification of T2D, premature mortality, late age at onset, multiple polymorphisms, and the genotypic and phenotypic heterogeneity of T2D (93).

Other evidence for the importance of genetic determinants comes from studies of mixed populations and from populations of different genetic backgrounds living in similar environments. Other data come from studies on populations residing in the same environment but within which there is a genetic admixture (8). For example, among the populations of the Gila River Indian Community, the prevalence of T2D is twice as great in full-blooded Pima Indians as in non-Indians, and the prevalence among those of half-Pima, half-non-Indian

ancestry is intermediate (8). Genetic susceptibility does appear to be a basic step for the development of T2D, but the expression of the disease is determined largely by environmental factors (8).

2.2.2.2 Environment

Many studies support the role of environment/lifestyle factors in the etiology of type 2 diabetes. The development of T2D is influenced by exposure to different environments. Some of the environmental effects can be assessed by comparing the frequency of the disease in migrants with that among people who remain in the original environment, assuming that both groups share similar genetic material.

There are many lifestyle factors that are thought to be involved in the development of T2D. Diet has been considered a possible cause of diabetes for centuries. Total caloric intake, as well as several components of diet has been considered, including carbohydrates and fats (57). High-fat diets have been associated with obesity and altered fat distribution. A higher dietary fat intake was associated with previously undiagnosed T2D and IGT in a random sample of Hispanics and non-Hispanic whites screened for glucose intolerance (94). Studies of severe food shortages during wars provide ecological evidence that diabetes mortality and morbidity declined abruptly with decreased caloric intake (58).

Some ecological studies (59, 60) suggest that T2D prevalence is consistently lower in populations with higher levels of habitual physical activity. Cross-sectional and retrospective studies have demonstrated that there is a lower prevalence of T2D at higher levels of physical activity. In the NHANES studies (61), physical activity was related to T2D only in Mexican Americans and not in U.S. Caucasians or African-Americans. In these studies, lower physical activity was reported after diagnosis of T2D, and this could have been the result of the diabetes

rather than its cause. Conversely, three prospective studies measured physical activity levels prior to T2D onset. In the Nurses' Health Study (62), women who stated they at least had weekly physical activity, over the next eight years, a relative risk of self-reported T2D of 0.8 (95% CI 0.7-0.9), compared with those with less activity. There was no dose-response relationship beyond weekly exercise. Five-year follow-up of a large cohort of male physicians (63) yielded a comparable estimate of the protective effect of at least weekly activity (RR=0.7). In these men, there was verification of dose-response, and the greatest effect was seen in men who were more overweight. The results of a 15-year follow-up (64) of male college alumni are consistent with these results. In these men, each 500 kcal of increased energy expenditure in leisure-time activity per week lowered the risk of T2D by 10%. This effect was also greater in more obese participants.

It has been hypothesized that this protective effect of physical activity on development of T2D is due to the prevention of insulin resistance. While this is generally accepted, some studies of the acute effects of physical training suggest a much more complex picture. Krotkieski *et al.* and Trovati *et al.* found that subjects who start an exercise program with high insulin levels responded with a drop in insulin levels (65,66). However, subjects who have lower baseline insulin levels increase their insulin levels with exercise. Furthermore, in some subjects undergoing physical training, there were no changes in insulin levels, but C-peptide levels (insulin secretion) and insulin sensitivity decreased (65).

2.2.2.3 Obesity

Obesity has been recognized as being associated with diabetes for a very long time. However, there is substantial controversy about the meaning of the relationship, since non-obese individuals develop T2D and many obese persons never develop T2D. There are several reasons

this might occur: 1) obesity is the etiologic pathway of a distinct subtype of T2D, 2) a similar genetic predisposition leads independently to both obesity and T2D, and 3) a similar genetic defect predisposes to both, but different additional genetic and/or environmental factors complete the sufficient causes for T2D and obesity (67).

Obesity itself is unlikely to completely justify inter-population difference in T2D frequency. For instance, Marshall *et al*. (68) found that Hispanics in San Luis Valley, CO have a twofold higher T2D prevalence and incidence, compared with non-Hispanic whites after adjustment for obesity, fat patterning, age, sex and family history of diabetes. Cowie et al. (69) demonstrated that a higher prevalence of type 2 diabetes was also found in Africa-Americans and Caucasians after adjustment for obesity and other risk factors. This racial disparity was present particularly at higher levels of obesity and the adverse effect of obesity was greatest in Black women.

Not only the presence but also the distribution of obesity influences the risk of developing T2D. Central obesity is associated with an increased possibility of developing T2D, as has been demonstrated in many different ethnic and racial groups. Central obesity in many populations is also associated with an increased incidence of coronary heart disease, hyperinsulinaemia, high serum triglyceride, low high-density lipoprotein (HDL) cholesterol levels, hypertension and disturbances in the patterns of sex hormones (91). Insulin resistance appears to be a central feature of this cluster of abnormalities related to abdominal obesity.

In addition to the level of obesity, duration has proven to also be an important risk factor for T2D. Maximum lifetime BMI was cross-sectionally associated with T2D, independent of current BMI (70). Everhart *et al*. (71) found that in Pima Indians who attained a BMI $\geq$30, the risk of T2D increased from 24.8/1,000 person-years in those who were obese for <5 years, to

35.2/1,000 for obesity of 5-10 years, to 59.8/1,000 for >10 years of obesity. However, in the majority of those participants with normal blood glucose, longer obesity duration was associated with lower fasting and post-load insulin concentrations. The authors speculated that this may have occurred if decreased insulin secretion followed prolonged obesity. It could also be due to a "survivor" effect, since individuals who converted to IGT or T2D were excluded from these analyses.

The distribution of body fat is also a strong risk factor for T2D, independent of the presence of obesity (72, 73). Even stronger associations have been found with better measurements of intra-abdominal fat, such as CT scans (74). Some longitudinal studies have demonstrated that, as individuals age, both weight gain and increased waist circumference occur; even in older persons who lose weight, waist circumference continues to increase (75). These trends may partially be responsible for the increased incidence of T2D with aging.

2.2.2.4 Pregnancy and Parity

It has been shown that increasing parity increases the risk of T2D in women. Some retrospective studies have found both positive (76) and no associations (77,78). It has also been argued that the effect of pregnancy operates through weight gain that accompanies pregnancy and that the numbers of births have no independent effects themselves (79). A study conducted in Rancho Bernardo, CA (80) found a positive association between increased parity and T2D, adjusted for current BMI, suggesting that parity may have an effect beyond that of obesity. Conversely, a prospective study of 113,606 U.S. female nurses proved that increased risk of T2D is secondary to obesity (81). In this study, there was a relative risk of 1.6 (95% CI 1.3-1.9) for women with ≥6 births compared with nulliparous women; however, adjustment for age and BMI

completely removed any effect of parity. Therefore, from this large prospective study, it has been shown that parity has no independent effect beyond its effect on weight gain.

2.2.2.5 Urbanization

Bennett found that urban residents have T2D rates higher than rural dwellers (82). A number of lifestyle factors implicated in the etiology of T2D (i.e., sedentary lifestyle, greater level of stress, and obesity) are associated with an urban lifestyle. The role of stress as a possible T2D risk factor has some support in studies of the neuroendocrine system, especially the sympathetic nervous system (83). An effect of stress may be mediated through abdominal obesity, or directly on glucose and/or insulin levels (84). However, there is little epidemiological evidence for this hypothesis.

2.2.3 Prevention and Intervention

Most previous T2D prevention studies have included programs that alter the lifestyle to reduce body weight. Currently, there is no evidence from randomized interventions that any manipulation of specific dietary components prevents progression from IGT to T2D. One randomized study of newly diagnosed T2D patients, a low-carbohydrate diet was compared with a modified-fat diet (85). The participants' weight decreased slightly more on the low-fat diet, but at one year there were no differences in fasting glucose and insulin levels. Weight reduction can reverse insulin resistance and, should prevent progression to T2D in at-risk-persons. However, long-term maintenance of a reduced body weight is difficult, and most patients regain the lost body weight within three years (67).

A few studies have shown that benefits of the addition of exercise programs to dietary interventions for enhancing long-term weight loss in obese individuals without diabetes (86). In

one study, obese T2D participants assigned to a 10-week diet and exercise intervention achieved significantly greater weight loss at one year follow-up than did subjects assigned to a diet intervention only (87). While most of the intervention studies in T2D patients showed improvements in blood glucose control in addition to weight loss, there are no data indicating the effectiveness of exercise-induced weight loss in preventing T2D in at-risk individuals (88).

The role of physical inactivity, dietary fat, and weight gain in the etiology of T2D is established. What remains to been seen is how these behavioral factors interact with the genetic factors to produce diabetes on the individual and population levels. A better understanding of the genetic-environmental interactions and of the heterogeneity of T2D would assist in designing ideal measures to prevent the disease.

2.3 PRE-DIABETES

2.3.1 Epidemiology

Pre-diabetes is becoming more common in the United States. The U.S. Department of Health and Human Services estimates that about one in four U.S. adults aged 20 years or older, or 57 million people, had pre-diabetes in 2007 (204). The Diabetes Prevention Program (DPP) illustrated those individuals with pre-diabetes are at extremely high risk for progression to overt diabetes (48). Those with pre-diabetes are likely to develop T2D within 10 years, unless they take steps to prevent or delay diabetes (204). The American Diabetes Association (ADA) previously defined pre-diabetes as either fasting glucose (IFG) = 6.1 to 6.9 mmol/L (110-125 mg/dL) and/or impaired glucose tolerance (IGT) (two-hour postload glucose of 7.8-11.0 mmol/L [140-199 mg/dL]). Recently, the ADA lowered the fasting glucose threshold value for IFG from 110 to 100 mg/dL (47).

Two recent studies of individuals without diabetes showed that higher fasting plasma glucose levels within the normoglycemic range constitute an independent risk factor for type 2 diabetes and that coronary disease is more severe in those patients with higher postload glycemia and hemoglobin A1c levels (51). The best ways to screen for pre-diabetes are with an oral glucose tolerance test and/or a fasting glucose. One can have a normal fasting glucose but an abnormal two-hour postprandial glucose level. The overlap between subjects with IFG and IGT is incomplete and suggests that they describe different pathophysiologic aspects of dysregulated glucose and fat metabolism. Multivariate analyses show that two-hour plasma glucose is closely associated with risk factors for diabetes and with cardiovascular variables, including triglycerides and apolipoprotein B (51).

2.3.2 Etiology

Currently, most experts agree that type 2 diabetes is a multi-organ disease involving defects of glucose and fat metabolism in several organs, including not only the pancreatic beta cell, liver, and skeletal muscle, but also other organs such as the intestines, kidney, brain, and nervous system. Diabetes begins as a pre-diabetes state characterized by insulin in many tissues, including the liver, adipose tissue, and muscle. Pre-diabetes is a central metabolic abnormality. Considerable information is available to suggest that a cluster of metabolic abnormalities related to insulin resistance and hyperinsulinemia increases cardiovascular risk and that these risk factors are present in insulin resistant patients who do not have diabetes (51). Patients with pre-diabetes may have a dyslipidemia characterized by high triglycerides and low high-density lipoprotein (HDL) levels. Pre-diabetes begins with an excessive intake of fatty acids in the diet. This excessive intake of fatty acids leads to an accumulation of triglycerides in adipose tissue. A

net spillover of fatty acids from adipose tissue to non-adipose tissues such as muscle, liver, and the pancreas occurs (51). The deposition manifests as the visceral accumulation of fat and can be measured by computed tomography (CT) scan (51). This visceral accumulation of fat also explains insulin resistance in the lean individual because it is the fat surrounding such organs as the liver that leads to insulin resistance, not necessarily subcutaneous fat (51).

2.3.2.1 Environment

Recent studies have shown that both lifestyle and pharmacologic therapy can alter the progression of pre-diabetes to overt diabetes. The three largest studies of pre-diabetes prevention to date include the Finnish, DPP, and the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) trials. In the Finnish Diabetes Prevention Study of more than 500 overweight subjects with impaired glucose tolerance (IGT) (49), the reduction in diabetes incidence in the intervention group was directly related to the degree of improvement in lifestyle intervention. The intervention group showed significantly greater improvement in each intervention goal. After 1 and 3 years, weight reductions were 4.5 and 3.5 kg in the intervention group and 1.0 and 0.9 kg in the control group, respectively. Measures of glycemia and lipidemia improved more in the intervention group (49).

In the STOP-NIDDM trial, 1429 subjects were randomized to receive acarbose or a placebo. The subjects experienced a 36% relative risk reduction in their likelihood of developing type 2 diabetes compared with subjects taking placebo (50). In the Diabetes Prevention Program (DPP), all 3234 participants were overweight and had pre-diabetes and 45% of the participants were from minority groups – African American, Alaska Native, American Indian, Asian American, Hispanic/Latino, or Pacific Islander. These factors are all well-known risk factors for the development of T2D as previously discussed. Participants were randomly divided into

different treatment groups. The first group, called the lifestyle intervention group, received intensive training in diet, physical activity, and behavior modification (204). By eating less fat and fewer calories and exercising for a total of 150 minutes per week, the participants aimed to lose 7 percent of their body weight and maintain that loss. The second group took 850 mg of metformin twice a day. The third group received placebo pills instead of metformin. Both of these groups also received information about diet and exercise but no intense motivational counseling. A fourth group was treated with the drug troglitazone (Rezulin), but this part of the study was discontinued after adverse affects were discovered (204).

The DPP's results demonstrated that millions of high-risk people can delay or avoid developing T2D by losing weight through regular physical activity and a diet low in fat and calories (204). The DPP also suggests that metformin can help delay the onset of diabetes. Metformin was effective in slowing progression of pre-diabetes to overt diabetes, although lifestyle changes were more effective. Those in the lifestyle intervention group reduced their risk of developing diabetes by 58% and this finding was true across all participating ethic groups and both sexes (204). These lifestyle changes worked particularly well for those aged 60 years and older, reducing their risk by 71%. About 5% of the lifestyle intervention group developed diabetes each year during the study period, compared to 11% of those in the placebo group.

Participants taking metformin reduced their risk of developing diabetes by 31%. Metformin was most effective in people 25 to 44 years old and in those with a BMI of 35 or higher (204). Approximately 7.8% of the metformin group developed diabetes each year during the study, compared to 11% of the placebo group (204). Because there is now clear evidence of the benefit from clinical intervention in the pre-diabetic condition, it is important to identify and intervene in people with pre-diabetes.

Cheng *et al* found in a cohort of young Africa-Americans, an ethnic group at high risk for developing diabetes, many subjects with pre-diabetes have IGT without IFG. Lowering the FPG threshold for IFG identifies more subjects with pre-diabetes, but still results in failure to detect most of the IGT-defined pre-diabetic cases. Furthermore, using the lower threshold causes the overall prevalence of individuals defined as having pre-diabetes to increase from 20.4% to 31.9%, substantially adding to the number of individuals labeled as having extremely high risk for developing diabetes. Without performing two-hour post-challenge testing, approximately one third of pre-diabetes cases would remain undiagnosed and at risk. Although use of FPG alone is currently favored clinically over two-hour PG because of the relative cost and inconvenience associated with OGTT, a substantial proportion of pre-diabetes subjects will be missed when FPG alone is used to screen African Americans (47).

2.3.2.2 Treatment

Although current treatment for pre-diabetes includes a pharmacological and lifestyle modification approach, lifestyle interventions are the cornerstone of treatment for this condition (52). Insulin resistance is part of the underlying pathology associated with metabolic syndrome, and patients identified with insulin resistance may have hypertension, dyslipidemia, visceral obesity, and vascular disease. Obesity, sedentary lifestyle, and high calorie, high-fat diets correlate with the development of insulin resistance. Lifestyle changes and therapeutic dietary intervention have been demonstrated to prevent or delay the development of diabetes.

Current recommended lifestyle changes include a reduction in energy intake and an increase in physical activity. Both are inversely associated with the degree of insulin resistance. Lifestyle changes can prevent the development of diabetes. A moderate decrease in caloric balance (500-1000 kcal/day) results in slow, progressive weight loss when coupled with regular

moderate-intensity physical activity (150 min/week of aerobic activity) (51). Reduction in saturated and trans fatty acids and cholesterol intake improves lipid status and insulin sensitivity.

Pharamacologic intervention also may prevent the development of diabetes. The DPP concluded that metformin may prevent progression to diabetes in insulin-resistant individuals. Participants in the STOP-NIDDM trial with impaired glucose tolerance randomized to acarbose had a 25% relative risk reduction in progression to diabetes after 3.3 years (50).

In the DPP, metformin was half as effective as diet and exercise in delaying the onset of diabetes and was nearly ineffective in older people aged > 60 years, or those with a BMI < 30 kg/m^2 (53). Metformin was as effective as lifestyle modification in those subjects aged 24-44 years or in those with a BMI of > 35 kg/m^2 (53). The role of pharmacologic intervention in those with pre-diabetes needs further definition and ongoing studies will answer those questions. Certainly, anti-obesity drugs are appropriate for some obese patients. Surgery also has a place in the treatment of these patients. Over the last several years, bariatric surgical intervention has played an increasingly important role in the care of morbidly obese patients (51). Numerous studies have demonstrated that in carefully selected patients there is significant weight loss (over 30% in some studies), decrease in BMI, reduction in blood pressure, and amelioration of insulin resistance (54). There is convincing evidence to suggest that pre-diabetes can be managed successfully with lifestyle and clinical interventions. However, getting patients to make and maintain behavior changes and adhere to treatment regimes requires a compelling approach.

Along with pharamacological interventions, several recent controlled trials on diabetes prevention have confirmed that lifestyle changes targeting diet, activity patterns, and weight regulation; however, there is still no consensus on a standard or systematic approach that supports sustained behavior change in any of these areas (51). A significant mediating factor

determining successful behavior change is self-efficacy, or one's belief about his or her ability to accomplish something (51). In addition to the challenges of changing engrained lifestyle habits, comorbid conditions such as depression can be a complicating factor when addressing any chronic medical condition (51).

Traditionally, diabetes education, which is similar to pre-diabetes education, has emphasized increasing knowledge about diabetes, risk factors, and diabetes self-care; however, many studies have shown that this didactic approach does not result in optimal clinical or behavioral outcomes (55). Biuso et al. believes that efforts should focus on improving coping, communication, and control by enhancing self-efficacy, increasing motivation to initiate and/or change behaviors, and facilitating an individualized plan of action that takes into account personal needs, barriers, and preferences (55). Therefore, considerable care must be taken to implement a behavioral change program that includes these components (51).

2.4 COMPLICATIONS IN PERSONS WITH DIABETES MELLITUS

Much of the burden of diabetes is due to the development of complications such as cardiovascular diseases, retinopathy and nephropathy. Most adults with diabetes have one comorbid condition, and as many as 40% have at least three comorbid conditions. As patients with diabetes get older, they are at higher risk for acquiring chronic diseases associated with age, such as osteoarthritis, dementia, and heart failure. Other chronic conditions, such as thyroid disease, other autoimmune disease, and any form of cancer can also complicate the medical management of diabetes. For instance, hyperthyroidism alters glucose metabolism and leads to hyperglycemia, whereas hypothyroidism leads to hypoglycemia. Cardiovascular diseases are the

leading causes of death for patients with type 2 diabetes, diabetic retinopathy is estimated to account for 5% of all cases of blindness globally (94), and up to 50% of patients receiving renal replacement therapy (RRT) have diabetic nephropathy (94). According to a 2007 fact sheet from the Centers for Disease Control and Prevention (89), the costs of medical care and indirect costs such as disability and premature death related to diabetes and associated complications totaled $174 billion.

There are both acute and chronic diabetes complications. Acute complications include diabetic ketoacidosis (DKA), lactic acidosis (LA), hypoglycemia, and hypersolmolar nonketotic state (HNS). Chronic conditions can be further divided into micro and macrovascular complications. Microvascular complications entail conditions related to the kidney or retina, neuropathy, which involves changes in the central nervous system (94). Macrovascular complications include coronary artery disease, cerebrovascular disease, peripheral vascular disease, or lower extremity arterial disease.

2.4.1 Chronic Complications

2.4.1.1 Microvascular Complications

Microvascular disease is the characteristic consequence of exposure to chronic hyperglycemia (94). Overall, the incidence of microvascular complications has declined in recent decades, due to improvements in the management of people with diabetes (94). For example, comparison of four cohorts of patients with type 1 diabetes whose disease was diagnosed between 1965 and 1984 demonstrated that the cumulative incidences of both diabetic nephropathy and proliferative retinopathy over the following 20 years were lowest in the most recently diagnosed cohorts (95). Similarly, for type 2 diabetes, studies in the United States have

revealed a marked decline in the proportion of patients with any degree of retinopathy, from 50% of patients in the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) in the early 1980s (96), to 10% in the Multi-Ethnic Study of Atherosclerosis (MESA) at the beginning of the 21st century (97).

Retinopathy

Diabetes, particularly diabetic retinopathy, is the main cause of new cases of blindness in people age 20-74 years in the United States (98). It has been estimated that more than 12% of new cases of blindness are attributable to diabetes, and approximately 8% of those who are legally blind are reported to have diabetes as the etiology. Those with diabetic retinopathy are 29 times more likely to be blind than those without diabetes (98). Diabetic retinopathy is characterized by alterations in the small blood vessels in the retina. Diabetic retinopathy has two stages: non-proliferative and proliferative retinopathy (98). The non-proliferative stage is characterized by retinal blot hemorrhages, microaneuryisms, exudates, and other lesions (98). The growth of abnormal blood vessels and fibrous tissues from the optic nerve or from the inner retinal surface are signs of proliferative retinopathy. Bleeding may occur during the growth of the abnormal tissue, which leads to vision loss (98). An estimated 97% of those who take insulin and 80% of those who do not take insulin who have had diabetes for more than 15 years have retinopathy; approximately 40% of insulin-taking and 5% of noninsulin-taking persons have the most severe stage, proliferative diabetic retinopathy (98). In the large Wisconsin epidemiological study, WESDR (90), proliferative retinopathy was present at baseline or after a 4-year follow-up in 23% of younger-onset (aged <30 years) diabetic individuals, and in 10% of older patients receiving insulin and in 3% of those not taking insulin. However, type 2 diabetes finally accounts for the higher absolute number of cases of proliferative retinopathy (90). The

main risk factors for developing proliferative retinopathy reported in WESDR were longer duration of diabetes, high blood glucose and, in the younger-onset group, higher blood pressure at base-line (90).

Estimates of rates of legal blindness in the United States have been reported by the National Society to Prevent Blindness from data of the Model Reporting Area (MRA) registry (99). It was estimated that 7.9% of people who were legally blind reported diabetes as the cause of their blindness (99). Kahn and Hiller demonstrated that prevalence rates for diabetes-related legal blindness increased with increasing age to a maximum in persons age 65-74 years; thereafter, the rates declined. This decline may have been due to excess deaths in the elderly diabetic population, in which the disease had already progressed to the stage of blindness (100). Rates for females were higher than for males (99). Higher rates of legal blindness were found in white females and in nonwhite males and females, compared with white males (99). Since the MRA registry data were based on self-reports and required registration at specific agencies in 16 states, the rates are thought to underestimate that actual prevalence of legal blindness by as much as 50%. Untreated proliferative retinopathy progresses to blindness within five years in roughly 20-50% of cases. Screening and proper care could prevent up to 90% of the cases of blindness attributed to diabetes. However, only approximately 60% of people with diabetes receive annual dilated eye exams (101).

Neuropathy

The mechanism of diabetic neuropathy is unclear; however, long-term hyperglycemia and tissue ischemia are considered the main pathogenic factors. Diabetic neuropathy of different degrees is thought to be present in as many as 60% of patients with diabetes and can be classified into prevalently motor, sensory, or autonomic forms (90). Motor neuropathy mostly induces

limb muscle atrophy and structural alterations in the feet. Sensory neuropathy alters tactile, thermal and pain-related functions. Autonomic neuropathy mainly affects the microcirculation and the heart (90). Sensory neuropathy plays a crucial role in the pathogenesis of diabetic foot: 60% of cases are in fact due to neuropathy and other cases to coexisting neuropathy and macro- and/or microangiopathy (90). The most common type of neuropathy is distal symmetric sensorimotor type, often referred to as distal symmetric polyneuropathy (DSP). DSP is characterized by pain, weakness, altered sensation, affecting the bilateral "stocking glove" pattern on the arms and legs (101). Because of the altered sensation, damage may not be detected until a secondary condition occurs, such as an infection. It has been shown that DSP is present in 12% of individuals at the time of diabetes diagnosis and in 25% after 25 years (101). Like other complications, the prevalence of neuropathy increases with age, poor glucose control and duration of diabetes (103).

Nephropathy

Diabetic nephropathy refers to the presence of elevated urinary protein excretion in a person with diabetes in the absence of other renal disease. Diabetic nephropathy is a frequent complication of type 1 and type 2 diabetes and involves about 30% of all diabetic patients. The severity of renal damage is a strong predictor of end-stage renal failure and is the second major cause of death during diabetes (90). Without specific intervention, 20-40% of diabetic patients with microalbuminuria will progress to overt nephropathy and, within 20 years, 20% of these will develop end-stage renal failure (90).

Diabetes is the leading cause of kidney failure, accounting for 44% of new cases in 2005 (89). In the United States, the incidence of diabetic nephropathy has increased by 150% in the past ten years, a trend that can also be seen in Europe (104). In 2005, 46,739 people with

diabetes began treatment for end-stage kidney disease in the United States and Puerto Rico (89). Diabetic nephropathy is typically more common in older and non-white populations and the risk of nephropathy is partly determined by genetics (101). Researchers have shown a familial clustering of nephropathy and high rates of cardiovascular events and hypertension among relatives of those with T2D and nephropathy (102). Additional risk factors of nephropathy include increased cholesterol levels, smoking, hypertension, elevated HbA1c levels, older age, insulin resistance, male sex, non-white race, and high dietary intake (105). Treatment of some of these conditions may reduce diabetes-related kidney disease by up to 50% (105).

2.4.2.1 Macrovascular Complications

Macrovascular complications associated with diabetes consist of coronary heart disease, cerebrovascular disease, lower extremity arterial disease, and peripheral vascular disease. These complications are more prevalent in those with diabetes compared with those who do not suffer from the disease. Coronary heart disease is two to four times more common in those with diabetes (106). In 2004, heart disease was noted on 68% of diabetes-related death certificates among those aged 65 years or older (89). Compared to those without diabetes, heart disease in those with diabetes appears earlier in life, affects women almost as often as men, and is more fatal. Adults with diabetes are more likely than those without diabetes to have hypertension, and dyslipidemia, but some of the increased risk of heart disease associated with diabetes appears to be independent of these factors. Insulin and glucose may act as cardiovascular disease risk factors, but data is inconsistent.

Diabetes is an important component of the complex of ‘common’ cardiovascular risk factors, and is responsible for acceleration and worsening of atherothrombosis. Coronary Heart Disease (CHD) causes about 65% of the total mortality in patients with diabetes (90). In terms

of major cardiovascular events, coronary heart disease and ischemic stroke are the main causes of morbidity and mortality in patients with diabetes. Data on cardiovascular disease among the diabetes population are limited. However, in 2000, 37.2% of persons with diabetes age 35 years and older reported receiving a diagnosis of a cardiovascular disease (40). Prevalence of ischemic heart disease among persons with diabetes was about 14 times the rate among those without diabetes in person 18 to 44 years of age (2.7% vs. 0.2%), 3 times as high in persons 45 to 64 years of age (14.3% vs. 4.7%), and almost twice as high in those 65 years of age or older (20% vs. 12%) (40). Other studies have shown that the absolute rates of cardiovascular disease in persons with diabetes are higher in men than in women (as in the general population), but the relative risk (comparing those with and without diabetes) is higher in women that in men (relative risk, 2 to 4 for women and 1.5 to 2.5 for men) (40).

About 80% of all diabetes patients die from cardiovascular events. Seventy-five percent of such deaths are due to coronary heart disease (CHD), and the remaining 25% to cerebrovascular, peripheral or other macrovascular disease (90). Age is a major additional factor for cardiovascular risk, and other main risk factors for cardiovascular morbidity and mortality are high total and low-density lipoprotein (LDL)-cholesterol and triglyceride levels, low high-density lipoprotein (HDL)-cholesterol, in addition to fasting plasma glucose, proteinuria and the presence of nephropathy and/or retinopathy (90).

The risk of developing an acute MI, as well as other acute coronary syndromes is increased 2 –to 4-fold (90), and in the Euro Heart Survey (91), which involved 5000 coronary patients, 30% had confirmed diabetes and silent myocardial ischemia was found in as many as 33% of patients with diabetes (91). In the OASIS (Organization to Assess Strategies for Ischemic Syndromes) register (92), diabetes increased the death rate of patients with unstable

angina pectoris by 75%, and it is also noteworthy that coronary syndromes and acute MI are more frequent in women with diabetes than men, and that the relative risk of fatal disease is much higher in women (90).

Previously unrecognized poor glucose tolerance recently emerged as a risk factor for severe outcome or death in patients with coronary syndromes. In the GAMI study (Glucose Abnormalities in Patients with Myocardial Infarction), 67% of all acute MI patients considered had an altered glucose tolerance during and/or after the acute episode (90). A large Finland-based population study on long-term cardiovascular mortality in diabetic or non-diabetic patients with or without a previous acute MI suggested that having diabetes could be considered an equivalent of a previous acute MI in a non-diabetic individual (93), but this concept has recently been questioned. Recently, even a higher than optimum fasting plasma glucose concentration without diabetes, has been shown to be a leading factor for cardiovascular mortality (93).

Peripheral vascular disease or LEAD (lower extremity arterial disease) includes such conditions as foot ulceration, gangrene, and intermittent claudication, which may lead to lower-level amputations (106). Peripheral arterial disease frequently occurs, and is more likely to be conducive to critical limb ischemia and amputation than in the absence of diabetes. An analysis of the 1999 to 2000 NHANES found that an estimated 8.1% of the diabetic population age 40 years or older have LEAD (40). Individuals with diabetes accounted for 51% of all lower level amputations of the toe or foot (106). An estimated 15% of persons with diabetes will have a diabetic foot ulcer during their lifetime; of these, 6% to 43% will ultimately undergo a lower-extremity amputation (40). Most of the same risk factors for CHD and stroke are also the risk factors for LEAD. Sex, age, hyperlipidemia, hypertension, and smoking have all been shown to be significant risk factors for the development of LEAD (106).

Although there is a large amount of morbidity associated with diabetes, much of it can be prevented (6-8). To prevent diabetes complications and to ultimately decrease diabetes-related morbidity and mortality, a team approach to diabetes care should be adopted. Patient self-care behaviors, provider recommendations and adherence to national standards, community support, and the use of clinical information systems should work in tandem to accomplish this goal (76,77).

It is essential for those with diabetes to take the central role in their diabetes self-management plan by having regular check-ups, being aware of unusual symptoms like vision problems or numbness in their feet, self-monitoring their blood glucose regularly, controlling their weight, participating in regular physical activity, and seeing a diabetes specialist if necessary (78-81). With the patient taking this role, the provider becomes more of a facilitator, making medication changes based on lab values, and ensuring that the standards of care for persons with diabetes are met (77,79). However, if a structure within the community is not in place in which the patient can be informed and activated and the provider cannot be prepared and proactive, diabetes-related morbidity and morality will continue to rise (1,37,86).

2.4.2 Acute Complications

Acute complications of diabetes include DKA, LA, HNS, and hyperglycemia. While HNS and DKA are associated with insulin deficiency, hypoglycemia results from the treatment of diabetes with either oral agents or insulin. LA is associated with other risk factors of diabetes, such as cardiovascular disease (40). Acute complications of diabetes have many precipitating risk factors, which include acute illness and poor compliance. Treatment of these complications often includes hospitalization or ambulatory care. This causes healthcare costs to increase and

therefore prevention is an important component in reducing healthcare costs related to diabetes (40).

2.4.2.1 Hyperosmolar Nonketotic State

HNS is clinically defined by the presence of relative insulin deficiency and hyperglycemia, usually >1,000 mg/dL with associated elevated serum osmolality, dehydration, stupor and progression to coma if untreated. These patients have sufficient circulating insulin to prevent ketosis and lipolysis (107). Hospital discharge data shows that HNS rarely occurs, and usually affects those with type 2 diabetes, who are Caucasian, female, and older than 65 years of age. Occurrence of HNS is caused by dehydration, medications such as steroids, or thiazides, acute illness, cerebral vascular disease, and older age (107).

Prevention of HNS in those with diabetes can be accomplished through education, self-care, self-monitoring of blood glucose, avoidance of dehydration, and awareness and avoidance, if possible, of medications that may trigger the disorder. Patients with this complication will respond well to hydration and small doses of insulin. These treatments will prevent the occurrence of mental disorientation (107).

2.4.2.2 Diabetic Ketoacidosis

Diabetic ketoacidosis is one of the major acute diabetic complications. DKA is defined by absolute insulin deficiency with hyperglycemia, increased lipolysis, ketone production, acidosis, and hyperketonemia (107). DKA usually occurs in those with type 1 diabetes and rarely occurs in those with type 2. When DKA occurs in those with T2D, it may represent a transition to insulin deficiency. The number of hospitalizations in the United States for which diabetic ketoacidosis was listed as the first diagnosis increased from 61,200 in 1980 to 99,913 hospitalizations in 2001 (40). Under-treatment of DKA can lead to coma and eventually death.

Some studies have estimated that DKA-related mortality ranges from 5-45% with the highest rates occurring in those aged 75 years and older (109). Deaths due to DKA are rare and have declines between 1980 and 2000 by 28% (32 to 23 per 100,000 diabetic population) (40). Incidence rates have been estimated between 4.6-13.4 per 1,000 diabetic-person-years (107;40) with rates being the highest in the younger age groups (<30 years old). Infection is the most precipitating factor of DKA, but other risk factors include acute illnesses, lack of diabetes education and training, noncompliance, poor self-care, and inadequate glucose monitoring (107).

Prevention remains the most important aspect of managing DKA in individuals with known diabetes. Prevention can be accomplished through appropriate education, improved self-care and compliance, and self-monitoring blood glucose. Some studies have demonstrated a 40-50% reduction in DKA hospitalizations accompanying patient education, follow-up care, and increased access to medical advice (107;108). However, for more severe cases of DKA, treatment includes hydration, insulin therapy, and electrolyte repletion (107).

2.4.2.3 Lactic Acidosis

LA is characterized by elevated lactic acid (lactic academia, ≥2.0 mmol/L) with acidosis (pH ≤7.3) and without ketoacidosis. Approximately half of the reported cases of LA have occurred in patients with diabetes (107). Currently LA is rarely seen in patients with diabetes, particularly since the withdrawal of Phenformin from the market. When LA occurred, it was predominately in individuals older than 45 years old, in women, in Caucasians, and in patients for whom diabetes was not listed on the hospital discharge summary (107). LA is usually precipitated by hypoxia and some medications such as Phenformin. Prevention of LA is very difficult. Often the predisposing conditions, such as acute myocardial infarction with hypoxia, or septic shock, are acute events and may not be amenable to immediate prevention other than

through long-term control and modification of risk factors. Usually, LA does not occur in conjunction with poorly regulated diabetes unless there is some additional event that produces hypoxia (107). Treatment of LA is similar to that of DKA in terms of hydration, restoration of electrolyte balance, correction of acidosis, and correction of hyperglycemia. Patients with LA are usually hospitalized. Hospitalization may be prolonged because of the underlying condition that my have led to the LA. This extended hospitalization has a considerable economic impact as well. The major morbidity associated with LA is neurological impairment and possible cerebral edema (107). The mortality rate from LA is high. The higher the lactic acid level in association with the acidosis, the higher the mortality rate. LA accounts for a very small portion of the total mortality in patients with diabetes (107).

2.4.2.4 Hypoglycemia

Hypoglycemia is a very common acute complication in those with diabetes, particularly occurring in patients who are treated with insulin, but can also occur in those people with diabetes who are on oral medications (107). Hypoglycemia may range from very mild lowering of glycemia (60-70 mg/dl) with minimal or no symptoms, to severe hypoglycemia with very low levels of glucose (<40 mg/dl) and neurological impairment. Patients with more severe hypoglycemia are more likely to need medical attention and thus are more readily ascertained for demographic data analysis. The Diabetes Control and Complications Trial (DCCT) accounted 62 hypoglycemic events per 100 patient-years from 1983-1989 in which assistance was required in the provision of treatment in the intensive therapy group, as compared with 19 such events per 100 patient-years in the conventional treatment group (110). However, it must be noted that the intensive-therapy group was rigorously treated with insulin. Since patients are less likely to this intensively treated, the incidence rate is likely to be lower in the general population.

Hypoglycemia is one of the largest contributors to hospitalizations in patients with diabetes. Nearly 64% of hospital records of patients with diabetes, list hypoglycemia in the discharge summary (111). Most hospital discharges for hypoglycemia in patients with diabetes occurred in patients older than 65 years old and hypoglycemia represents a greater proportion of hospitalizations in females and African-American patients (107).

To reduce the frequency of hypoglycemic events, consistent self-monitoring of blood glucose is necessary. It is also important for the patient with diabetes to avoid skipping meals after taking insulin. Prevention of hypoglycemia depends on education regarding diabetes management and self-care, self-monitoring of glucose levels, and factors that may precipitate hypoglycemia (107).

The major morbidity associated with hypoglycemia is temporary neurological deficit and coma, seizures with central nervous system injury, and permanent neurological impairment if treatment is delayed (107). Death related to hypoglycemia in diabetes rarely occurs. There were no deaths recorded in the DCCT (111). The majority of patients with hypoglycemia survive the event.

3.0 GEOGRAPHIC INFORMATION SYSTEMS

When Geographical Information Systems (GIS) were first developed in the early 1960's, they were no more than a set of innovative computer-based applications for map data processing that were used in a small number of government agencies and universities only. Today, GIS has become an important field of academic study, one of the fastest growing areas of the computer industry, and, most important, an essential component of the information technology (IT)

infrastructure of modern society (112). Spatial analyses using GIS have become widespread and well accepted. A GIS is an information system where the database consists of observations on spatially distributed features, activities or events, which are definable in space as points, lines, or areas. A GIS manipulates data about these points, lines, and areas to retrieve data for ad hoc analyses.

3.1 Definitions of GIS

Unfortunately, attempting to define GIS is not a very simple task. Some people see GIS as a general branch of Information Technology; others see it more specifically as a computer-assisted mapping and cartographic applications, a set of spatial-analytical tools, a type of database systems, or a field of academic study. The United States Geographical Survey defines GIS as "a system of hardware, software, and procedures designed to support the capture, management, manipulation, analysis, modeling, and display of spatially referenced data for solving complex planning and management problems" (113). Rhind defines GIS as "a computer system capable of assembling, storing, manipulating, and displaying geographically referenced information, i.e., data identified according to their locations" (114). Based on these two definitions, GIS can be simply defined as computer-based systems specially designed and implemented for two subtle but interrelated purposes: managing geospatial data and using these data to solve spatial problems.

GIS is a special class of information systems. The word "geographic" in GIS carries two meanings: "Earth" and "geographic space" (112). By "Earth," it implies that all data in the system is pertinent to Earth's features and resources, including human activities based on or associated with these features and resources. By "geographic space," it means that the

commonality of the data in the systems and the problems that the systems aim to solve is spatial (or geographic) in nature, i.e., location, distribution, pattern, and relationship within a specific geographical reference framework. This focus on geospatial data and their applications for spatial problem solving makes GIS unique among information systems.

Depending on the nature of the data that they process, information systems in general can be classified as spatial information systems and non-spatial information systems. Non-spatial information systems are designed for processing data that are not referenced to any position in geographic space. Systems for accounting, banking, human resources management, and goods inventory are typical examples of non-spatial information systems (112).

Spatial information systems are those designed for processing data pertaining to real-world features or phenomena that are described in terms of locations. However, only those spatial information systems that are used for processing and analyzing geospatial data, of geospatially referenced data, can be labeled as GIS (112). Geospatial data are a special form of spatial data that is characterized by two crucial properties: 1) the reference to geographic space, which means that the data are registered to an accepted geographical coordinate system of Earth's surface, so that data from different courses can be spatially cross-referenced and integrated and 2) the representation at geographic scale, which means that the data are normally, recorded at relatively small scales and, as a result, must be generalized and symbolized (112). GIS not only represents the skills and procedures for collecting, managing, and using geospatial information but also entails a comprehensive body of scientific knowledge from which these skills and procedures are developed.

3.1.2 The Evolution of GIS

Both the technology and functions of GIS have undergone considerable changes since its inception in the early 1960's. GIS as we understand it today, is very different from its predecessors. The Canada Geographic Information System (CGIS) has been recognized as the first GIS ever produced in the 1960s and 1970s (115). The purpose of CGIS was to address the needs of land and resource information management of the federal government of Canada. In 1973, the USGS started the development of the Geographical Information Retrieval and Analysis (GIRAS) to handle and analyze land-use and land-cover data. The 1960s and 1970s were important formative years of GIS. During this time, hundreds of software packages for handling and analyzing geographic information were produced (115). These early systems were developed and used mainly by government agencies and universities for very specific data management and research objectives.

In 1982, Environmental Systems Research Institute, Inc. (ESRI) released ArcInfo, designed to run on minicomputers. This particular GIS software package was on the first vector-based GIS to use the geo-relational data model that employed a hybrid approach to geographic data processing (116). Graphical data are stored using the topological data structure, while attribute data are stored using the relational or tabular data structure. This software is the most widely used package today and is very user friendly for academics and businesses alike.

The development of GIS was greatly accelerated by the growth of computer technology in the 1990s. With advances in operating systems, computer graphics, database management systems, and computer-human interaction, GIS became multiplatform applications that ran on different computer platforms as stand-alone applications and as time-sharing systems (112). At the same time, as quantitative and analytical techniques were developed in the social and

physical sciences, and as more data were collected about different aspects of human activities and the environment, the need to find suitable tools to take advantage of the new techniques and data became more pressing than ever before (112). The increasing access to computers and the urgent need for effective geospatial data management together pushed the use of GIS to a new height. The applications of GIS were no longer limited to the traditional areas of land and resource management but quickly extended to new areas that included facility management, vehicle navigation, market research, and business decision support (112).

Today, GIS has popularized the use of geospatial information by empowering individuals and organizations to use such information in areas that earlier generations of GIS users could never had thought of. It is now common for people to use GIS to check the weather and traffic conditions before they leave for work, locate the nearest ATM, and find information about the city they are about to travel to. At the same time, GIS has become and indispensable tool for government officials to manage land and natural resources, monitor the environment, enforce laws, and deliver social services (112).

3.1.3 Components of GIS

3.1.3.1 The Data Component of GIS

A GIS, as an information system, is made up of three components, data, technology, and application. Geographical data record the locations and characteristics of natural features or human activities that occur on or near Earth's surface. Geospatial data are represented by three basic forms that include vector, raster, and surface. Vector data represent the real world by means of discrete points, lines, and polygons (112). This data is better for depicting natural and artificial features that can be individually identified. Raster data represent the real world by

means of a grid of cells with attribute values. This data is not good for representing individually identifiable features but is ideal for a variety of spatial analysis functions (112). Surface data depict the real world by means of a set of selected points or continuous lines of equal values. They can be analyzed and displayed in two or three dimensions and are most suited for natural phenomena with changing values across an extensive area (112).

3.1.3.2 The Technology Component of GIS

The technology component of GIS can be explained in terms of hardware and software. The hardware of GIS is made up of a configuration of core and peripheral equipment that is used for the acquisition, storage, analysis, and display of geographic information. The central processing unit (CPU) of the computer is the center of the GIS hardware and performs all the data processing and analysis tasks. On the software side, GIS was conventionally developed using a hybrid approach that handled graphical and descriptive components of geospatial data separately. It is now possible to build application software modules with programming languages such as Visual C++, and to integrate them with the GIS functions originally supplied by the software vendor (112). GIS applications can obviously benefit from this new approach to software development.

3.1.3.3 The Application Component of GIS

The application component of GIS can be explained from three perspectives: areas of applications, nature of applications, and approaches of implementation. Academic, business, government, industry, and military sectors are the major areas of GIS application today. As the areas of applications have become more diversified, the nature of GIS applications has also undergone significant changes over the years (112). The most important changes occurred when GIS started to be implemented within computer networks and with the advent of the Internet.

With these additions, GIS became a virtual global system that offers all kinds of geospatial information services via a world-wide system of computer networks (112).

3.2 Spatial Analysis

It is necessary to distinguish between spatial analysis and spatial statistical analysis. Spatial analysis is the study of a spatial pattern using the basic GIS operations such as spatial query and join, buffering, and overlaying. Spatial statistical analysis is the application of statistical theory and techniques to the description and modeling of spatially referenced data (128).

In his article, Mayer (124) discusses two ways that spatial analysis can increase our understanding of disease pathogenesis. First, geographical studies may suggest possible causal factors. Associations between disease and place imply that the population living there possesses inherent traits that make it more susceptible to disease or that it may experience some increased level of exposure to a risk factor such as air pollution. Second, spatial analysis can help identify how populations adapt and relate to their environment. Such adaptations may be beneficial and protective or maladaptive and detrimental to health (124). Adaptation to air pollution risk provides a good example. In areas that experience high pollution events, individuals may reduce their exposure on high pollution days by staying indoors or avoiding strenuous exercise, or they may underestimate the risk and proceed with their daily activities as though no excess risk is present (124). In the latter case, the maladaptive behavior may increase their risk of illness or death.

Data for spatial analysis must contain two types of information (127). The first class includes attributes of spatial features measured in interval or ratio variables such as population size, mortality rates, population estimates, or ordinal and nominal variables such as disease

severity, name, or soil type. The second type involves the location of a spatial feature described by position on a map measured in one of many geographic coordinate or referencing systems (125). In bringing these two classes of information together, spatial analysis seeks to assess non-independence or association in values of attributes at the same or nearby locations or locations likely to experience spatial interaction (e.g., airports with connections to other distant airports).

Because much of the available health and covariate data is collected for purposes other than spatial analysis, data integration and quality control are important precursors to the application of spatial-analytic techniques. A recent user-needs assessment survey of 30 health professionals in Canada revealed data availability, consistency, and cost as the main challenge to the expanded use of GIS and allied methods for health surveillance. Although over 80% of the respondents said they planned to expand the use of spatial analysis in health research and policy, many expressed concern about the data needed to support such analyses (126). In the United States and some European countries, the myriad of private medical care suppliers will probably make the task of developing national-level data capable of supporting spatial analysis even more difficult. Institutional structures for data collection, management, and dissemination lag behind the statistical techniques and technology available for spatial analysis (127).

Although all studies do not follow the same steps, they tend to take the following steps: (1) getting data into GIS; (2) transforming data; (3) spatial analysis; (4) spatial statistical analysis; and (5) visualization or mapping. The first two steps constitute data preprocessing stage; the next two constitute data processing stage. The last step is usually the ultimate goal of using GIS to visualize the findings.

3.2.1 Data Preprocessing Stage

Although there are several options for getting data into GIS, perhaps geocoding, a tool for translating location information into corresponding latitudes and longitudes in health databases, is increasingly more popular (128). Automated geocoding coupled with automatic address standardization and cleaning functions, has helped promote GIS-based analysis of data. Geocoding levels vary depending on the reference data used. The most accurate geocoding comes from the use of tax parcel-level database. The Topologically Integrated Geographic Encoding and Referencing (TIGER) system that provides a national computer-readable map database for geocoding operations enables street-level geocoding. Geocoding with census tracts or zip codes (or zip + 4 codes) can be available for lesser accuracy (128).

Transformation processes constitute data preprocessing stage. Correlated or redundant information is also removed in this stage. Also the same scale of observation is applied to all maps before looking for a spatial pattern. Determining the degree of aggregation and simplification is made in this stage as well. Spatial data analysis often requires transformation of data formats. There are basically two types of geographic data: vector data, based on coordinates, comes as points, lines, or polygons, while raster data, based on grids or pictures, is more commonly associated with spatial analysis (128). Points represent a single location and generally have associated data for the specific even or location. Polygons represent areas, and most often have aggregated data associated with them. Raster data does not have direction or inside/outside features, but does have a cell size and extent with data attached to each cell (128). While the data is numeric, it can represent measurements or categories. GIS tools are available for converting one format to another before spatial analysis is taken. Data may also be in different units or at different scales. One might have counts per county, or city, zip code, or

census tract. Location information in health data (e.g., death certificates, hospital discharge, and health care provider data) is most often available at the level of zip code. Census data come in different spatial units. A GIS allows users to combine all this information in a meaningful way, using overlay, buffering, geoprocessing, zonal averages, and proportional allocation (128).

3.2.2 Data Processing Stage

In general, things that are closer together tend to be more alike than things that are farther apart. This "local" spatial structure is a fundamental geographic principle for spatial analysis. GIS users define local neighborhoods using their preferred spatial proximity measures. Once the spatial structure is defined by the chosen spatial proximity measure, a local spatial analysis can be done. That is, an observed value for each region can be replaced with a "local" value calculated on the basis of values for the neighboring regions with a pre-specified contributing weight. For example, O'Neill (129) created distance between the pair of residential zip code and nearest hospital emergency department using transportation-specialized GIS software. Instead of the Euclidean distance, the distance was defined as the shortest path along the road network (in minutes) between centroids. Then this distance measure was exported to SAS to do a logistic regression analysis to estimate the probability of in-hospital mortality and emergency admission as a function of hospital distance.

3.3 Spatial Statistical Analysis

Smoothing and Cluster Detection Statistics

Statistical methods such as smoothing and approaches to identify clusters provide objective tools for measuring data quality and for accounting for data uncertainties in mapping

and assessment of spatial patterns. In public health spatial statistical analysis, various smoothing procedures are used to eliminate variance instability in disease rates or proportions. Observed rates are often extreme when the population at risk is too small (e.g., rural areas) or the disease being studied is rare. Its ultimate goal is to control this high variance, find areas with an excess rate, and interpret its categories (128). The most popular methods for smoothing are kernel density smoothing, Empirical Bayes smoothing, and locally weighted regression.

If disease data have been geographically coded to their latitude and longitude coordinates, or to quite small areas such as zip code, census tracts, census block areas, or to other small postal code areas, they can be spatially aggregated in very flexible ways according to the needs of the user. One popular technique for creating a continuous map from such "point" data is kernel density smoothing (128). A point data is mapped by creating a grid using an inverse distance weighting function. GIS software allows users to select the distance or the number of points to be smoothed and create a grid of user-selected fineness (128). Each point is averaged with the weighted value of every other point within a specified distance of that point based on a specified weight scheme such as the inverse square of the distance (128). For example, Talbot et al. (129) used kernel density smoothing techniques while working with the numbers of low birth weights (LBW) as well as the total number of births aggregated for each zip code in New York State. All births in a particular zip code were then assigned to the geographical coordinates of the population-weighted zip code centroid. Then this zip code was overlaid with a layer with 1-km spacing of the grid points. The nearest zip code centroid to the grid point is located. If the number of births is less than the minimum number, then the next nearest zip code centroid is located and the number of births are added to those from the previous zip codes. This process is continued until the total number of births captured is greater than or equal to the minimum

number of births. At this point, the total number of births and LBWs captured in the selected zip codes are assigned to the grid point.

Many disease mapping studies use empirical Bayes smoothing. In this technique, observed rates are calculated as disease cases/population at risk. The rates are assumed to follow a binomial, or Poisson, random variable (128). Empirical Bayes methods shrink observed rates differentially toward the mean of the distribution of rates in proportion to their expected variability based on the number of observations in the small areas. For example, when the observed rates are based on small populations the Bayes estimator is closer to the prior mean (much local smoothing). However, when the population is large, the Bayes estimator approaches the observed rate (little local smoothing) (128).

Unlike the first two methods, a locally weighted regression (LOESS) is a nonparametric smoothing method. In locally weighted regression, points are weighted by proximity to the current value in question using a kernel. A regression is then computed using the weighted points. It performs a regression around a point of interest using only data that are "local" to that point (128). The estimator variance is minimized when the kernel includes as many points as can be accommodated by the model. Too large a kernel includes points that degrade the fit; too small a kernel neglects points that increase confidence in the fit (128). There are a number of ways one can set the smoothing parameter. As the parameter decreases, the regression becomes more global. The variance-based method usually gives the best performance (128).

There are some issues regarding the use of spatial statistical analyses in the health field. First, commercial GIS packages such as ArcGIS or MapInfo, do not allow the users to do spatial analyses without leaving their systems. Studies had to leave GIS systems to use other programs to make meaningful spatial statistical analyses (127-129). Secondly, health data come in

different units from different sources. Health researchers who deal with various data sources often have to aggregate data. The third issue is the intrinsic nature of data that are often available to health researchers: health data are mostly count data aggregated over a geographical region. Some smoothing methods used were originally designed for continuous spatial data such as elevation readings, agriculture crop, or mining deposit. So applying smoothing methods originally developed for raster (image) data to the polygons for which health data are commonly available can be very arbitrary (128). HIPAA compliance issues can also prevent researchers from having detailed health data. In this case, the technique for disaggregating rather than aggregating data may be demanded by health researchers. For example, when screening data is available for zip codes and cancer incidence data is available for census tracts, area interpolation is needed to estimate the screening rates for census tracts (128). The efforts to expand the use of GIS to other than traditional GIS-favorite fields have not been successful at least in terms of use of spatial statistical analyses in GIS. More statistical tools suitable for health data should be integrated into GIS.

The analytic capabilities of geographic information systems have developed rapidly in recent years. Public health is now presented with the opportunity to examine key relationships between the health characteristics of populations and physical, environmental and human characteristics. It is evident that there is now a need for the development of a more structured, organized system of disease surveillance in which geo-referenced data systems are available. GIS will be valuable in identifying certain areas where there are higher disease prevalence and risk factors. This could later lead to the development of focused programs that can reduce risk factors and possible disease rates.

4.0 GEOGRAPHIC INFORMATION SYSTEMS AND PUBLIC HEALTH

Today, GIS are increasingly being used to investigate diverse public health and medical problems. For example, environmental health researchers are using GIS to conduct risk analyses of the spatial diffusion of air and water pollutants. Epidemiologists are using GIS to investigate possible etiological risk factors of various acute and chronic diseases. Community health scientists are using these systems to study the disparities in disease and mortality rates among various ethnic and racial groups. Emergency planning and management researchers are studying their anticipated responses to possible natural disasters and terrorist attacks at various geographic locations (123).

Advances in computer technology, the encouragement of its use by the federal government, and the wide availability of academic and commercial courses on geographic information systems are responsible for the growing use of GIS in public health and medicine. The greatest potential of GIS lies in their abilities to clearly and convincingly show the results of complex analyses through maps. Unlike tables and spreadsheets with seemingly endless numbers, maps produced by GIS have the ability to transform data into information that can be quickly and easily communicated. These systems also extend the range of problems that can be solved using technology by allowing users to more efficiently complete complex problems (123).

Certain environmental aspects play an important role in the prevention and treatment of chronic diseases. Studies have shown that access to health care, diet, physical activity, housing, income, and environmental exposures contribute to chronic disease, which are all part an individual's environment or community (130, 131, 132). While there are many ways to define community, geographic location is one important way to understand the context in which people

live. What has been lacking, until recently, is a valid method for defining and analyzing geographic areas which make up a community where these risk factors and chronic diseases may cluster. Geographical modeling may allow for better identification of the geographic area of communities which can provide information regarding risks for chronic disease. There is great variability in the health and well being of residents depending upon where they live. Health-promotion interventions may need to be designed to target the geographic areas that represent clusters of health problems and unhealthy lifestyles.

Associations between disease and place imply that the population living there possesses inherent traits that make it more susceptible to disease or that it may experience some increased level of exposure to a risk factor. Second, spatial analysis can help identify how populations adapt and relate to their environment.

Chronic diseases are preventable and can be controlled with intervention. However, some areas may not have resources that would enable its residents to lead a healthy lifestyle. Geospatial mapping techniques can be used to show areas with higher prevalence of chronic diseases and where funds need to be targeted. These maps can provide important clues about the geographic variability of risk factors, disease states and clinical services utilization.

4.1 The Built Environment

The built environment refers to human-modified places such as homes, schools, workplaces, parks, industrial areas, farms, roads, and highways (154). The built environment encompasses all buildings, spaces and products that are created or modified by people. It extends overhead in the form of elective transmission lines, underground in the form of waste disposal sites and subway trains, and across the county in the form of highways (154). It impacts indoor and

outdoor physical environments (e.g., climatic conditions and indoor/outdoor air quality) as well as social environments (e.g., civic participation, community capacity and investment) and subsequently our health and quality of life (154). The built environment has an influence on health since 80% of North Americans live in cities and towns and spend 90% of their time indoors (155). Much discussion of the built environment has focused on the challenges of providing adequate transportation, urban sprawl, air pollution and the diminishing natural environment.

New evidence, however, increasingly recognizes that the places we live and work clearly affect our health (155,156). Access to green open space can increase physical activity and mental wellbeing, because most sustained exercise is incorporated into daily routine activities (163). Recent research explores the effect the built environment on physical activity (157), asthma (158), obesity (159), cardiovascular disease, lung cancer mortality (160), and mental health (161,162). The growing health burdens and rising economic costs associated with higher chronic disease incidence require such research efforts. These complex diseases are attributable to an interaction of genetic and environmental influences, and many of the latter can be directly connected to the built environment. Research investigating the association between public health and quality-of-life benefits of sustainable communities is necessary.

4.1.1 Housing, Transportation, and Sedentary Lifestyles

The association between substandard housing and health has long been recognized (164,165). However, only recently has a growing body of evidence emerged suggesting that physical and mental health problems – anxiety, depression, attention deficit disorder, substance abuse, aggressive behavior, asthma, heart disease, and obesity – related to the built environment,

particularly to poor urban planning and inadequate housing (158,166). Housing disrepair exposes individuals to lead, pests, air pollution, contaminants, and greater social risk (158).

Over decades, unimproved sidewalks decay as utility crews dig up concrete, tree roots push up paved areas, and weather erodes surfaces. Many cities lack the resources to repave or replace sidewalks as frequently as needed. As a result, neighborhoods frequently have broken or impassable sidewalks. While sharply contrasting with the problem of no sidewalks in may rural communities, broken sidewalks in urban areas have a similar result, less leisure walking (172). Lack of safe sidewalks in growing urban areas has resulted in a reduction in the number of children walking or biking to schools, and adults walking to work or for recreation. Today, only 10% of children walk or bicycle to school – a 40% reduction over the last 20 years (154). This has contributed to an increasingly sedentary lifestyle for children, possibly factoring into the growing rates of childhood obesity (154).

Mounting evidence suggests that there are social, health, and economic consequences to isolated and sedentary lifestyles (154). Unfortunately, the physical and social construct of the urban environment promotes isolation (154). Certain features of the built environment such as cul de sacs, lack of parks, and high speed traffic may function to discourage activity and ultimately increase obesity risk (169). Studies find that people who live close of parks are more likely to use them and to be physically active than those who live farther from them (154,169). Neighborhoods with a mixture of land use types including commercial, industrial, residential, and office, also appear to promote physical activity (170), while neighborhoods consisting exclusively of housing seem to dampen activity (171). Higher rates of television viewing, increased computer usage, concern about crime, little contact with neighbors, and geographic isolation have created communities that are not interconnected (154). This isolation may result

in a lack of social networks, which can contribute to obesity, cardiovascular disease, mental health problems, and increased rates of mortality (167,168).

Coinciding with the health risk of physical inactivity is the reality of food insecurity. Many older neighborhoods no longer have a local supply of fresh, healthful food and they often lack transportation access to supermarkets (172). Supermarkets are less likely to locate in inner cities and rural areas and small stores are more likely to sell low quality, non-fresh food and have higher prices, a situation that would contribute to poorer nutrition and lower health status (172).

4.2 GIS and Disease Mapping

GIS analysis can be further used to identify geographic regions in which disease is localized. The use of GIS is an important way in which to better illuminate how individuals interact with their environment in terms of their health. While there are many ways to define community, geographic location is one important way to understand the context in which people live. There is great variability in the health and well being of residents depending upon where they live (119). GIS-based analysis can be used to identify these areas. Health-promotion interventions can then be designed to target the geographic areas that represent these clusters of health problems and unhealthy lifestyles.

There have been significant developments in disease mapping in the past few decades. The continual development of statistical methodology in this area is responsible for the growing popularity of disease mapping because of its potential usefulness in regional health planning, disease surveillance and intervention, and allocating health funding.

Geographic information systems are increasingly used to analyze the geography of disease, specifically the relationships between pathological factors (causative agents, vectors and

hosts, people) and their geographical environments. GIS applications in the United States have described the sources and geographical distributions of disease agents, identified regions in time and space where people may be exposed to environmental and biological agents, and mapped and analyzed spatial and temporal patterns in health outcomes (117).

Some of the earliest GIS applications with implications for the study of disease involved mapping point sources releasing toxic chemicals into the environment (117). The Agency for Toxic Substances and Disease Registry (ATSDR) was an early supporter for the use of GIS in environmental health studies, adopting the technology in 1990 and sponsoring a workshop on GIS applications in public health and risk analysis in 1994, underscoring its commitment to GIS as a tool for assessing "real risks to real people" (118). Researchers have been using GIS to describe environmental health studies for quite some time. Information on environmental contamination is integrated with population or human health outcome data in a GIS. Studies limited to modeling the sources and distributions of environmental agents have evolved, and now GIS are being used to implement EPA recommendations for managing sources of groundwater contamination in wellhead protection areas, integrating data from a variety of sources on the distribution of agents (117).

An example of how GIS is often used in environmental studies is a pilot study conducted by Hunter (120), of carcinogens in water drawn from domestic wells in Anne Arundel County, Maryland, used a GIS to determine which wells to sample. The GIS application identified areas potentially at risk for contamination based on commercial and industrial land use associated with volatile organic compounds (120).

Because of data limitations, investigating the sources and geographical distribution of biological agents of disease using GIS has proven more difficult than modeling environmental

sources (117). Air and water quality monitoring systems have traditionally emphasized monitoring physical and chemical properties rather than detection of biological agents. Indeed, the presence of these agents is often determined after a disease outbreak. In the case of infectious diseases which are transmitted directly from person to person, unlike diseases transmitted though air and water, monitoring the distribution of the disease agent is essentially reduced to surveillance of people who carry the disease. This is controversial because of threats to privacy and confidentiality and also because health service providers and their business partners have a proprietary interest in administrative records. Over the past several decades, administrative data rather then data from publicly maintained disease surveillance systems have been an important source of data on population morbidity (117), but only for those who have access to the data. Because there are geographical differences in the availability and utilization of health services, the underlying spatial pattern of morbidity in the population may not be accurately captured in these data (117).

Numerous empirical studies have been conducted to investigate whether minority and low-income populations are disproportionately exposed to pollution and GIS have clearly played a role in these studies. In a study using 1990 census population data and 1995 geographical data from the City of Minneapolis, two proximity measures commonly used in GIS-based assessment of environmental equity were used to evaluate potential exposure to airborne chemicals for minorities, the poor, and children (121). A geographic randomization methodology was developed to assess the significance of the results derived from the proximity measures.

Health agencies in the United States have long been involved in the preparation of atlases to display the spatial distributions of health outcomes. These projects are now taking advantage

of advances in computer-assisted cartography, GIS, and online mapping. Some of these directly address disparities by racial, ethnic, and income groups.

Research conducted in San Diego explored whether residences near highly traveled roads were associated with asthma in children from low-income households (122). The locations of residences of 5996 children 14 years old or younger diagnosed with asthma in 1993 were compared to a random control group of children with non-respiratory diagnoses including 2284 diagnoses. The number of medical care visits made by children with asthma was also evaluated in relation to traffic levels. Traffic counts at the highest traffic street, the nearest street, and all streets within a 500-ft buffer around the residence were calculated from available traffic data. Analysis of the distribution of cases and controls by quintiles and 90^{th}, 95^{th}, and 99^{th} percentiles showed no significantly elevated odd ratios. Among children with asthma, however, children whose nearest street had low traffic flows to have made two or more medical visits for asthma during the year than to have made only one visit. The results suggest that exposure to motor vehicle exhaust may aggravate symptoms among those diagnosed with asthma.

The analytic capabilities of geographic information systems have developed rapidly in recent years. Public health is now presented with the opportunity to examine key relationships between the health characteristics of populations and both physical environmental and human characteristics. From reviewing these studies, it is clear that there is a need for a system of disease surveillance which also uses geographical data. GIS will be valuable in identifying certain areas where there are higher disease prevalence and risk factors. This could later lead to the development of focused interventions that can reduce these risk factors and possible disease rates.

Trooskin et al. (181) conducted a study aimed to use GIS to document the non-random distribution of hepatitis C (HCV), identify infection cluster areas, and describe the demographic characteristics of these areas. The investigators conducted spatial analysis of newly reported positive hepatitis C cases using the Connecticut Hepatitis C Reporting Database. Spatial filtering was used to eliminate random noise generated by sparsely populated towns or small number of cases per town. Cluster analysis was used to determine whether cases of HCV infection tend to occur closer in space to other cases than would be expected by chance alone. The study determined that areas with the highest concentration of HCV reports roughly correspond to the major metropolitan areas of Connecticut. Four of the six significant clusters indentified were located in the most densely populated and most urban areas in the state. All but one identified cluster had been described previously as areas of substantial injection drug use. The findings of this study suggest that spatial analysis may assist in the identification of clusters that would not otherwise be suspected based on local demographics or other characteristics (181).

Timander and Mclafferty (182) performed an exploratory spatial analysis of breast cancer clustering in the community of West Islip on Long Island, New York. Using address-level data from a survey of women in this community, the researchers analyzed the existence and locations of breast cancer clusters among long-term community residents. Spatial and geographical methods were used to estimate a logistic regression model of disease as a function of known risk factors and to analyze spatial clustering among the cases of breast cancer not explained by the modeled risk factors (182). This method determines the actual locations of clusters so that if there is a potential causal factor in the environment it can be identified for further study. Although the researchers found little evidence of clustering, the methods they described have a utility for exploratory spatial analysis in many different health contexts.

Jacquez and Greiling (183) conducted a two-part study that employed a multi-methods approach to elucidate geographic variation in cancer incidence in Long Island, New York, and to evaluate spatial association with air-borne toxics. The researchers used the local Moran statistic to identify cancer hotspots and spatial outliers. They evaluated the geographic distributions of breast cancer in females and colorectal and lung cancer in males and females in Nassau, Queens, and Suffolk counties, New York. The researchers identified significant local clusters of high and low standard mortality rate (SMR) and significant spatial outliers for each cancer-gender combination (183). This study did not consider any economic, ethic, or environmental exposure data so these factors could not be related to the clusters.

4.2.1 GIS in Diabetes and Obesity Research

Few spatial analysis studies have been conducted that investigate diabetes, obesity or risk factors related to these conditions. Since spatial analysis was mainly used for environmental studies, most spatial analysis public health studies focused on environmental exposure studies.

Obesity in the United States has been linked to individual income and education. Drewnowski et al. (132) conducted a study to determine whether obesity rates in King County, Washington, at the zip code scale, were associated with area-based measures of socioeconomic status and wealth. In a model adjusting for covariates and spatial dependence, property values were the strongest predictor of the area-based smoothed obesity prevalence (132). Geocoding of health data provides new insights into the nature of social determinants of health. Disparities in obesity rates by zip code area were greater than disparities associated with individual income or race/ethnicity (132).

Gesler et al. (130) used GIS technology in diabetes health intervention research. Successful intervention programs to prevent diabetes require information about where target populations live and carry out their activities. Gesler and colleagues used geographic analysis to obtain this information by using maps of where people live and carry out their daily activities to plan diabetes intervention programs. Researchers used Global Positioning System and GIS technologies to map residences, activity spaces using symbols and standard deviational ellipses (SDEs), and sites where diabetes information has the potential to be welcomed, for a sample of low income African American, Latino, and white females and males in a small, rural, southern town. Standard deviational ellipses are particularly effective at capturing the spatial characteristics of a population group (e.g., places participants visited in the past week) and have been widely used in crime analysis and social studies. SDEs were derived from spatial locations and weighted by the total amount of time spent at each point (130). The ellipses produced represent approximately 95% of the group's activities. The maps produced by this study provided data on the best locations for diabetes prevention programs and educational materials to target individuals at high risk for the development of type 2 diabetes (130).

The high prevalence of obesity may result from the interaction of environmental, behavioral, and genetic factors. Broadly defined environmental factors such as changes in agriculture, food processing and marketing, transportation, and the contextual effect of residential areas create the context for the population distribution of adiposity (192). Environmental characteristics that have recently received attention as determinants of physical activity include aspects of urban sprawl (193), accessibility of recreational resources (194,195), and neighborhood safety (196,197).

In addition, food availability at the neighborhood level has recently received attention as a possible environmental determinant of health. Researchers have documented disparities in the costs of foods (198-200) among areas, while others have shown differences in the availability of certain types of food stores (198-203). Moreland, Roux, and Wing (192) conducted multilevel modeling in order to calculate prevalence ratios of the associations between the presence of specific types of food stores and cardiovascular disease risk factors. The researchers used 2004 data from a cross-sectional study of men and women participating in the third visit (1993-1995) of the Atherosclerosis Risk Communities (ARIC) Study. This analysis demonstrated that the presence of supermarkets was associated with a lower prevalence of obesity and overweight (obesity prevalence ratio [PR] = 0.83, 95% CI=0.75-0.92; overweight PR=0.94, 95% CI=0.90-0.98), and the presence of convenience stores was associated with a higher prevalence of obesity and overweight (obesity PR=1.16, 95% CI=1.05-1.27; overweight PR=1.06, 95% CI=1.02-1.10). The results from this study suggest that characteristics of local food environments may play a role in the prevention of overweight and obesity (192).

Inagami et al. (206) found residents in poor neighborhoods have a higher body mass index (BMI) and eat less healthfully. One possible reason might be the quality of available foods in their area. The researchers examined the location of grocery stores where individuals shop and its association with BMI. The 2000 U.S. Census data were linked with the Los Angeles Family and Neighborhood Study (L.A.FANS) database, which consists of 2620 adults sampled from 65 neighborhoods in Los Angeles County between 2000 and 2002. Inagami and colleagues used multilevel linear regressions to estimate the associations between BMI and socioeconomic characteristics of grocery store locations after adjustment for individual-level factors and socioeconomic characteristics of residential neighborhoods. They found that individuals had a

higher BMI if they reside in disadvantaged areas and in areas where the average person frequents grocery stores located in more disadvantaged neighborhoods. Those who own cars and travel farther to their grocery stores also had a higher BMI. When controlling for grocery store census tract socioeconomic status (SES), the association between residential census tract SES and BMI became stronger. They were able to conclude that where people shop for groceries and distance traveled to grocery stores are independently associated with BMI.

Another study describing diabetes used a spatial scan statistic method to test for the presence of diabetes clusters. The spatial scan statistic, which works by aggregating together the unique combinations of small-area geographies which have a high probability of being clusters, is an especially powerful tool to use in low-prevalence and low-incidence situations. Green et al. (131) used GIS to identify the socio-demographic, environmental, and lifestyle factors associated with the geographic variability of diabetes. Predictor and outcome data were aggregated for analysis using the spatial scan statistic to aggregate study data into highly probable diabetes prevalence clusters. Predictor and outcome data were aggregated to existing administrative health areas. Analysis of variance and spatial and non-spatial linear regression techniques were used to explore the relationship between predictor and outcome variables. Mapping and statistical analysis revealed substantial clustering in the prevalence of diabetes in the City of Winnipeg, Canada. The observed variations were associated with variations in socioeconomic, environmental, and lifestyle characteristics of the population (131).

Samuelsson and Löfman (204) investigated geographic clusters of type 1 diabetes in children and adolescents in south east Sweden. Ordinary kriging was used for estimation of spatial distribution of incidence and the population at risk was obtained directly from the population registry for the years and geographical area levels used for the cases. The researchers

found a clear geographical variation in the risk for children and adolescents to develop type 1 diabetes between the municipalities in the south east region of Sweden. They further explained that apart from chance, the most probable explanation of this is that local environmental factors play a part in the process leading to the development of type 1 diabetes (204).

5.0 ACCESS TO HEALTH CARE IN RURAL AREAS

Patients in rural areas may use less medical care than those living in urban areas (133). This difference in access to health care in rural areas may be dependent on a number of variables. These include patient-specific factors such as age, race, ethnicity, and perceptions of quality, as well as extrinsic factors such as insurance coverage and health care costs (133). Another potential factor related to health care utilization is travel time and distance (134,135). Research has suggested that utilization is adversely affected by long travel times. Indeed, patients may forgo free care if it is greater than 20 miles away (134). Several state health departments have proposed a standard in which rural residents should not have to travel more than 30 minutes to see a physician (133).

Our current framework of the rural-urban hierarchy of care is one in which rural areas are very dependent on urban ones for health care, in particular specialty care. In this "hub-and-spoke model," rural patients must, and be willing to, travel long distances for their care. However, more recently, a much less dependent model had been put forward, wherein most specialty care is obtained in larger rural cities (e.g., rural cities of >25,000 population) (133). Most research studies determine rural status of a geographical area by linking the patient zip code to its rural-urban commuting area code (RUCA) (136). This rural-urban taxonomy is typically selected because RUCAs are now the basis of a wide range of federal programs. RUCAs use Census Bureau information to differentiate areas based on their city/town size and work commuting patterns to larger cities and towns. There are four categories designated by the RUCA: urban (population 50,000 or greater), large rural city (in or associated with a large rural city of 10,000-49,999), small rural town (in or associated with a rural town of 2,500-9,999), and

isolated rural town (in a town of less than 2,500 population and/or not associated significantly with a larger town via work commuting flows (133).

5.1 Access to Care

Chan, Hart and Goodman (133) used Medicare billing data from 1998 to study geographic access to health care for rural Medicare beneficiaries living in Alaska, Idaho, North and South Carolina, and Washington. The authors found that 96% of visits by those living in urban communities were either in the patient's home zip code or in an urban area. In contrast, only 21% of visits by those living in large rural areas were in urban areas. The vast majority (75%) of these visits were in large rural areas or in the patient's home zip code. Only about 30% of visits by those living in a small and isolated rural area were in urban areas. The majority of these visits took place in other rural areas. Thus, rural residents received the vast majority of their visits within rural areas.

The authors also found that rural residents have fewer overall visits and see fewer medical specialists and more generalists for their care than their urban counterparts. In addition, they found residents of small and isolated rural areas have greater travel distance and time compared to those living in urban areas. Median one-way travel time was less than 30 minutes for all patients, including those living in isolated small rural areas. However, some patients with specific diagnoses or undergoing specific procedures needed to travel much farther. Less than 30% of those living in all rural areas traveled to urban areas for their care. The vast majority were seen in their area or traveled to a larger rural location (133).

The impact of health status of the disparity in geographic access to medical specialists remains unclear. These differences certainly create costs for rural residents, including increased

money for travel; increased time spent traveling, and the possibility of delays in care. Some research suggests that rural residents do not rely on urban areas for the majority of their care (133,134). Only about 30% of visits by those living in small and isolated rural areas were in urban areas. Indeed, for those living in large rural areas, this figure was only 20% (133). This has several implications. First, it appears that patients are unwilling or are unable to travel great distances for their care. Secondly, these individuals rely heavily on care by generalists, such as internists and those in family practice (134). Overall, this research suggests that those living in small and isolated rural areas have decreased geographic access to health care providers, in particular medical specialists, and rely heavily on generalists for the majority of care. Additionally, these individuals have fewer visits overall (9.9% fewer for those in isolated rural areas) and must travel longer distances to access certain types of care (133).

Rural older adults are often viewed as especially vulnerable for a number of reasons. Rural areas are frequently characterized by poorly developed and fragile economic infrastructures, resulting in fewer available per capita hospital beds, doctors, nurses, and other health care services (135). In addition to socioeconomic hardships rural residents face substantial physical barriers, including a lack of public transportation, difficult terrain, and long distances to services (136,137). It still remains unclear how rural elders perceive barriers to health care access and how they cope with those perceived barriers. Researchers Goins, Williams, Carter, Spencer, and Solovieva (134) examined what barriers rural elders report experiencing when accessing needed health care. To determine this, the authors conducted focus groups with community-dwelling rural elders in six rural counties in West Virginia to discuss the barriers they believe prevent them from accessing care in general. In response to the questions posed to the focus group participants, five categories of barriers to health care emerged from the

discussions: transportation difficulties, limited health care supply, lack of quality health care, social isolation, and financial constraints (134).

Discussion regarding health care supply included concerns about the limited number of physicians and long-term care options. The limited number of physicians included difficulty with recruitment and retention, need for more specialists, overall limited choice of physicians, and aging of local doctors (134). Many rural residents depend on care provided by physician assistants (PAs) and international medical graduates (IMGs), which can be perceived as a problem. Comments regarding IMGs concerned rural elders' reluctance to see these doctors or their dissatisfaction with past experiences, primarily due to perceived language barriers.

Lack of quality health care emerged as a third barrier. Issues included difficulty getting accurate diagnoses, lack of trust in health care providers, physicians' perceived lack of interest in patients, difficulty scheduling an appointment, and/or long waiting times at such appointments. Some participants felt that physicians were not interested in them as patients, particularly since they were older adults. Participants also expressed dissatisfaction with waiting too long to be seen by their physician.

Social isolation reflected some aspects of rural norms and values, such as the strong sense of self-reliance and reluctance to use formal services. Some participants were unaware of or did not have accurate information about available services. Participants also suggested that it would be helpful if older adults had information on services that might help meet their needs (134).

Financial constraints posed considerable barriers to accessing needed health care among study participants, including issues related to health care expense, inadequate health care coverage, income ineligibility to Medicaid, and the high cost of prescription medications. Participants commented they were not poor enough to qualify for Medicaid but did not have

enough financial resources to afford health care (134). Rural areas have significant gaps in the continuum of care since home-based and community-based long-term care services are often unavailable (136). Beyond having a limited supply of health care providers, rural respondents also reported physicians are inadequate and lack professionalism. In rural areas, local physicians are often perceived as having poor interpersonal skills and/or lower quality care than what is available in more populated areas (138).

5.2 Access to Transportation and Driving Distance

One of the most often cited attributes of rural areas that affects health care utilization is low population density, isolation, and large distances between residences and services (139). The opportunity for health care consumers to have a vehicle to transport them to a practitioner or facility is especially important in rural settings where distances are relatively great, roads may be poor quality, and public transportation is seldom available (139).

The South Carolina Rural Health Research Center took advantage of a highly detailed, nationally representative survey of travel conducted by the U.S. Department of Transportation, the 2001 National Household Travel Survey (NHTS) to explore the potential for disparities in access associated with rural residence. The NHTS asks participants to record each of their trips and its purpose; one purpose was medical/dental care. The researchers found that nationally, the average distance traveled for medical/dental care was 10.2 miles (205). Rural trips averaged 17.5 miles, versus 8.3 miles for urban residents. In multivariate analysis, they found that rural residents remained more likely to travel more than 30 minutes for care (OR 1.80, CI 1.09-2.99) (205). Rural populations, more likely to perceive the price of gas as a problem, are likely to be particularly affected by current gasoline prices (205).

Conceptually, transportation can be examined from two perspectives. Within the Health Behavior Model, it is an important enabling factor for accessing health care (144), particularly in rural areas. Recent analyses have begun to focus on the effects of transportation access in rural communities. Lovett and colleagues (146) use geographic information system analysis to show that in rural areas of the United Kingdom, there are pockets in which car journeys to the nearest general practitioner are greater than 10 miles and there is no regular bus service. These pockets of limited transportation have the highest health need indicators. Nemet and Bailey (147) measured perception of ease in getting a needed ride among rural elders in Vermont. Their measure of transportation access ("If you have to get somewhere in a car, how difficult is it for you to get there? -very difficult, somewhat difficult, not at all difficult?") was not significant in predicting health care visits in the face of distance from provider. Gesler et al. (148) found that over 85% of the transportation for health care visits in the previous year among the residents of two rural North Carolina communities was by private car, with 13.5% having walked. However, an important finding was that those who drove themselves to care and those who had to be driven (car riders) formed two groups with distinct characteristics. Car riders in both towns were more likely to be older, female, African American (vs. white), unmarried, poor, and less educated than those who drove themselves. Car riders were also more likely to be in fair or poor health as opposed to good or excellent health, to lack medical insurance, and to travel 20 minutes or more annually to health care.

A need for transportation programs will only increase as the rural population ages during the coming decades; it is the elderly who have the greatest limitations in the use of personal transportation (driving a car) as well as a great need for health care (142). Damiano et al. (145) found that those individuals in Iowa City, IA, who used public transportation had four more

annual chronic care visits that those who did not. Access to public transportation for health care in rural communities is far from universal, and where it is available, it is often restricted to those with special characteristics, such as older adults and those with certain kinds of chronic conditions. Providing effective public transportation systems is difficult. These are expensive services that are more easily cut during difficult economic periods than are direct patient services.

5.2.1 Diabetes Health Care Access

According to the Rural Healthy People 2010 survey, diabetes was identified as the third highest ranking rural health concern (177). In this national survey of local and state rural health leaders, diabetes was ranked third among the most frequently nominated rural priorities, after access and heart disease and stroke (178). Diabetes was also among the top five priorities in all four geographic regions of the survey. The prevalence of diabetes also varies by urbanicity and degree of rurality. In 1995, the self-reported 3.6% prevalence of diabetes in non-metropolitan statistical areas (MSAs) of the United States was higher than in central cities (3.19%) and all MSAs (3.24%) (179).

Despite the availability of effective treatments, many patients with diabetes do not receive optimal glycemic control. As previously discussed for all health care, travel burden may be one of many obstacles for diabetes patients, especially in rural areas. Travel burden includes arranging transportation, the time required to travel, arranging child care, the cost of missing work, and the cost of the transportation. Driving distance is one aspect of travel burden, and may serve as a marker for at least some of the burden of obtaining diabetes care. Strauss et al. (149) examined the relationship between glycemic control and the driving distance from a patient's

home to the site of primary care. The authors found that driving distance was significantly associated with glycemic control in their population of older, rural subjects. Each 22 miles of driving distance was associated with a 0.25% increase in HbA1c. The effect was more pronounced among insulin users. Several mechanisms may contribute to this relationship. Longer driving distances may mean fewer office visits and less monitoring (149). In addition, those who live farther away may be perceived to be at greater risk for hypoglycemic complications, leading to less aggressive care (149). Littenberg et al. (150) found that the greater the driving distance for adults with diabetes to their source of primary care, the less likely they are to be using insulin. The authors suggest that patients and physicians are concerned about the risks of insulin and are reluctant to use it if they feel the patient lives too far away from care for rescue in the event of hypoglycemia. Travel burden might influence therapy through the frequency of medical contact (150). It may be useful to minimize travel burden for patients with diabetes, perhaps by enhanced public transportation, more clinic locations in rural areas, telephone or other electronic links, or home care.

In the face of a steadily increasing prevalence of diabetes, the health care system has failed to prevent, detect, and manage diabetes adequately, especially in rural areas. Rural residence is a significant risk factor for never receiving an ophthalmic examination, which can detect early signs of diabetic retinopathy (178). When rural residents do see a doctor, they are more likely to see a generalist than a specialist for treatment of diabetes and related complications. Rural patients with a history of gestational diabetes are at high risk for developing T2D, yet only 30% have adequate follow-up by their physicians (179).

Because diabetes self-management education has been shown to be effective at improving short-term behavioral and physiologic outcomes for patients with diabetes, decreased

access to education is an important barrier in rural settings. In addition, busy rural primary care practices often lack the organizational support and computerized tracking systems to initiate practical interventions to improve diabetes care (151). The Park County Diabetes Project, a partnership between three primary care clinics, the Livingston Memorial Hospital, and the Montana Diabetes Control Program, initiated a collaborative effort in October 2000 to improve diabetes care and community awareness among Park County residents (151). Beginning in October 2000, the Park County Diabetes Project made a number of changes in the delivery of diabetes care and patient education. These included establishing and maintaining the patient registries, nurses conducting mail and telephone outreach to patients in need of services, and providing ongoing continuing education workshops. This is one of only a few studies documenting improved diabetes care, outcomes, and reduced self-management barriers in a rural population. The changes in diabetes self-management barriers are notable, as in the decrease in the A1c and blood pressure values for this patient population over the three-year period. For rural communities, one of the key areas in which change is needed may be improving access to diabetes education. This could be accomplished through distance communication strategies, such as telemedicine, or through the provision of educational support and resources to assist health professional to improve their diabetes education skills and their ability to develop quality education programs (151). These findings suggest that system changes in primary care practices and the implementation of accessible diabetes education can improve care and reduce barriers for rural patients with diabetes on a countywide level.

6.0 CONCLUSION

Diabetes is a complex chronic disease with many causes, complications and management needs. It affects a large proportion of people of varying ages, income levels, races/ethnicities and geographic areas. Diabetes is becoming more common in the United States. From 1980 through 2007, the number of Americans with diabetes increased from 5.6 million to 17.9 million (2). It is estimated that another 5.7 million Americans are undiagnosed (2). Approximately 762,000 or 7.0% of Pennsylvanians have been diagnosed with diabetes and is responsible for nearly 4,000 deaths in Pennsylvania (6). Diabetes is a major public health challenge due to the enormous impact on the affected individual, their families and the health care system. However, recent research has shown that diabetes related mortality and morbidity can be prevented or delayed by controlling risk factors (7).

Certain environmental aspects play an important role in the prevention and treatment of chronic diseases such as diabetes. Studies have shown that access to health care, diet, physical activity, housing, income, and environmental exposures contribute to diabetes, which are all part an individual's environment or community (4,5). While there are many ways to define community, geographic location is one important way to understand the context in which people live. Until recently, there has not been a valid method for defining and analyzing geographic areas that make up a community where these risk factors and chronic diseases may cluster. Geographical modeling may allow for better identification of the geographic area of communities that provide risk for diabetes. There is great variability in the health and well being of residents depending upon where they live. Health-promotion interventions may need to be

designed to target the geographic areas that represent clusters of health problems and unhealthy lifestyles.

Geographical Information Systems (GIS) may allow investigators to conduct spatial analysis that can to be used to increase comprehension of chronic disease pathogenesis. Geographical studies may suggest possible causal factors based on geography and play an important role in the understanding of the development and control of diabetes. Associations between disease and place imply that the population living there possesses inherent traits that make it more susceptible to disease. However, it has been shown that there are certain risk factors that cluster in these areas that cause increased risk for disease. Also, spatial analysis can help identify how populations adapt and relate to their environment. More research is needed to study how the built environment relates geographically to chronic diseases such as diabetes in order to develop public health prevention programs and improve diabetes management and outcomes.

There is a growing recognition that the built environment has an impact on health. For example, one may expect more physical activity and healthier diets among persons in communities with convenient, safe walking paths and accessible sources of fresh fruits and vegetables. On the other hand, poorer health indicators may be expected among residents of communities with high crime rates, few parks or walking paths, numerous alcohol and tobacco outlets, and little access to fresh food. Low-income and/or rural communities are more likely to be sites of hazards and less likely to be conducive to physical activity and healthy eating. Chronic diseases, such as diabetes, are leading health concerns which are influenced by the built environment. Decisions about zoning, transportation, land use and community design influence the distances people travel to health care facilities, the convenience of purchasing healthy foods,

and the safety and attractiveness of neighborhoods for walking. It is clear from the health implications of these decisions that public health should be a strong ally to ensure that decisions about neighborhood design are made with the health of community members at the forefront.

However, decisions about the built environment have traditionally been made without active inclusion of public health. To facilitate public health's participation, this project provides a concrete example that demonstrates the importance of the built environment as well as illustrates potential roles for public health. A greater understanding of opportunities to improve health outcomes through altering the built environment will strengthen linkages between public health, city planners and others involved in community design.

7.0 METHODS

7.1 OBJECTIVE AND SPECIFIC AIMS

In order to provide the public health community with another tool to enhance our understanding of the factors that affect the numbers and types of diabetes cases in Pennsylvania, it is important that we undertake a project that will support the analysis of geographic and geospatial factors in terms of associated risk factors. Geospatial analysis tools can be used to discover and analyze relationships based on geographic proximities. These factors include the location of various disease prevention and healthcare facilities (pharmacies, foot and eye care centers hospitals, rural health clinics, physcians' offices), locations of healthier food options (large supermarkets, farmers markets, full-service restuarants) and areas for physical activity (parks, recreational centers, golf courses, gyms) and public transportation routes and sidewalk availability to identify areas in greater need of these services. The concentration of diabetes cases in areas of greater need of services will also lend information regarding issues of access and the potential consequences these issues.

This study proposes to investigate geographical patterns of diabetes hospitalizations, risk factors for diabetes complications and glycemic control among individuals with type 2 diabetes in rural regions. Geographic data will be used to explore the geographic distribution of diabetes hospitalization rates in rural Southwestern Pennsylvania in Allegheny, Armstrong, Cambria, Greene, Indiana, Fayette, Somerset, Washington, and Westmoreland counties. This geographic data will be juxtaposed with a variety of potentially related geographic, economic, and health risk factors. As a part of this investigation, we aim to:

1. To identify an association between county rurality hospitalization rates for uncontrolled diabetes in southwestern Pennsylvania.

a: Individuals who reside in counties with increased rurality will be more likely to be hospitalized for uncontrolled diabetes than counties that are more urbanized.

2. To determine if there is an association between the availability of disease prevention and health care facilities, the local food environment and risk factors for complications of diabetes in Southwestern Pennsylvania.

a. The presence of supermarkets, full-service restaurants, physicians' offices, hospitals and pharmacies will decrease the likelihood of having the risk factors for diabetes complications in individuals with type 2 diabetes.

3. To examine the association between glycemic control and improvement in individuals with type 2 diabetes, and travel burden to diabetes management centers in southwestern Pennsylvania.

a. Individuals who have uncontrolled diabetes will be less likely to live as close to their diabetes management center as those who are in glycemic control. Also, those who live closer will be more likely to have improved glycemic control than those who live farther from the diabetes centers.

7.2 STUDY DESIGN

7.2.1 Overview

This study is an observational, ecological cross-sectional study that took place in rural Southwestern Pennsylvania including Allegheny, Armstrong, Cambria, Fayette, Greene, Westmoreland, Indiana, Somerset, and Washington Counties.

7.2.2 Data Collection

In an effort to improve diabetes education and care, the University of Pittsburgh Diabetes Institute started a regional health care collaboration, the Pittsburgh Regional Initiative for Diabetes Education (PRIDE). Nine counties (Allegheny, Armstrong, Cambria, Fayette, Greene, Indiana, Somerset, Washington, and Westmoreland) were selected from the study area where the partners of PRIDE diabetes centers are located. The patient data was collected using a data management system, Delphi. This system was used by the University of Pittsburgh Diabetes Institute in order to collect data on individuals with diabetes attending diabetes centers throughout southwestern Pennsylvania. The participating centers include: The Center for Diabetes Care at the Indiana Regional Medical Center, Community Medical Services, Centerville Clinics, Inc., Conemaugh Diabetes Institute, The Diabetes Center at Uniontown Hospital, Highlands Hospital Diabetes Center and the Washington Hospital Diabetes Education & Management Program. The Delphi Data Management System allowed the staff of these centers to enter patient data into an organized system. Individual-level data such as home addresses, demographics, lab test data, medications, health indicators, comorbid conditions, and complications were entered into this data system from June 2005 to January 2007. The variable list is included in Table 9.6, Appendix B. All of the individuals 18 years and older that were entered into the Delphi system (n=3367) were diagnosed by their physician with diabetes prior to be being referred to the diabetes center.

Data from the Pennsylvania Health Care Cost Containment Council (PHC4) was obtained to determine diabetes hospitalization rates in the counties of interest (PCH4, 2006). PCH4 is an independent state agency responsible for addressing the problem of escalating health costs. The council collects, analyzes and makes available to the public data about the cost and quality of

health care in Pennsylvania. PHC4 collects over 4.5 million inpatient hospital discharge and ambulatory/outpatient procedure records each year from hospitals and ambulatory surgery centers in Pennsylvania. This data, which includes hospital charge and treatment information as well as other financial data, is collected on a quarterly basis and is then verified by PHC4. The Council also collects data from managed care plans on a voluntary basis. The Council shares this data with the public through free public reports. The PHC4 data used for this study is a customized data set obtained through the Council's *Special Requests* division. The data set included all hospitalizations with any diagnosis of diabetes or diabetes-related complications in the counties within the study area. Control patient data was also obtained for those hospitalized with a primary diagnosis for fractures (ICD-9 codes 800-829) in the same counties. The variable list is included in Table 8.8, Appendix A.

All persons who were hospitalized during the 2007 calendar year with a diagnosis for diabetes in any diagnosis code fields were used to calculate the hospitalization rates. Hospitalizations rates per 10,000 adult residents were calculated for diabetes as the principal diagnosis only and any listed diagnosis (includes the admitting, principal, or any of the eight secondary diagnoses). For these events, the International Classification of Diseases, Ninth Revision, Clinical Modification codes (ICD-9) for diabetes (250.xy; where, x = 0,1,2,3,4,5,6,7,8,9 and y = 0, 1, 2, 3) as the diagnosis code were used to calculate rates. The hospitalization rates were age and sex-adjusted using the standard 2000 U.S. population estimates from the U.S Census Bureau (207). The hospitalization rates for uncontrolled diabetes (250.02; 250.03) as any listed diagnosis and long-term complications of diabetes (250.xy; where, x = 4,5,6,7,8,9 and y = 0,1,2,3) as any-listed diagnosis were also calculated. The hospitalization rates for short-term complications diabetes (250.xy; where, x = 1,2,3 and y = 0,1,2,3) as any

listed diagnosis and end stage renal disease (250.40-250.43, 996.62, 996.73, and 996.81) as any listed diagnosis were calculated as well. A more descriptive listing of these ICD-9 codes is displayed in Table 8.7, Appendix A. Age-adjusted rates were calculated by stratifying the population into four age groups: 18-44, 45-64, 65-74, and 75 years of age and greater. These age categories were used to follow the age categories of the Centers for Disease Control and Prevention (CDC) (211). The zip code of the patients' residence was used to define the county of residence, and to prevent calculating rates for the county in which the patient was hospitalized. Since this study is interested in the geographical variance associated with the patients' residence and not necessarily hospitalizations rates due to diabetes, it was important to make this distinction.

Municipal data such as county, city and political borders were downloaded in shape file format from the United States Census website (www.census.gov) (180-184). The Census website was also used to download demographic and socioeconomic information such as percent of the population living below the poverty level, median household income, population by age, and education levels for each county, zip code and census tract (185,186). Road centerline data was collected by a project partner, L. Robert Kimball & Associates, from each county municipal office (187). The locations of waterways such as lakes and streams, public recreational areas such as parks and state forests, and industrial sites such as brown fields were downloaded from the Pennsylvania Spatial Data Access website (www.pasda.psu.edu) (188). Business data such as locations of restaurants, supermarkets and grocery stores, convenience stores, fresh fruit and vegetable markets, meat and fish markets, fitness and other recreational centers, and health care facilities (including rural health clinics, private physicians offices, diabetes clinics, dialysis centers, eye care, and hospitals) were purchased from ESRI, a GIS and mapping software

company that also provides geographical datasets (189). With the exception of the business data, all of these geographical data sets are publicly available.

7.2.3 Address Geocoding

The type of data used for this project is known as quasi geospatial data because by using the addresses alone it is not possible to pinpoint locations on a map and to integrate address-based data with other forms of geospatial data for spatial analysis (112). To locate addresses on a map, it is necessary to determine their grid references in an accepted geo- referencing system. Address geocoding, also known as address matching, is the process by which grid references (e.g. latitude/longitude) are added to point locations described by street addresses from the county road centerline data (112). Address geocoding is an important geospatial data input function in many GIS software packages, including the software used for this project, ArcView GIS.

The Concept of Address Geocoding

The objective of address geocoding is to match addresses in data files that have grid references (the reference theme) to those addresses in data files that do not (the event table). The primary source of reference theme data in this project will be the road centerline data acquired from each individual county. When this reference theme data was unavailable, either TIGER (Topologically Integrated Geographic Encoding and Referencing) files from the Bureau of the Census or StreetMap from ESRI will be used. Although the structures of different reference theme data files may be different from one another, they all contain the street network and the address ranges on both sides of the street that are necessary for geocoding (112). On the other hand, addresses in the event table are normally recorded as text strings that contain components

such as house number, street name, city name, and postal code. The event table was stored in the specific format of a database file as a dBASE dbf file.

The software module that performs geocoding is usually referred to as the geocoding editor. It is necessary for the two types of data to be in a compatible format in order to compare the reference theme data with event table data in address geocoding. This means the creation of a geocoding index from the geographical reference theme by the geocoding editor. The geocoding index is a database table. An associated geocoding information file is also created to record the characteristics of the geocoding index, such as address style and the address attribute fields. During the address geocoding process, the application software first reads the records in the event table one by one (112). It pareses the address into separate components (i.e., street number, street name, city name, and postal code) and standardizes the components according to the specifications of a selected address style supported by the geocoding editor. It then determines the street segment where the particular address is found by geocoding index. The actual grid reference of the address within the street segment is finally computed by interpolating between the two end points of the street segment according to the numerical relationship between the street number and the address range of the street segment (112).

The Process of Address Geocoding

Address geocoding is multi-step process that can be carried out in batch or interactive modes, or a combination of both. The procedure of geocoding can be generalized into the following sequence of steps (Figure 1):

1. *Data preparation*. The objective of this step is to prepare the reference theme and the event table for geocoding. For the reference theme, it is necessary to ensure that the address style used is one of the address styles supported by the geocoding editor, for example, U.S. street

address with zone, U.S. street address without zone, ZIP + postal codes, and five-digit ZIP postal codes (112).

All addresses for both patients and businesses were standardized to support one address style, U.S. street address with zone. For the event table, it was made certain that all components of the street address were stored according to the format specified by the geocoding editor in ArcView. All abbreviations were spelled out. Addresses with rural routes or former highway numbers were compared to standardized 9-1-1 address databases and were corrected. If PO Boxes were the only address provided, then the 9-1-1 address database was used to locate the street address associated with the PO Box. The geocoding editor supports some name aliases (e.g. City Hall, St. Patrick's Hospital) in addition to the street addresses, so a separate alias table for common place names was created.

2. *Loading the reference theme and event table*. The reference theme and the event table were loaded into the geocoding editor, which then built the geocoding index and the geocoding information file for using information from these two input files. (112). Street centerline data provided by each county municipal office was used as the reference theme. ArcView Street Map was also used to provide another layer of detail for the reference theme table.

3. *Geocoding*. The geocoding process was performed in both batch and interactive modes. The process was started in batch mode, which let the geocoding editor run until the last record of the event table was reached. At the end of the batch run, a dialog box showing the number of matches that were made was displayed. There were various reasons why a perfect match was not achieved, such as spelling mistakes, incorrect house numbers, and outdated data in the reference theme or event table. At this point, an interactive rematch was performed by

which each of the unmatched addresses was examined and geocoded with the aid of the geocoding editor.

4. *Saving and populating the geocoding data*. On completion of the interactive geocoding process, the results to data files were saved as required by the geocoding editor so that they could be used for further analysis.

Once the addresses in the event table were geocoded, they were integrated with other types of geospatial data to create new maps and perform spatial analysis. A typical map is called an electronic pin map, which displays the locations of various events by address. Geocoded addresses were also used in advanced spatial query and analysis, such as location-allocation modeling to determine the optimal locations of new service centers or facilities.

7.2.4 Network Analyst

The ArcGIS Network Analyst extension was used in this study to find driving distances between study subjects and various outcome locations. Network Analyst allowed us to build a network dataset and perform analysis on a network dataset (212). This extension is composed of a number of parts: a wizard to create a network dataset (in ArcCatalog), a dockable Network Analyst window (in ArcMap), a Network Analyst toolbar (in ArcMap), and a number of geoprocessing tools contained within ArcToolbox. A network dataset includes highways connecting to cities, streets interconnected to each other at street intersections, and sewer and water lines that connect to houses (212).

7.2.4.1 Building a Network Dataset

First, the sources for appropriate roles inside the network dataset must be prepared. The sources should have fields that represent the network impedance values such as distance, travel

time, etc. For best results, these fields should be named the same as the units of the impedances, as these fields will automatically be detected by the New Network Dataset wizard (212). If one-way streets are modeled, the edge sources should have a field specifying one-way street information. The network dataset can then be created using the Network Dataset Wizard. The Wizard will wizard will walk the user through naming the network dataset, identifying the network sources, setting up the connectivity, identifying elevation data, if necessary, specifying turn sources, if necessary, defining attributes (such as costs, descriptors, restrictions, and hierarchy), and setting up the directions reporting specifications (212). Finally, when a network dataset is created or an existing network dataset is edited, it must be built. Building is a process of creating network elements, establishing connectivity, and assigning values to the defined attributes (212).

7.2.4.2 Route Analysis

Creating a route can mean finding the quickest, shortest, or most scenic route, depending on the impedance chosen. If the impedance is distance, as used in this study, then the best route is the shortest route. Thus, the best route can be defined as the route that has the lowest impedance, or least cost (212). Any cost attribute can be used as the impedance when determining the best route. When e a new route analysis layer is created, it is displayed in the Network Analyst Window, along with related three categories which are stops, barriers, and routes (212).

The stops feature layer stores the network locations that are used as stops in route analysis. In this study, the diabetes management center that the subjects visited was used as the location stops. Barriers are used in route analysis to denote points from which a route cannot

traverse through. The Route feature layer stores the resultant route of route analysis. Once the best route is found, it is displayed on the Network Analyst Window.

7.2.4.3 Creating an Origin-Destination Cost Matrix

Using Network Analyst, an origin-destination (OD) cost matrix was created for the homes of subjects to each diabetes centers they visited. The parameters for the OD cost matrix were specified and paths from each home to the particular center they visit.

There are four components of an OD cost matrix analysis layer: origins, destinations, barriers, and line feature classes. The origins layer stores the network locations that are used as origins in OD cost matrix analysis. In this study, the home addresses of the subjects were used as the origins. Destinations feature layer stores network locations that are used as destinations in OD cost matrix analysis. In ArcMap, this layer behaves exactly like the Origins feature layer. In this study, the diabetes management centers were used as the destinations. Barriers feature layers are used in closest facility analysis to denote points where a route cannot traverse and were not needed in this study. The Lines feature layer stores the resultant paths of OD cost matrix analysis (212).

7.3 STATISTICAL ANALYSIS

Before any hypotheses were tested, the distribution of and descriptive statistics for all variables of interest were performed to determine mean, range, distribution, and other characteristics necessary to determine appropriate statistical analyses to be performed. The measures of central tendency (e.g. means, standard deviations, medians, proportions, etc.) were also used for all of the descriptive analyses.

Specific Aim 1:

Nine Pennsylvania counties (Allegheny, Armstrong, Cambria, Fayette, Greene, Indiana, Somerset, Washington, and Westmoreland) were selected from the study area. These counties were chosen for this specific aim because these are the counties in the study area for all three manuscripts. Age and age-sex-standardized diabetes hospitalization rates were calculated for each of the nine counties using the patient data collected by PHC4. Demographic information included with this data set was used to calculate diabetes hospitalization rates per 10,000 people for each county with respect to population information from Census 2006 data. The dataset was stratified into four groups: 18-44, 45-64, 65-74, and 75 years and older.

Each county was ranked by rurality based on criteria from the United States Department of Agriculture Economic Research Service (USDA) (210). Based on the continuum from the USDA, the definitions of the nine counties in this study are as shown in Table 8.6 in Appendix A. The counties were further ranked based on total population, population density, miles of roads/highways, and daily vehicle miles traveled, miles of highways/roads in combination with the USDA's continuum codes (Table 8.5, Appendix A). The counties were ranked for rurality on a scale from 1 to 9 with respect to the previously described measures above. The overall rankings of rurality were calculated for each county by averaging the scores for each of the six measures. The population data was obtained from the Census 2000, which was obtained from the U.S. Census Bureau, 2005 (207,208). The traffic-related data was obtained from the Pennsylvania Department of Transportation (209).

This specific aim seeks to determine whether diabetes hospitalization rates were associated to area-based measures of race/ethnicity, income, poverty, type of hospital admission, and type of insurance. Multi-level analysis using logistic regression/General Estimating

Equations (GEE) was used to test the association between uncontrolled diabetes rates and county rurality by calculating odds ratios (OR) and their 95% confidence intervals (CI). A binary variable for the outcome was calculated for those individuals hospitalized for uncontrolled diabetes (= 1) versus those hospitalized for all other diabetes ICD-9 codes (= 0). Individual variables that were thought to be important characteristics in those with diabetes such as age, race, and gender were added to the model. Age was entered into the model as both a continuous individual variable and as a county mean age to assess differences between the counties. Since this data was not available at the individual-level for these hospitalization events, the study employed county averages of the percentage of residents living below the poverty level and the percentage of residents with a high school diploma or higher degree to determine the distribution of socioeconomic data for each county. The insurance information for each patient was also included in the analysis as a measure of poverty. In the full model, gender and percent living below the poverty level were not statistically significant. Each of these variables was removed from the model individually with no changes to the model. However, due to the importance of the two variables to diabetes outcomes, they remained in the final regression model. Statistical analyses were performed with SAS 9.1, GeoDa, and Excel to determine the odds ratios, county rankings, and spatial autocorrelation. All estimates of significance were at $p = .05$ level.

Choropleth maps of the hospitalizations rates for each of the counties were created using ArcMap Software (Figures 8.12-8.16, Appendix A). These maps use a color gradient to symbolize the classifications of rates. GeoDa Software was employed to analyze spatial autocorrelation and whether the hospitalization rates of in one county correlate with neighboring counties. The presence, absence, or characteristics of some spatial objects may sometimes have significant impacts on the presence, absence, or characteristics of the neighboring objects (7).

Moran's I was the indicator used to examine spatial autocorrelation between the county's rates (Figures 8.9 – 8.11, Appendix A).

Specific Aim 2:

The distribution of and descriptive statistics for all variables of interest were performed to determine distribution, mean, median, and other characteristics necessary to determine appropriate statistical analyses to be performed. To estimate odds ratios (OR) of diabetes complications risk factors associated with the presence of different types of food stores, multi-level logistic regression was performed using the PROC GENMOD program in SAS 9.1 (28). This is a multilevel test that takes census tract and individual-level data into account and the repeated measures option was used to account for the clustering of subjects within the census tracts. Each of the risk factors of hypertension, hypercholesterolemia, overweight, obese, and hyperglycemia was modeled separately. First, dichotomous variables characterizing 'any' versus 'none' of that type of facilities within the census tract were created for each type food service place (fast food, limited-service, and full-service restaurants), food store (supermarkets, grocery stores, and convenience stores), offices of physicians and pharmacies. Indicator variables were also created to represent the presence of specific combinations of types of food stores: (a) Supermarkets only, (b) Grocery stores only, (c) Convenience stores only, (d) Supermarkets, grocery stores, and convenience stores, (e) None, (f) Combination of stores; and food service places: (a) Full-service restaurants only, (b) Limited-service restaurants only, (c) Fast food restaurants only, (e) None, and (f) Combination of places. The dichotomous variables were modeled for each of the risk factors, while controlling for age, gender, and duration of diabetes. Since individual-level socioeconomic status (SES) information was not available, census tract information was used in the model to control for these factors. The percentage of residents

living below the poverty level, percentage of residents reporting Black as their race, median household income, and percentage of residents with a high school education or higher for each census tract were also considered in the regression models. Descriptive analysis was conducted to calculate the mean and percentages of laboratory values, age, gender, duration of diabetes, co-morbidities and complications of diabetes.

Specific Aim 3:

The analyses for specific aim 3 will build on the analyses for specific aims 1 and 2. Again, descriptive statistics for all variables of interest were performed to determine distribution, mean, median, and other characteristics necessary to determine the appropriate statistical analyses to be conducted. Patient outcomes such as BMI, blood pressure, LDL, HDL, HbA1c from the Delphi database was used to make comparisons between those that are in glycemic control and those who are not.

Travel burden will calculated by determining the shortest distance from the subject's home to the diabetes management center they visited. The subjects will be categorized dichotomously as living less than or greater than ten miles from the diabetes center. The driving distances of subjects that are in glycemic control and those who are not will be compared with X^2 tests. Multi-level logistic regression will be used to test the association between control (present or absent) and each marker of travel burden (distance in miles and dichotomous variable) by calculating odd ratios. The analysis will be adjusted for individual level factors such as age, sex, BMI, type of insurance, and duration of diabetes as well as community level factors such as percent of census tract living below the poverty level, median household income, and percent of census tract with a high school degree or higher.

8.0 MANUSCRIPT 1:

ANALYSIS OF UNCONTROLLED DIABETES HOSPITALIZATIONS IN RURAL AREAS

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8.1 ABSTRACT

Objective - To consider an association between county rurality and hospitalization rates for uncontrolled diabetes in southwestern Pennsylvania.

Hypothesis: Individuals who reside in counties with increased rurality will be more likely to be hospitalized for uncontrolled diabetes than those in counties that are more urbanized.

Research Design and Methods: Nine counties in Southwestern Pennsylvania (Allegheny, Armstrong, Cambria, Fayette, Greene, Indiana, Somerset, Washington, and Westmoreland) were selected from the study area where diabetes centers are located. Age-standardized diabetes hospitalizations rates using Pennsylvania Health Care Cost Containment Council were calculated. Each of the counties was ranked by rurality based on criteria from the United States Department of Agriculture Economic Research Service. Statistically significant contributions to the diabetes hospitalization rates by each of the independent individual and county level covariates (county rank, age, gender, race, poverty, education, income) were examined by logistic regression/GEE analysis.

Results: The analysis included 54,703 patients from nine counties who were hospitalized with a diagnosis of diabetes (ICD-9 250.0-250.9) during the 2007 calendar year. Patients were predominantly older (59.2% age 65 or more), female (53.6%), and Caucasian (88.9%). Allegheny County had the highest percentage of Blacks (19.8%) and Washington County had the highest mean age (68.2 years old). During 2007, diabetes was the principal diagnosis upon admission in 14.5 per 10,000 adult residents, and for any-listed diagnosis in 246.8 per 10,000 adult residents for the entire study area. Hospitalization rates for uncontrolled diabetes (ICD-9 codes 250.02; 250.03) as any-listed diagnoses upon admission were also calculated for the study

area. The rate was 8.2 per 10,000 adult residents. The results indicated that residing in a more rural area (OR = 1.11, P = <0.0001), being younger (OR = 0.98, P = <0.0001), non-white (OR = 1.25, P = 0.002), being uninsured or receiving Medicaid (OR = 0.96, P = <0.0001) and having a high school degree or higher (OR = 0.89, P = <0.0001) were significant contributors to being admitted to the hospital for uncontrolled diabetes while gender was not significant (OR = 1.04, p = 0.46).

Conclusions: Results of this study indicated an association between the rurality of a county and the diabetes hospitalization rates of the county's residents. Residents of more rural counties are 11% more likely to be hospitalized for uncontrolled diabetes compared to those living in areas that are less rural for every increase in rurality ranking.

8.2 INTRODUCTION

There are 23.6 million children and adults in the United States, or 7.8% of the population, who have diabetes. While an estimated 17.9 million have been diagnosed with diabetes, unfortunately, 5.7 million people (or roughly 25%) are unaware that they have diabetes. Diabetes affects approximately 7.0% of the population of Pennsylvania (5). This disease is a major public health challenge due to the enormous impact on the affected individual, their families and the health care system. However, recent research demonstrates that diabetes related mortality and morbidity can be prevented or delayed by controlling risk factors (1).

Studies demonstrate that access to health care, diet, physical activity, housing, income, and environmental exposures contribute to chronic disease, which are all part an individual's environment or community (2-4). Environmental factors associated with rurality may contribute to geographical differences in diabetes-related hospitalization rates. Areas with a higher rurality ranking in terms of population density, miles of highways/roads, median household income, and average daily vehicle miles may have higher rates of diabetes hospitalizations. These more rural areas typically have less public transportation, fewer health care facilities and services, lower levels of education, and lower income. Patients in rural areas may use less medical care than those living in urban areas (4). This difference in access to health care in rural areas may be dependent on a number of variables. These include patient-specific factors such as age, race, ethnicity, and perceptions of quality, as well as extrinsic factors such as insurance coverage and health care costs (4). Another potential factor related to health care utilization is travel time and distance (27,28). Research has suggested that utilization is adversely affected by long travel times. A study found that rural patients may forgo free care if it is greater than 20 miles away

(27). Several state health departments have proposed a standard in which rural residents should not have to travel more than 30 minutes to see a physician (4).

There is great variability in the health and well being of residents depending upon where they live. Health-promotion interventions may need to be designed to target the geographic areas that represent clusters of health problems and unhealthy lifestyles as well as those that are socioeconomically disadvantages.

The objective of the current study was to identify an association between county rurality and hospitalization rates for uncontrolled diabetes in southwestern Pennsylvania. We hypothesized that individuals who reside in counties with increased rurality will be more likely to be hospitalized for uncontrolled diabetes than those in counties that are more urbanized.

8.3 METHODS

8.3.1 Study Population

In an effort to improve diabetes education and care, the University of Pittsburgh Diabetes Institute started a regional health care collaboration, the Pittsburgh Regional Initiative for Diabetes Education (PRIDE). Nine counties (Allegheny, Armstrong, Cambria, Fayette, Greene, Indiana, Somerset, Washington, and Westmoreland) were selected from the study area where the partners of PRIDE diabetes centers are located. The participating centers included: The Center for Diabetes Care at the Indiana Regional Medical Center, Community Medical Services, Centerville Clinics, Inc., Conemaugh Diabetes Institute, The Diabetes Center at Uniontown Hospital, Highlands Hospital Diabetes Center and the Washington Hospital Diabetes Education & Management Program.

As prevalence of diabetes could not be directly measured, data were obtained from the PHC4 to estimate the prevalence of diabetes in the study area. The Pennsylvania Health Care Cost Containment Council (PHC4) is an independent state agency responsible for addressing the problem of escalating health costs. The council collects, analyzes and makes available to the public data about the cost and quality of health care in Pennsylvania. This data, which includes hospital charge and treatment information as well as other financial data, is collected on a quarterly basis and is then verified by PHC4. The Council also collects data from managed care plans on a voluntary basis. The PHC4 data used for this study is a customized data set obtained through the Council's *Special Requests* division. The data set included all hospitalizations with any diagnosis of diabetes or diabetes-related complications in the counties within the study area.

8.3.2 Study Design

Each county was ranked by rurality based on criteria from the United States Department of Agriculture Economic Research Service (6). The USDA ERS used Rural-Urban Continuum Codes (6) to form a classification scheme that distinguishes metropolitan (metro) counties by the population size of their metro area, and non-metropolitan (nonmetro) counties by degree of urbanization and adjacency to a metro area or areas. The metro and nonmetro categories were subdivided into three metro and six nonmetro groupings, resulting in a nine-part county codification. All U.S. counties and county equivalents were grouped according to their official metro-nonmetro status announced by the Office of Management and Budget (OMB) in June 2003, when the population and worker commuting criteria used to identify metro counties were applied to results of the 2000 Census. Metro counties were distinguished by population size of the Metropolitan Statistical Area of which they are part. Nonmetro counties were classified

according to the aggregate size of their urban population. Within the three urban size categories, nonmetro counties were further identified by whether or not they have some functional adjacency to a metro area or areas. A nonmetro county was defined as adjacent if it physically adjoins one or more metro areas, and has at least two percent of its employed labor force commuting to central metro counties. Nonmetro counties that do not meet these criteria are classed as nonadjacent. Based on the continuum described above, the USDA defines the nine counties in this study as shown in Table 8.6 in Appendix A.

The counties were further ranked based on total population, population miles of highways/roads in combination with the USDA's continuum codes (Table 8.5, Appendix A). The counties were ranked for rurality on a scale from 1 to 9 with respect to the previously described measures above. The overall rankings of rurality were calculated for each county by averaging the scores for each of the six measures. The population data was obtained from the Census 2000, which was obtained from the U.S. Census Bureau, 2005 (13, 14). The traffic-related data was obtained from the Pennsylvania Department of Transportation (15).

8.3.3 Case Definitions

The hospitalization data for adults 18-106 years of age obtained from PHC4 contained the admitting, principal, and eight secondary diagnosis codes for each hospitalization event that occurred within in the study area during 2007. The Principal Diagnosis Code is the ICD.9 diagnosis code assigned at discharge as the reason for the hospitalization as supplied by the facility. It may differ from the admitting diagnosis. The secondary diagnosis codes 1-8 are additional ICD.9 diagnosis codes assigned to describe additional conditions that coexist at admission or are discovered during the hospitalization as supplied by the facility. The age

variable was calculated by PHC4 and outliers were investigated through their research department. The outliers were verified to the best of the researcher's knowledge and remain in the analysis. All persons who were hospitalized during the 2007 calendar year with a diagnosis for diabetes in any diagnosis code fields were used to calculate the hospitalization rates. Hospitalizations rates per 10,000 adult residents were calculated for diabetes as the principal diagnosis only and any listed diagnosis (includes the admitting, principal, or any of the eight secondary diagnoses). For these events, the International Classification of Diseases, Ninth Revision, Clinical Modification codes (ICD-9) for diabetes (250.xy; where, x = 0,1,2,3,4,5,6,7,8,9 and y = 0,1,2,3) as the diagnosis code were used to calculate rates. The hospitalization rates were age and sex-adjusted using the standard 2000 U.S. population estimates from the U.S Census Bureau (13). The hospitalization rates for uncontrolled diabetes (250.02; 250.03) as any listed diagnosis and long-term complications of diabetes (250.xy; where, x = 4,5,6,7,8,9 and y = 0,1,2,3) as any-listed diagnosis were also calculated. The hospitalization rates for short-term complications diabetes (250.xy; where, x = 1,2,3 and y = 0,1,2,3) as any listed diagnosis and end stage renal disease (250.40-250.43, 996.62, 996.73, and 996.81) as any listed diagnosis were calculated as well. A more descriptive listing of these ICD-9 codes is displayed in Table 8.7, Appendix A. Age-adjusted rates were calculated by stratifying the population into four age groups: 18-44, 45-64, 65-74, and 75 years of age and greater. These age categories were used to follow the age categories of the Centers for Disease Control and Prevention (CDC) (17). The zip code of the patients' residence was used to define the county of residence, and to prevent calculating rates for the county in which the patient was hospitalized. Since this study is interested in the geographical variance associated with the patients' residence and not necessarily hospitalizations rates due to diabetes, it was important to make this

distinction. To control for individuals hospitalized more then once in the 2007 calendar year, a unique patient identifier was used to calculate the hospitalization rates. This unique number was randomly generated for each patient in the data set and supplied by PHC4. The rate presented reflect only one hospitalization event per unique identification number.

8.3.4 Statistical Analysis

The multi-level data was analyzed using General Estimating Equations (GEE) regression to test the association between uncontrolled diabetes rates and county rurality by calculating odds ratios (OR) and their 95% confidence intervals (CI). This data is considered multi-level because the dataset contains both individual and county level variables. A binary variable for the outcome was calculated for those individuals hospitalized for uncontrolled diabetes (= 1) versus those hospitalized for all other diabetes ICD-9 codes (= 0). Individual variables that were thought to be important characteristics in those with diabetes such as age, race, and gender were added to the model. Race was coded for non-whites and whites so that the minorities were grouped together due to low numbers in this category. Age was entered into the model as both a continuous individual variable and as a county mean age to assess differences between the counties. Prior studies cited factors related to educational attainment and income as contributing to poor health outcomes (8-12). Since this data was not available at the individual-level for these hospitalization events, the study employed county averages of the percentage of residents living below the poverty level and the percentage of residents with a high school diploma or higher degree to determine the distribution of socioeconomic data for each county. The insurance information for each patient was also included in the analysis as a measure of poverty. In the full model, gender and percent living below the poverty level were not statistically significant. Each

of these variables was removed from the model individually with no changes to the model. However, due to the importance of the two variables to diabetes outcomes, they remained in the final regression model. Statistical analyses were performed with SAS 9.1, GeoDa, and Excel to determine the odds ratios, county rankings, and spatial autocorrelation. All estimates of significance were at $p = .05$ level.

Cloropleth maps of the hospitalizations rates for each of the counties were created using ArcMap Software (Figures 8.12-8.16, Appendix A). These maps use a color gradient to symbolize the classifications of rates. GeoDa Software was employed to analyze spatial autocorrelation and whether the hospitalization rates of in one county correlate with neighboring counties. The presence, absence, or characteristics of some spatial objects may sometimes have significant impacts on the presence, absence, or characteristics of the neighboring objects (7). Moran's I was the indicator used to examine spatial autocorrelation between the county's rates. The Queen weighting algorithm was used, which defines neighboring counties as those that meet around the borders. Moran's I statistic is based on a scale of 1 to -1; 0 indicates no correlation and 1 indicates perfect correlation (Figures 8.9 – 8.11, Appendix A).

8.4 RESULTS

8.4.1 Description of the Population

The analysis included 54,703 patients from nine counties who were hospitalized with an ICD-9 code for diabetes, any-listed diagnosis during 2007. They were predominantly older (59.2% age 65 or more), female (53.6%), and Caucasian (88.9%). Allegheny County had the highest percentage of Blacks (19.8%) and Washington County had the highest mean age (68.2 years

old). Table 8.4 includes the population characteristics by county. Based on the county rurality ranks, Armstrong and Greene Counties were ranked the most rural; Westmoreland and Allegheny Counties were ranked the least rural.

Age-adjusted adult diabetes hospitalization rates (per 10,000 residents) among those with diabetes for each county are displayed in Figures 8.0-8.8, Appendix A. The unit of analysis for these rates is the individual; the total number hospitalizations were unavailable therefore, the total number of diabetes hospitalizations was used to calculate the following rates. During 2007, diabetes was the principal diagnosis among all diabetes hospitalizations upon admission in 14.5 per 10,000 adult residents, and the any-listed diagnosis in 246.8 per 10,000 adult residents for the entire study area. Allegheny County, which ranked as the least rural county, had the highest age-adjusted diabetes hospitalization rate as a principal diagnosis (17.8 per 10,000). This rate was also high in Washington County (14.1 per 10,000), which also ranked among the least rural. The age-adjusted rates per 10,000 adult residents for the other counties in order from most rural to least are as follows: Armstrong (7.9); Greene (4.4); Fayette (11.9); Cambria (7.4); Indiana (9.7); Somerset (12.5); and Westmoreland (12.7) (Figure 8.1). At a rate of 49.1 per 10,000, non-Hispanic Black residents had hospitalization rates for diabetes as a principal diagnosis 3.6 times that of non-Hispanic Whites (13.4 per 10,000). At a rate of 409.1 per 10,000, non-Hispanic Black residents had hospitalization rates for diabetes as any-listed diagnosis 1.5 times that of non-Hispanic whites (282.3 per 10,000).

Uncontrolled diabetes as any-listed diagnoses upon admission hospitalization rates were also calculated for the study area, 8.2 per 10,000 adult residents (Table 8.4). The hospitalization rates for all types of diabetes diagnoses examined in this study were slightly higher in male than in females in all counties; Hospitalization rates for uncontrolled diabetes as an any-listed

diagnosis was 7.9 per 10,000 adult residents in males and 7.2 per 10,000 adult residents in females; 15.2 and 12.6 per 10,000 adult residents for diabetes as a principal diagnosis, respectively; and 237.9 and 211.4 per 10,000 adult residents for diabetes as an any-listed diagnosis at hospitalization. Additionally, the highest rates of uncontrolled diabetes hospitalization occurred in the 45-64 years age group. In general, males and females had similar hospital admission rates for diabetes in 2007, 16.8 and 15.2 per 10,000 adults respectively. Similar rates were also found in uncontrolled diabetes hospitalization rates as well as hospitalization rates due to diabetes complications.

The hospitalization rates for short-term complications of diabetes were the highest in Somerset and Westmoreland Counties (5.2 and 4.8 per 10,000, respectively) and the lowest in Armstrong, Greene and Indiana Counties (2.3, 2.5 and 2.5 per 10,000, respectively (Figure 8.6, Appendix A). Similarly, hospitalization rates for long-term complications of diabetes were highest in Washington and Westmoreland Counties (58.6 and 45.1 per 10,000) and lowest in Greene County (13.9 per 10,000 adult residents) (Figure 8.7). Hospitalization rates for End-Stage Renal Disease were highest in Washington and Cambria Counties (16.5 and 10.8 per 10,000) and lowest in Greene and Indiana Counties (2.5 and 6.8 per 10,000 residents) (Figure 8.8, Appendix A).

The proportion of hospitalizations by type of patient insurance was calculated for each county. The proportion of patients with Medicare was the highest type of insurance coverage among all counties ranging from 48.9% in Cambria County to 66.2% in Armstrong County (Table 8.4). The proportion of hospitalizations by type of admission was also calculated. Individuals who were hospitalized for uncontrolled diabetes were overwhelmingly more likely to be an emergency or urgent admission (67.9% - 96.3%). An emergency admission was defined

by PHC4 as the patient required immediate medical intervention as a result of severe, life threatening, or potentially disabling conditions. An urgent admission was defined as the patient required immediate attention for the care and treatment of a physical or mental disorder; an elective admission occurred when the patient's condition permitted adequate time to schedule the availability of a suitable accommodation. A trauma admission was defined as a visit to a trauma center/hospital involving trauma activation.

8.4.2 GEE Regression

Univariate analysis was conducted to explore differences between the counties for age, gender, race and the measures of poverty. The differences among counties for all four of these variables were found to be significant. The significant p-value attained for the race variable was accounted for by the considerably higher percentage of Black residents in Allegheny County. Using GEE regression, county rurality rank, age, gender, and race, percentage of residents living below the poverty level, percentage of residents with a high school degree or higher, and percentage of patients who are uninsured or receiving Medicaid were assessed for their contribution to the adult uncontrolled diabetes versus all other diabetes hospitalization rates for any-listed diagnosis. The results indicated that residing in a more rural area (OR = 1.11, P = <0.0001), being younger (OR = 0.98, P = <0.0001), non-white (OR = 1.25, P = 0.002), percent uninsured or receiving Medicaid (OR = 0.96, P = <0.0001) and percent with a high school degree or higher (OR = 0.89, P = <0.0001) were significant contributors to the model while gender was not significant (OR = 1.04, p = 0.46) (Table 8.1).

Table 8.1: Odds Ratios and 95% Confidence Intervals (CI) for Likelihood of Being Hospitalized for Uncontrolled Diabetes Compared to All Other Diabetes Diagnoses

Parameter	P-value	Odds	95% CI
County Rurality Rank	<0.0001	1.11	1.06, 1.17
% Uninsured/Medicaid	<0.0001	0.97	0.96, 0.98
Age (continuous)	<0.0001	0.98	0.98, 0.99
Race - Non-white	0.005	1.23	1.06, 1.41
Sex- Male	0.47	1.04	0.94, 1.14
% Graduated High School	<0.0001	0.91	0.87, 0.95
% Living Under Poverty Level	0.10	1.02	1.00, 1.04
County Mean Age	0.001	1.28	1.09, 1.50

The diabetes hospitalization rates for uncontrolled and all diabetes for each county were entered into GeoDa software to examine spatial autocorrelation. The Moran's I for rates of diabetes as the principal and any-listed diagnosis as well as uncontrolled diabetes as any-listed diagnosis indicated no significant spatial autocorrelation to neighboring counties (-0.11, -0.19, -0.29, respectively). Moran's I graphs are included in Figures 8.9 – 8.11.

8.5 CONCLUSIONS

Results of this study indicate an association between the rurality of a county and the diabetes hospitalization rates of the county's residents. Residents of more rural counties were 11% more likely to be hospitalized for uncontrolled diabetes compared to all other diabetes hospitalizations, for every increase in rurality rank. For example, a resident in Armstrong County (Rurality Rank = 1) is 27% more likely to be hospitalized for uncontrolled diabetes than a resident in the same age category, gender, and race in Allegheny County (Rurality Rank = 9). This relationship may not be reflected in the hospitalization rates that were calculated for each county because these are rates that are based on the total population of the county and is per 10,000 adult residents of said

county. The relationship that was explored here analyzed the relationship between those hospitalized for uncontrolled diabetes compared to those hospitalized for all other diabetes-related diagnoses. This is an important distinction to address and is explored in more detail in the following sections. Furthermore, the diabetes hospitalization rates may be higher in those counties that are less rural, however, according to data from the Pennsylvania Department of Health, the diabetes and cardiovascular disease mortality rates are higher in more rural counties (Table 8.2). This may indicate that those with diabetes in more urban counties are seeking health care at a greater rate but those in more rural counties are dying from diabetes-related causes. This may be reflected in the results from this study that indicated that residing in a more rural area (OR = 1.11, P = <0.0001), being younger (OR = 0.98, P = <0.0001), non-white (OR = 1.25, P = 0.002), percent uninsured or receiving Medicaid (OR = 0.96, P = <0.0001) and percent with a high school degree or higher (OR = 0.89, P = <0.0001) were significant contributors to the model while gender was not significant (OR = 1.04, p = 0.46). Furthermore, these findings reflect the estimates from the National Center of Health Statistics which found that in 1995, the self-reported prevalence of diabetes in non-metropolitan statistical areas (NMSAs) of the U.S. (3.6 percent) was higher than in central cities (3.19 percent) and all MSAs (3.24 percent) (17).

Diabetes is the sixth leading cause of death and imposes a costly burden on the American health care system (1). It is important to examine the rates of hospitalization in order to find solutions to reduce the number of hospital visits in those with diabetes. Diabetes is a chronic, lifelong disease with no cure. Further, those with diabetes undergo costly treatment with less than half achieving clinical goals (5). According to the National Hospital Discharge Survey, diabetes is the sixth leading cause of hospitalization in the U.S. for men at least 45 years old, and

the seventh overall for women of comparable ages (21). In 1996, diabetes was listed as a discharge diagnosis in 3.8 million individuals (21).

According to the Rural Healthy People 2010 survey, diabetes was identified as the third highest ranking rural health concern (16). In this nationwide survey of state and local rural health leaders, diabetes was ranked third among the most frequently nominated rural health priorities, after access and heart disease and stroke (16). The issue of rural-urban disparities for diabetes is quite complex; however, the prevalence appears to be higher in developed rural areas, such as the areas examined here, and lower in undeveloped ones (18-20). As the difference between rural and urban lifestyle disappear, higher rural prevalence may reflect differences in socioeconomic, racial/ethnic, or age status, more so than rurality *per se*. Several measures of socioeconomic status (SES) were used here to explore these differences among the study counties. The proportion of individuals that were uninsured (self-pay or charity/indigent care) or receiving Medicaid was significantly higher in Cambria County (27.5%) and Somerset County (25.3%) compared to the other counties in the study area. The other measures of SES were at the county-level and are described in Table 8.5.

One way to monitor the cost and quality of care received by individuals with diabetes is to examine the number and type of hospital admissions for diabetes (ref). These admissions add to the high cost of this disease and suggest that individuals with diabetes might not have sufficient access to appropriate preventive care (ref). Furthermore, in 2007, 15.2 percent of patients with diabetes in the study area were hospitalized two or more times, perhaps confirming other studies. This study chose to focus on uncontrolled diabetes. Hospital admissions for uncontrolled diabetes reflect the quality of outpatient care, self-management and other aspects of health care, and are of interest to comprehensive health care delivery systems (5). Admissions

for uncontrolled diabetes can be prevented and therefore reduce the number of hospitalizations. This could lead to a decrease in health care related costs due to diabetes. Hospitalizations for diabetes, particularly for uncontrolled diabetes, may be preventable because appropriate care can generally be provided on an outpatient basis (1). If a patient reaches the point where hospitalization for diabetes is required, a breakdown in care, or access to care, may have already occurred. It is important to note that an overwhelming proportion of the uncontrolled diabetes hospitalizations were emergency or urgent admissions. In this study, these hospitalizations may be due to Type 1 diabetes for acute hyper or hypoglycemia could be prevented with proper self-management through diabetes education and access to quality diabetes care. Those that were hospitalized for uncontrolled diabetes were significantly younger than those who were hospitalized for other diabetes-related causes. This may be because some of the hospitalizations for uncontrolled diabetes were attributed to Type 1 Diabetes, which is seen in the younger population.

A study conducted by the American Diabetes Association (ADA) estimated that in 2007, the direct medical costs attributable to diabetes reached $116 billion (22). People diagnosed with diabetes, on average, have medical expenditures that are roughly 2.3 times higher than those without diabetes (22). Diabetes-related hospitalizations totaled 24.3 million days in 2007, an increase of 7.4 million from the 16.9 million days in 2002 (23). The average cost for a hospital inpatient day due to diabetes is $1,853 and $2,281 due to diabetes-related chronic complications, including neurological, peripheral vascular, cardiovascular, renal, metabolic, and ophthalmic complications (23).

During 2007, diabetes was the principal diagnosis upon admission in 14.5 per 10,000 adult residents, and the any-listed diagnosis in 246.8 per 10,000 adult residents for the entire

study area. The hospital rates that examined principal diagnosis suggest that the reason for the admission was a direct result of diabetes and therefore an important distinction to make. Hospital admission rates for diabetes increased with age; the highest rates were found in those in the 75 years and older age category. At a rate of 49.1 per 10,000, non-Hispanic Black residents had hospitalization rates for diabetes as a principal diagnosis 3.6 times that of non-Hispanic whites (13.4 per 10,000). At a rate of 409.1 per 10,000, non-Hispanic Black residents had hospitalization rates for diabetes as any-listed diagnosis 1.5 times that of non-Hispanic whites (282.3 per 10,000). According the Centers for Disease Control and Prevention non-Hispanic Blacks are 1.6 times as likely to have diabetes as non-Hispanic whites of similar age, on average.

Short-term complications of diabetes include acute, life-threatening events, such as diabetic coma and diabetic ketoacidosis. Hospitalization admission rates for these events may be an immediate reflection of how well patients are managing their diabetes. PHC4 found that the hospitalization for short-term complications in the state of Pennsylvania was 4.9 per 10,000 residents in 2004. Similar any-listed diagnosis hospitalization rates were found in the study area, ranging from 2.3 – 5.2 per 10,000 residents. Also, it should be noted that the figures presented by PHC4 reflect hospitalizations, not persons. An individual hospitalized on two separate occasions during 2004 was counted twice. This may account for the over-estimation of their hospital rates.

Long-term complications of diabetes include chronic problems such as stroke, kidney disease, neurological complications, etc. that develop over a period of years. Hospitalizations for these events may be a reflection of how well individuals are managing their diabetes over a long period. Rates for these any-listed diagnosis hospitalizations in the study are ranged from 13.9-58.6 per 10,000 adult residents.

The literature demonstrates that diabetes encompasses behavioral, environmental, social, and clinical factors, all which play an important role in the management of the disease. It is assumed that behavioral characteristics of individuals with diabetes are affected by their access to health care and disease prevention facilities, a healthy local food environment and physical activity locations. Furthermore, it is believed that those living in more rural areas have less access to these locations and therefore will have higher rates of disease. We believe that our work in this report will provide further evidence for this theory.

This current study also adds to the existing literature by describing a population at the individual-level for a small geographic area. Most of the data collected for diabetes rates are extrapolated from larger random surveys and exact rates are not available at the county-level for many states. This study uses individual-level data to calculate county-level data. It also focuses on hospitalizations for uncontrolled diabetes which can be an indication of how well the health care system in an area is performing. The majority of the literature on the geographic variation of chronic diseases and diabetes examines urban areas and does not focus on rural populations. The rurality of an area is difficult to define and several factors were considered in this study. Larger differences between the rural counties and less rural counties may have been found if different or other factors were accessed. Population density and daily vehicle miles traveled may not be the most important determinants of rurality in terms of diabetes care.

Green et al. (24) used GIS to identify the socio-demographic, environmental, and lifestyle factors associated with the geographic variability of diabetes. Mapping and statistical analysis revealed substantial clustering in the prevalence of diabetes in the City of Winnipeg, Canada. The observed variations were associated with variations in socioeconomic, environmental, and lifestyle characteristics of the population (24). High rates of diabetes prevalence were strongly

correlated with indicators of low socioeconomic status, and poor environmental air quality. These prevalence rates were based on aggregate data from the Canadian Health Service, and did not include individual-level data.

Samuelsson and Löfman (25) investigated geographic clusters of type 1 diabetes in children and adolescents in south east Sweden. The authors sought to estimate the spatial distribution of incidence. The population at risk was obtained directly from the population registry for the years and geographical area levels used for the cases. The researchers found a significant geographical variation in incidence rate were found between the municipalities ($p<0.001$) but not between the counties. The variation became somewhat weaker when excluding the six largest municipalities ($p<0.02$). They further explained that apart from chance, the most probable explanation of this is that local environmental factors play a part in the process leading to type 1 diabetes (25). The authors did not further investigate the environmental factors that my attribute to the increased rate in some areas.

This is the first study, to our knowledge, to consider diabetes hospitalization rates at the geographic scale of the county-level and link it to the rurality of the county. The methodology used in this study can be transported to any other geographical area to determine disparities in urban and rural areas. Furthermore, it is one of the only studies to focus on hospitalizations for uncontrolled diabetes, which may be a predictor of a breakdown in health care or access to care. This study did have limitations. First, this study did not have the number of total hospitalizations for 2007 in the study area. This did not allow for the calculation of rates based on all hospitalizations and allow for comparisons of age, gender, and race for those who were not hospitalized for diabetes. Although a number of potential confounders were controlled for in the multivariate analyses, residual confounding by unmeasured variables such as health care

insurance cannot be ruled out. A distinction between the principal diagnosis and any-listed diagnosis was also made. Oftentimes although diabetes is the underlying cause of the hospitalization, other diagnoses are listed as the principal diagnosis by hospitals. By looking at both principal and all of the secondary diagnoses, a clearer picture of the burden of diabetes becomes apparent (Figures 8.0, 8.1). Ideally, as many counties as possible should be considered in the analysis to include a larger geographical scale. However, due to funding issues, this geographical area was chosen. The results of this study may not be generalizable to all other geographical areas and may be unique to Southwestern Pennsylvania. This area has many unique characteristics in terms of geography, climate, public health infrastructure, and cultural norms that make it an important are to study for health disparities.

Based on the findings of this study, residents of rural counties have higher rates of uncontrolled diabetes hospitalizations compared to all diabetes hospitalizations. This is significant to public health because diabetes is a serious, costly disease, in which hospitalizations continue to rise. It is responsible for $174 billion in direct medical costs and indirect (work loss, disability, premature death) medical expenditures every year. Diabetes also has an enormous impact on the affected individual, their families, and the health care system. Understanding where gaps in health care and diabetes management education exist may lead to changes in policy and the local neighborhood environment to increase the access of rural residents. It is important to further investigate the access residents of these counties have to health care facilities, other disease prevention facilities, and the local food and physical activity environments. This will shed more light on how the environment of individuals with diabetes affects their overall health and their ability to control their diabetes.

8.6 TABLES

Table 8.2 Measures of Rurality and SES and Rankings of Nine Counties in Pennsylvania

County	% Under Poverty Level[a]	Median Household Income[a]	% High School Diploma[a]	Total Pop.[a]	Population Density (persons/mi^2)[a]	Miles of Hwys/ Roads[b]	Daily Vehicle Miles Traveled[b]	% Black Residents[a]	Age-Adjusted Diabetes Mortality Rates[d]	Age-Adjusted CVD Mortality Rates[d]	USDA Rural-Urban Continuum Codes[e]	Overall Rank[c]
Armstrong	13.3	50,007	87.0	72,392 (8)	106 (7)	1,855 (7)	23.6 (8)	0.8	27.4	280.6	1	9
Greene	18.0	36,647	83.1	40,672 (9)	69 (9)	1,468 (9)	40.5 (1)	3.9	28.4	**349.4**	6	8
Fayette	19.7	31,637	81.9	144,556 (5)	183 (5)	2,081 (6)	21.3 (9)	4.0	**38.6**	**318.7**	1	7
Cambria	12.6	34,387	85.7	144,995 (4)	211 (4)	1,724 (8)	24.5 (7)	3.4	23.8	**325.5**	3	6
Indiana	16.0	38,735	84.6	87,690 (6)	107 (6)	2,090 (5)	29.5 (5)	2.0	**31.0**	265.8	4	5
Somerset	12.3	33,837	81.4	77,861 (7)	72 (8)	2,287 (4)	38.3 (2)	2.2	23.8	302.9	4	4
Washing-ton	10.0	45,789	87.9	205,553 (3)	240 (3)	2,873 (3)	35.1 (3)	3.3	29.8	277.4	1	3
Westmore-land	9.3	45,289	89.9	369,993 (2)	353 (2)	3,731 (2)	32.6 (4)	2.2	23.1	302.2	1	2
Allegheny	12.4	45,266	90.6	1,281,666 (1)	1670 (1)	5,688 (1)	28.0 (6)	12.7	22.1	294.9	1	1

a Data from U.S. Census Bureau (13)
b Data from the Pennsylvania Department of Transportation (15)
c Average of the four measures of rurality and SES (9 = most rural to 1 = least rural)
d Data from PADOH; A rate that appears in bold for a county denotes a significantly higher value compared to the state's rate (26)
e United States Department of Agriculture Economic Research Service (6)

Table 8.3 Age-Adjusted Diabetes Hospitalization Rates, per 10,000 Adult Residents, by County, 2007

County	Armstrong n =1,156	Greene n =465	Fayette n =3,293	Cambria n =3,386	Indiana n =1,779	Somerset n =2,151	Washington n =5,954	Westmoreland n =11,258	Allegheny n =25,261	Total Area N =54,703
Uncontrolled Diabetes, Any-Listed Diagnosis	2.1	5.5	9	3.7	10.8	6.3	12.3	10	8.2	7.9
Diabetes, Principal Diagnosis	7.9	4.4	11.9	7.4	9.7	12.5	14.1	12.7	14.5	17.8
Diabetes, Any-Listed Diagnoses	230.1	138	243.6	138	242.6	288.4	314.9	322.6	221.7	246.8

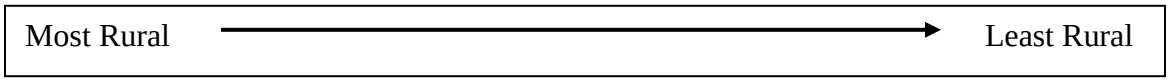

Table 8.4 Population Characteristics, by County, N = 54,703 subjects

County	Allegheny n =25,261	Armstrong n =1,156	Cambria n =3,386	Fayette n =3,293	Greene n =465	Indiana n =1,779	Somerset n =2,151	Washington n =5,954	Westmoreland n =11,258	Total Area N =54,703	p-value
Age											<. 0001
Mean [sd]	66.5 [14.8]	66.9 [14.7]	67.3 [14.1]	65.9[14.1]	63.7 [14.2]	67.1 [14.5]	68.1 [13.7]	68.2 [13.93]	67.9 [14.4]	66.9 [14.5]	
Range	18 - 105	19 - 98	18 - 102	18 - 101	19 - 93	18 - 96	18 - 98	19 - 106	18 - 106	18 - 106	
Race n(%)											<. 0001
Asian/Isl. Pac.	50(0.2)	1(0.1)	3(0.1)	3(0.1)	0(0.0)	2(0.1)	3(0.1)	9(0.2)	11(0.1)	82(0.2)	
Black	4993(19.8)	14(1.2)	113(3.3)	113(3.4)	3(0.4)	12(0.7)	7(0.2)	290(4.9)	392(3.5)	5941 (10.9)	
Native American	13(0.1)	0(0.0)	1(0.03)	2(0.1)	0(0.0)	1(0.1)	0(0.0)	2(0.03)	3(0.03)	22(0.04)	
White	20200 (79.9)	1141(98.7)	3269 (96.5)	3175(96.4)	463(99.6)	1764 (99.1)	2141 (99.7)	5653(94.9)	10852 (96.4)	48658 (88.9)	
Gender n(%)											0.022
Female	13671 (54.1)	645(55.8)	1853 (54.7)	1754(53.3)	257(55.3)	967(54.4)	1119 (52.0)	3169(53.2)	5888(52.3)	29323 (53.6)	
Male	11590 (45.9)	511(44.2)	1533 (45.3)	1539(46.7)	208(44.7)	812(45.6)	1032 (48.0)	2785(46.8)	5370(47.7)	25380 (46.4)	
Insurance n(%)											<.0001
Uninsured	307(1.2)	4(0.4)	929(27.5)	22(0.7)	6(1.3)	122(6.9)	544(25.3)	45(0.8)	183(1.6)	2162(4.1)	
Medicare	15159 (60.1)	765(66.2)	160(48.9)	2139(65.2)	270(58.2)	1130 (63.5)	1091 (50.8)	3753(63.2)	7264(64.6)	31731 (59.7)	
Medicaid	1951(7.7)	93(8.0)	211(6.3)	417(12.7)	69(14.9)	118(6.6)	100(4.7)	453(7.6)	631(5.6)	4043(7.6)	
Comm./Govt	7668(31.0)	283(25.4)	567(17.3)	678(21.4)	117(25.6)	390(23.0)	396(19.2)	1642(28.4)	3048(28.1)	14789 (27.8)	
Unknown	154(0.6)	10(0.9)	20(0.6)	28(0.9)	2(0.4)	19(1.1)	16(0.8)	48(0.8)	112(1.0)	409(0.8)	
Admission Type n(%)											<.0001
Emergency	12072 (47.8)	571(49.4)	1503 (44.4)	1501(45.6)	50(10.8)	292(16.4)	961(44.7)	1508(25.3)	4848(43.1)	23306 (42.6)	
Urgent	2270(8.9)	122(10.6)	24(0.7)	319(9.7))	170(36.6)	581(32.7)	16(0.7)	2557(42.9)	998(8.9)	7057 (12.9)	
Elective	8487(33.6)	235(20.3)	1708 (50.4)	617(18.7)	124(26.7)	596(33.5)	1129 (52.5)	1185(19.9)	3605(32.0)	17686 (32.3)	
Trauma	97(0.4)	2(0.2)	39(1.2)	6(0.2)	1(0.2)	6(0.3)	1(0.1)	22(0.4)	29(0.3)	163(0.3)	
Unknown	2335(9.2)	226(19.6)	112(3.3)	850(25.8)	120(25.8)	304(17.1)	44(2.0)	682(11.5)	1778(15.8)	6491 (11.9)	

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9.0 MANUSCRIPT 2:

ANALYSIS OF THE AVAILABILITY OF THE LOCAL FOOD AND HEALTH CARE ENVIRONMENT AND DIABETES

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9.1 ABSTRACT

Objective: To determine if there is an association between the availability of disease prevention and health care facilities, the local food environment and risk factors for diabetes complications.

Hypothesis: The presence of supermarkets, full-service restaurants, physicians' offices, hospitals and pharmacies will decrease the likelihood of having the risk factors for diabetes complications in individuals with type 2 diabetes.

Research Design and Methods: Data on 3367 individuals with diabetes were collected from seven diabetes centers. Data containing the 2007 location of businesses including fast food, limited-service and full-service restaurants, convenience and grocery stores, and supermarkets; physicians' offices, hospitals and pharmacies were geocoded to the census tract level. Individual risk factors included hypertension, hypercholesterolemia, overweight, obesity and A1c level. GEE regression was used to estimate odds ratios (OR) for having each risk factor and their association with the presence of different types of food stores and health care locations, controlling for individual level (age, race, gender, duration of diabetes) and community level (percent living below the poverty level, median income, percent of Black residents, and percent with a high school degree or higher) factors.

Results: The analysis included 3,367 individuals with diabetes from seven diabetes centers in Southwestern Pennsylvania. They were predominantly older (mean age = 67.9), female (56.8%), and Caucasian (94.6%). Over 75% of the individuals had hypertension, 52.7% had hypercholesterolemia, 68.7% were overweight, 46.4% were obese and 50.4% had uncontrolled diabetes. Nearly 57% of the individuals lived in census tracts with convenience stores, while only 24.3% lived in census tracts with large supermarkets. Sixty-percent of individuals lived in

census tracts with fast food restaurants while only 41.0% lived in areas with full-service restaurants. Approximately 57% of the population lived in census tracts with a physician's office, 56.7% lived in an area with a pharmacy and only 8.0% lived near a hospital.

While supermarkets and grocery stores were associated with a decrease in the likelihood of hypertension, hypercholesterolemia, being overweight and obese, the presence of convenience stores was associated with an increase in the likelihood of individuals having hypertension, hypercholesterolemia, being overweight, obese, and hyperglycemia, after adjusting for individual and community level factors.

A similar trend was found in food service places. The presence of full-service and limited-service restaurants was associated with a decrease in the likelihood of having hypertension, being overweight and obese while the existence of fast food restaurants was associated with an increased likelihood of having these factors. The presence of any of the health care locations was associated with a decrease in the likelihood of having these factors.

Conclusions: Results from this study indicate that the local food and health care environment at the neighborhood level is a possible ecological determinant of health. There is a clear association between the presence of food stores and service places, and health care locations with risk factors for diabetes complications among individuals with diabetes. The local environment has a significant impact on public health by possibly restricting a population's food and health care choices and opportunities that affect health.

9.2 INTRODUCTION

Diabetes has reached epidemic proportions and continues to grow as one of the most significant public health issues of modern times. Individuals with diabetes are at increased risk for vascular disease, including microvascular complications (i.e., retinopathy, nephropathy, and neuropathy), macrovascular complications (i.e., stroke, coronary heart disease, lower extremity arterial disease). Certain environmental aspects play an important role in the prevention and treatment of chronic diseases including as diabetes and its complications. Studies show that access to health care, diet, physical activity, housing, income, and environmental exposures contribute to chronic diseases, which are all part an individual's environment or community (1,2,3). Diet is an important part of the treatment of diabetes and maintenance of glycemic control. The American Diabetes Association recommends that people with diabetes consume a diet low in fat and high in fiber-containing foods such as fruits, vegetables, and whole grains. The availability of these and other recommended foods in neighborhood food stores may influence the food choices of adults with diabetes (29). Risk factors for diabetes complications include obesity and overweight, hypertension, hyperglycemia and high cholesterol. These risk factors may be associated with certain environmental aspects of a population.

An increasing number of studies in the public and environmental health literature demonstrate that individuals' health and health behaviors are affected by their surroundings (12-14). Recently, researchers in Canada determined that areas in which the number of places selling wine increased, wine consumption by residents also increased (15). Investigators more than a decade ago found that physical proximity to a medical facility or doctor's office affected utilization of healthcare resources (16).

The role that diet plays in the causation and prevention of diabetes and diabetes-related complications has been studied for several years. An individual's ability to meet dietary recommendations for a healthy diet has been a concern of public health researchers and practitioners for many years as well. Previous work demonstrates that dietary choices may be influenced by many factors including taste, nutrition, weight control, convenience, and cost (17). Some studies show that cost is the most significant predictor of dietary choices, making healthy eating habits difficult to achieve for the economically disadvantaged (18-20). Research also suggests that low-income individuals generally cannot afford healthier foods (21). Other data indicates that food costs more for people of low socioeconomic status because purchases are made in lesser quantities at convenience and small grocery stores and there is more reliance on processed food. Residents in lower income areas may need to depend on these smaller stores with limited selection of foods at substantially higher prices (22).

Cost is an important barrier; however, very few studies have attempted to focus on locality as a factor that may inhibit a population's ability to acquire a healthy diet. A study conducted in San Diego, CA compared supermarkets, neighborhood grocery stores, convenience stores (i.e., Seven-Elevens), and health food stores. The authors found that supermarkets had twice the average number of "heart-healthy" food compared to neighborhood grocery stores and four times the average number of such foods compared to convenience stores (23). There is little other data on the contents of convenience stores, but they are assumed to carry a larger proportion of energy-dense foods. Since the food choices that people make are limited to what is available to them, and convenience is an important predictor for food habits (24, 17), it is hypothesized that individuals living in areas with few food choices other than convenience stores

may be more likely to adopt an energy-dense diet. Alternatively, food environments offering a greater variety of healthy food options at affordable prices may lead to healthier food choices.

Despite the availability of effective treatments, many patients with diabetes do not receive optimal care. Driving distance is one aspect of travel burden, and may serve as a marker for at least some of the burden of obtaining diabetes care (28).

In the face of a steadily increasing prevalence of diabetes, the health care system has failed to prevent, detect, and manage diabetes adequately, especially in rural areas. When rural residents do see a doctor, they are more likely to see a generalist than a specialist for treatment of diabetes and related complications (28).

The impact of location of food stores and food service has on individuals' diets remains unclear. The few studies that have addressed locality have not investigated if the number and types of food stores and food services places are associated with risk factors of residents (8). Additionally, those with diabetes who reside rural areas are believed to be less likely to visit a physician than their urban counterparts, and fewer of them have insurance coverage for medications (8). No studies at the time of publication explore the association of risk factors and numbers of local physicians' offices and pharmacies. Therefore, this study aims to describe the local food and health care environment, where residents can obtain food, care and pharmaceuticals in their neighborhood.

It is our objective to determine if there is an association between the availability of food stores, food service places, health care locations and the risk factors associated with complications of diabetes in a rural area. Because of the previous positive associations between diet and availability of supermarkets (25) and full-service restaurants, it is hypothesized that the presence of supermarkets, full-service restaurants, physicians' offices, and pharmacies will be

associated with a lower prevalence of risk factors for diabetes complications in individuals with diabetes.

9.3 METHODS

9.3.1 Study Population

In an effort to improve diabetes education and care, the University of Pittsburgh Diabetes Institute started a regional health care collaboration, the Pittsburgh Regional Initiative for Diabetes Education (PRIDE). Nine counties (Allegheny, Armstrong, Cambria, Fayette, Greene, Indiana, Somerset, Washington, and Westmoreland) were selected from the study area where the partners of PRIDE diabetes centers are located. Data on individuals with diabetes were collected using a data management system, Delphi. This system was used by the University of Pittsburgh Diabetes Institute in order to collect data on individuals with diabetes attending diabetes centers throughout southwestern Pennsylvania. The participating centers include: The Center for Diabetes Care at the Indiana Regional Medical Center, Community Medical Services, Centerville Clinics, Inc., Conemaugh Diabetes Institute, The Diabetes Center at Uniontown Hospital, Highlands Hospital Diabetes Center and the Washington Hospital Diabetes Education & Management Program. The Delphi Data Management System allowed the staff of these centers to enter patient data into an organized system. Individual-level data such as home street addresses, demographics, lab test data, medications, health indicators, co-morbid conditions, and complications were entered into this data system from June 2005 to January 2007. The variable list is included in Table 9.6, Appendix B. All of the individuals 18 years and older that were entered into the Delphi system (n=3367) were diagnosed by their physician with diabetes prior to be being referred to the diabetes center.

9.3.2 Measurement of the Local Environment

Data containing the 2007 location of businesses for the study area was purchased from the Environmental Sciences Research Institute (ESRI), Redlands, CA. Types of businesses in this data set include fast food, limited-service and full-service restaurants, convenience and grocery stores, and supermarkets; physicians' offices, hospitals and pharmacies. A list of these variables is displayed in Table 9.7, Appendix B. Characteristics and the location (shape files for geocoding) of zip codes were obtained from the U.S. Census Bureau, 2000. The 1997 North America Industry Classification System (NAICS) codes were modified to define the types of food stores. Supermarkets were defined as large corporate owned "chain" food stores (e.g. Giant Eagle, Shop and Save). These stores contain frozen and canned foods, bakery items, fresh fruits and vegetables, meat, fish, poultry, and may have delicatessens. Grocery stores were distinguished as smaller non-corporate-owned food stores. Convenience stores included all food stores that carry a limited selection of foods, mostly snack foods, whether or not attached to gas station. In addition to food stores, other types of places where residents buy food were classified as full-service restaurants, franchised fast food (e.g. McDonald's, Burger King, Pizza Hut), and limited-service restaurants. Cafeterias were grouped with full-service restaurants. Carry-out eating places such as sandwich shops, delis, ice cream and smoothie shops were included with limited-service restaurants. Other types of places to obtain food, not mentioned above were not included in these analyses because of their small proportion of annual sales of foods and beverages in the United States. Also, establishments that sell food items in bulk were excluded since they require a membership (Table 9.7, Appendix B).

This study was only interested in the availability of food stores and food service places through local, routine sources. Consequently, churches, community centers, schools, nursing

homes, and hospitals were excluded. Shopping areas and places that are primarily for entertainment such as bowling alleys were also excluded because it can be assumed that few individuals rely on these places for a significant portion of their diet. Physicians' offices that do not pertain to diabetes and related complications (i.e. pediatricians, plastic surgeons, psychologists) were excluded from the data set since patients were unlikely to visit such offices for purposes important to this study.

Census tracts, national geographic boundaries containing approximately 3000 to 4000 individuals, were used as proxies for neighborhoods. The Delphi patients were collected from a total of 168 census tracts throughout six counties. ArcGIS software (ESRI, Redlands, CA) was used to calculate the number of facilities in each census tract (Table 9.1).

Table 9.1: Location Descriptions for the Entire Study Area Containing 1383 Locations in 168 Census Tracts

	n	Number of Census Tracts with the Location Type
Locations (N=1383)		
Local Food Environment		
Supermarkets	45	36(21.4)
Grocery Stores	124	86(51.2)
Convenience Stores	142	90(53.6)
Full Service Restaurants	92	67(39.9)
Limited Service Restaurants	98	60(35.7)
Fast Food Restaurants	187	88(52.4)
Health Care		
Hospitals	15	13(7.8)
Pharmacies	166	82(48.8)
Physicians' Offices	514	101(60.1)

9.3.3 Definitions of Outcomes

Laboratory values of the patients who were entered into the Delphi Data Management System were used to define the risk factor values for diabetes complications. The first lab values that

were entered for each patient were used in the analysis. Two categories of body weight (overweight and obesity), hypercholesterolemia and hypertension were created because of their importance as risk factors for diabetes complications and their association with diet. Body Mass Index (BMI) was calculated as [weight in kilograms/height in meters^2]. Individuals with a BMI ≥25 were classified as overweight and those with a BMI ≥30 as obese. Individuals were categorized as having hypercholesterolemia if they had a LDL >100 mg/dL, and/or who reported taking cholesterol lowering medications in the system. Patients were considered to have hypertension if they had a systolic blood pressure measurement ≥130 mmHg or a diastolic measurement ≥80 mmHg and/or if they reported taking anti-hypertensive medications. Subjects were classified as having hyperglycemia if they had an A1c level > 7.0% or reporting taking anti-diabetic medications.

9.3.4 Statistical Analysis

To estimate odds ratios (OR) of diabetes complications risk factors associated with the presence of different types of food stores, generalized estimating equations (GEE) logistic regression was performed using the PROC GENMOD program in SAS 9.1 (28). This is a multilevel test that takes census tract and individual-level data into account and the repeated measures option was used to account for the clustering of subjects within the census tracts. Each of the risk factors of hypertension, hypercholesterolemia, overweight, obese, and hyperglycemia was modeled separately. First, dichotomous variables characterizing 'any' versus 'none' of that type of facilities within the census tract were created for each type food service place (fast food, limited-service, and full-service restaurants), food store (supermarkets, grocery stores, and convenience stores), offices of physicians and pharmacies. Indicator variables were also created to represent

the presence of specific combinations of types of food stores: (a) Supermarkets only, (b) Grocery stores only, (c) Convenience stores only, (d) Supermarkets, grocery stores, and convenience stores, (e) None, (f) Combination of stores; and food service places: (a) Full-service restaurants only, (b) Limited-service restaurants only, (c) Fast food restaurants only, (e) None, and (f) Combination of places. The dichotomous variables were modeled for each of the risk factors, while controlling for age, gender, and duration of diabetes. Since individual-level socioeconomic status (SES) information was not available, census tract information was used in the model to control for these factors. The percentage of residents living below the poverty level, percentage of residents reporting Black as their race, median household income, and percentage of residents with a high school education or higher for each census tract were also considered in the regression models. Descriptive analysis was conducted to calculate the mean and percentages of laboratory values, age, gender, duration of diabetes, co-morbidities and complications of diabetes.

9.4 RESULTS

9.4.1 Description of the Population

The analysis included 3,367 individuals with diabetes from seven diabetes management centers in Southwestern Pennsylvania. They were predominantly older (mean age = 67.9), female (57.6%), and Caucasian (94.6%). Over 75% of the individuals had hypertension, 52.7% had hypercholesterolemia, 68.7% were overweight, 46.4% were obese and 50.4% have uncontrolled diabetes. Nearly 57% of the individuals lived in census tracts with convenience stores, 51.6% lived near grocery stores, while only 24.3% lived in census tracts with large supermarkets. A

similar trend can be seen in food service places; 59.8% of individuals lived in census tracts with fast food restaurants while only 41.0% lived in areas with full-service restaurants. Fifty-seven percent of the population lived in census tracts with a physician's office, 56.7% lived in an area with a pharmacy and only 8.0% lived near a hospital.

9.4.2 GEE Regression

The associations between the food and healthcare locations and the diabetes complications risk factors are presented in Table 9.3. The associations were adjusted for individual-level factors such as age, duration of diabetes, race, and gender. Since individual-level SES variables were unavailable, census track information for the percentage of residents living below the poverty level, median household income, percentage of residents with a high school education or higher, and percentage of residents reporting Black as their race were included in the model adjustment. Multi-collinearity was assessed between median household income, poverty level, and education. Theses variables were significantly correlated however the R value was low and the model did not change significantly when all three of these factors were entered into the model, so they were all included in the final model.

The existence of supermarkets in the census track was associated with a lower likelihood of having hypertension and hypercholesterolemia. Individuals who resided in a census tract with at least one supermarket were 13% less likely to have hypertension (OR=0.87, 95% confidence interval [CI] =0.78, 0.97) and 17% less likely to have hypercholesterolemia (OR=0.83, 95% CI =0.70, 0.89) than those living in census tracts without supermarkets, after adjusting for individual and census tract level characteristics. Individuals who lived in an area with a grocery store were 5% less likely to have hypertension (OR =0.95, 95% CI =0.79, 1.14), 15% less likely

to be overweight (OR=0.85, 95% CI =0.51-0.91), and 6% less likely to be obese (OR =0.94, 95% CI 0.72-0.99) compared to those without a grocery store in their census track. Conversely, the presence of at least one convenience store was associated with a higher likelihood of risk factors. Those with a convenience store in their census track were 58% more likely to have hypertension (OR=1.58, 95%CI =1.31, 1.91), 19% more likely to have hypercholesterolemia (OR= 1.19, 95% CI = 1.00, 1.42), 82% more likely to be overweight (OR= 1.82, 95% CI= 1.47, 2.26), 45% more likely to be obese (OR= 1.45, 95% CI= 1.23, 1.72), and 19% more likely to have uncontrolled diabetes (OR= 1.19, 95%CI= 1.00, 1.41).

The presence of food service locations was also found to have an effect on risk factors for diabetes complications. Individuals with diabetes who lived in an area with a full-service restaurant were 39% less likely to have hypertension (OR=0.61, 95% CI= 0.50, 0.74), 36% less likely to be overweight (OR= 0.64, 95% CI= 0.52, 0.79) and 25% less likely to be obese (OR= 0.75, 95% CI= 0.59, 0.83). Those who reside in a census tract with at least one limited-service restaurant were 22% more likely to have hypercholesterolemia (OR= 1.22, 95% CI = 1.16, 1.73), 80% more likely to be overweight (OR= 1.79, 95% CI 1.36, 2.37) and 43% more likely to be obese (OR= 1.43, 95% CI 1.17, 1.74) compared to those who do not have this restaurant in their census tract. The presence of fast food restaurants was also associated with an increased likelihood of having risk factors of diabetes complications. Individuals in the study who lived in a census tract with at least one fast food restaurant, were 78% more likely to have hypertension (OR= 1.78, 95% CI = 1.45, 2.19), 22% more likely to have hypercholesterolemia (OR=1.22, 95% CI 1.01, 1.47), 62% more likely to be overweight (OR= 1.62, 95% CI=1.28, 2.06), and 61% more likely to be obese (OR= 1.61, 95% CI= 1.34, 1.94) compared to those who lived in a census tract without a fast food restaurant.

The existence of health care locations within an individual's census track was also associated with a decrease in the likelihood risk factors. Those who lived in an area with at least one pharmacy were 38% less likely to have hypertension (OR= 0.62, 95% CI = 0.51, 0.76) and 31% less likely to have hypercholesterolemia (OR= 0.69, 95% CI= 0.58, 0.83). The presence of a pharmacy was not significantly associated with being overweight, obese, or having and A1c > 7.0%. Compared to those who lived in an without an office of a physician, those who resided in a census tract with at least one office were 15% less likely to have hypertension (OR=0.85, 95% CI= 0.72, 0.90), 25% less likely to have hypercholesterolemia (OR=0.75, 95% CI= 0.65, 0.78) and 34% less likely to be overweight (OR=0.66, 95% CI= 0.53, 0.82). Individuals who resided in a census tract with a hospital were 30% less likely to have hypertension (OR=0.70, 95% CI= 0.52, 0.95) and 37% less likely to have hypercholesterolemia (OR= 0.63, 95% CI= 0.47, 0.85) compared to those who do not have a hospital within their census tract. Complete results are reported in Table 9.3.

The associations between certain combinations of food stores and service locations and risk factors were also explored. These associations compare the likelihood of risk factors among individuals with diabetes in census tracts with different combinations of types of local food environment locations to those who live in a census tract with no locations. The ratios displayed in Table 9.4 are adjusted for individual level age, race, gender and duration of diabetes, census level SES variables, and the presence of health care locations (pharmacies, offices of physicians, and hospitals). Individuals who lived in a census tract with only one or more supermarkets were 60% less likely to have hypertension (OR=0.40, 95% CI= 0.28, 0.57), 36% less likely to have hypercholesterolemia (OR=0.64, 95% CI= 0.47, 0.86), 20% less likely to be overweight (OR=0.80, 95% CI= 0.67, 0.94), 47% less likely to be obesity (OR=0.53, 95% CI=0.37, 0.75)

compared to those who had no food stores in their census tracts. Individuals with only a grocery store in their census tract were 29% (OR=0.71, 95%=0.51, 0.99) less likely to have hypertension, 43% more likely to have hypercholesterolemia (OR=1.43, 95% CI= 1.06, 1.93), and 10% less likely to be overweight (OR=0.90, 95% CI= 0.85, 0.98) compared to those who have no food stores in their area. Those who resided in a census tract with only convenience stores were 68% more likely to have hypercholesterolemia (OR=1.68, 95% CI= 1.24, 2.27), 26% more likely to be overweight (OR= 1.26, 95% CI= 1.17, 1.94), and 37% more likely to be obese (OR=1.37, 95% CI= 1.01, 1.85). Subjects who lived in a census tract with all three types of food stores were nearly 4 times more likely to have hypercholesterolemia (OR=3.79, 95% CI= 2.49, 5.77) and 7% less likely to be overweight (OR=0.93, 95% CI= 0.28, 0.98).compared to those without a food store in their area. There were no significant associations found between the combinations of food stores and glycemic control.

Associations between risk factors for diabetes complications and certain combinations of restaurants within each census tract were also explored. These associations followed a similar pattern to the food stores. For example, those who lived in areas with only full-service restaurants were 59% less likely to have hypertension (OR=0.41, 95% CI = 0.30, 0.55), 63% less likely to be overweight (OR=0.37, 95% CI= 0.26, 0.50), and 55% less likely to be obese (OR=0.45, 95% CI=0.34, 0.60) compared to those who lived in census tracts without any restaurants. Subjects who lived in census tracts with only fast food restaurants were 71% more likely to have hypertension (OR= 1.71, 95% CI= 1.12, 2.61), 98% more likely to be overweight (OR=1.98, 95% CI=1.17, 3.35) and 67% more likely to be obese (OR=1.67, 95% CI=1.19, 2.33). Those who lived in areas with only limited-service restaurants were 62% more likely to have hypercholesterolemia (OR=1.62, 95% CI=1.09, 2.40), 85% more likely to be overweight

(OR=1.85, 95% CI=1.02, 3.38). Individuals who resided in areas with all three types of restaurants were 56% more likely to have hypertension (OR=1.56, 95% CI 1.06, 2.31), 2.3 times more likely to have hypercholesterolemia (OR= 2.3, 95% CI= 1.61, 3.29) compared to those without any restaurants in their census tracts. Having more than one type of restaurant in your area is associated with a 73% increase in the likelihood of having hypertension (OR=1.73, 95% CI= 1.23, 2.44), 2.5 times more likely to be overweight (OR=2.53, 95% CI= 1.64, 3.92), and 50% increase in the likelihood obesity (OR=1.50, 95% CI= 1.12, 2.01) compared to those who do not have any restaurants in their census tract, adjusting for individual and community level factors..

9.5 CONCLUSION

Results from this study indicated that the local food and health care environment at the neighborhood level is a possible ecological determinant of health. There is a clear association between the presence of food stores and service places, and health care locations with risk factors of diabetes complications among individuals with diabetes. The study subjects have type 2 diabetes and many have risk factors for diabetes complications such as retinopathy, nephropathy, and neuropathy, macrovascular complications (i.e., stroke, coronary heart disease, lower extremity arterial disease). Over 75% of the individuals had hypertension, 52.7% had hypercholesterolemia, 68.7% were overweight, 46.4% were obese and 50.4% had A1c values > 7.0%. Many of the subjects are from rural areas of Southwestern Pennsylvania, where it has become apparent that there is less access to healthy food and health care. Nearly 57% of the individuals lived in census tracts with convenience stores, while only 24.3% lived in census

tracts with supermarkets. A similar trend was observed for food service places; 59.8% of individuals lived in census tracts with fast food restaurants while only 41.0% lived in areas with full-service restaurants. Roughly 57% of the population lived in census tracts with a physician's office, 56.7% lived in an area with a pharmacy and only 8.0% lived near a hospital. While supermarkets and grocery stores were associated with a decrease in the likelihood of hypertension, hypercholesterolemia, being overweight and obese, the presence of convenience stores was associated with an increase in the likelihood of individuals having hypertension, hypercholesterolemia, being overweight, obese, and an A1c > 7.0%, after adjusting for individual and community level factors.

A similar trend was found in food service places. The presence of full-service and limited-service restaurants was associated with a decrease in the likelihood of hypertension, being overweight and obese while the existence of fast food restaurants was associated with an increase in these factors. The presence of any of the health care locations was associated with a decrease in the likelihood of these factors in those with Type 2 diabetes.

Additionally, analyses were conducted to determine associations between risk factors and specific combinations of food locations and food service places. Individuals who resided in a census tract with only a supermarket or only a grocery store were less likely to have hypertension, hypercholesterolemia, be overweight and obese, while those who lived in a census tract with only a convenience store were more likely to have these risk factors, compared to those who live in a census tract with no food stores, adjusted for individual and community level factors. Furthermore, those who lived in census tracts with more than one type of store or all type of stores were more likely to be obese and have hypertension. This may be because the presence of a convenience store in the census tract was driving the model. As expected, a similar

trend was found in the restaurant models. Subjects who lived in a census tract with only at least one full-service restaurant were less likely to have hypertension, be overweight and obese while those with only a fast food restaurant in their area were more likely to have hypertension, be overweight, or obese compared to those living in a census tract with no restaurants in their area. The local food and health care environment was not as associated with glycemic control as the other risk factors. It was only associated with the presence of fast food restaurants. This may be an artifact of the variability of A1c values over time.

These findings expand on those of Moreland, Roux, and Wing (8) who conducted multilevel modeling in order to calculate prevalence ratios of the associations between the presence of specific types of food stores and cardiovascular disease risk factors. The researchers used 2004 data from a cross-sectional study of men and women participating in the third visit (1993-1995) of the Atherosclerosis Risk Communities (ARIC) Study. This analysis demonstrated that the presence of supermarkets was associated with a lower prevalence of obesity and overweight (obesity prevalence ratio [PR] = 0.83, 95% CI=0.75-0.92; overweight PR=0.94, 95% CI=0.90-0.98), and the presence of convenience stores was associated with a higher prevalence of obesity and overweight (obesity PR=1.16, 95% CI=1.05-1.27; overweight PR=1.06, 95% CI=1.02-1.10). The results from this study suggest that characteristics of local food environments may play a role in the prevention of overweight and obesity (8). Although our study focused on those with diabetes and risk factors of complications, and Moreland et al. used a cross-sectional population from major metropolitan areas, the results strengthen the associations between the local food environment and health.

Inagami et al. (27) found residents in poor neighborhoods have a higher body mass index (BMI) and eat less healthfully. One possible reason might be the quality of available foods in

their area. The researchers examined the location of grocery stores where individuals shop and its association with BMI. The 2000 U.S. Census data were linked with the Los Angeles Family and Neighborhood Study (L.A.FANS) database, which consists of adults sampled from 65 neighborhoods in Los Angeles County. Inagami and colleagues aimed to estimate the associations between BMI and socioeconomic characteristics of grocery store locations after adjustment for individual-level factors and socioeconomic characteristics of residential neighborhoods. They found that individuals had a higher BMI if they reside in disadvantaged areas and in areas where the average person frequents grocery stores located in more disadvantaged neighborhoods. They were able to conclude that where people shop for groceries and distance traveled to grocery stores are independently associated with BMI. Our study also demonstrated that after controlling for SES factors of the census tract, the significant associations between food stores, food service places, and health care locations and risk factors for complications remained.

Our study also investigated the associations between health care locations and risk factors for diabetes complications. Results indicate that individuals who live in census tracts with at least one pharmacy or hospital were less likely to have hypertension and hypercholesterolemia. Those with an office of a physician within their census tract were less likely to have hypertension, hypercholesterolemia or be overweight. Several mechanisms may contribute to this relationship. Longer driving distances may mean fewer office visits and less monitoring of these risk factors. Some researchers have also found that rural residence is a significant risk factor for never receiving an ophthalmic examination, which can detect early signs of complications such as diabetic retinopathy (26).

Travel burden might influence therapy through the frequency of medical contact. The route distance used in this study is a proxy for many factors that affect an individuals' travel burden. Conceptually, transportation distance can be examined from many perspectives. The physical distance an individual has to travel may affect how often they visit the management center or the time between visits. The longer the distance, the less likely they may be the travel for visits. Distance may also be a psychosocial barrier. Individuals that have a greater distance to travel may perceive this distance as a barrier to accessing care. Individuals may also be in denial as to the severity of their disease. In addition, traveling greater distances may cause an individual to change their health care seeking behavior. Within the Health Behavior Model, it is an important enabling factor for accessing health care (144), particularly in rural areas. Recent analyses have begun to focus on the effects of transportation access in rural communities. Lovett and colleagues (146) use GIS analysis to show that in rural areas there are pockets in which car journeys to the nearest general practitioner are greater than 10 miles and there is no regular bus service. These pockets of limited transportation have the highest health need indicators. Nemet and Bailey (147) measured perception of ease in getting a needed ride among rural elders. Their measure of transportation access ("If you have to get somewhere in a car, how difficult is it for you to get there? -very difficult, somewhat difficult, not at all difficult?") was not significant in predicting health care visits in the face of distance from provider.

It may be useful to minimize travel burden for patients with diabetes, perhaps by enhanced public transportation, more clinic locations in rural areas, telephone or other electronic links, or home care. It is important to note that the results from this study demonstrate that the food environmental factors were more significant in contributing to risk factors of diabetes complications that the health care locations. The models adjusted for risk factors of diabetes

complications that can not be controlled such as age, gender, race, and the SES factors at the census tract level. However, even after adjusting for these factors, the controllable environmental factors still had a significant association with risk factors. This is evidence that the environment can play a role in the health of residents and should be changed in order to control important risk factors.

This is the first study, to our knowledge, to examine the impact of the built environment and risk factors for diabetes complications. This study also used patient-level data in combination with community-level factors that may contribute to the likelihood of risk factors. The use of the census tract level was also a unique aspect of this study.

Although this study demonstrates the need for greater attention on the local food and health care environment, there were some limitations in the study. The patient data was collected from a clinic population who are making office visits and may be healthier than a population with diabetes that do not visit a diabetes management center. This may skew the results away from the null. The subjects were not surveyed on where they shopped, the restaurants in which they ate, or where they went for health care, so misclassification may have occurred if the census tract did not represent the area where the subjects patronage. Also, market research has an impact on where food stores, food service and health care places are located (8). Businesses may be located in more populated areas or areas with a higher SES. Also, the food and health care locations were aggregated to the census tract level, which was used as a proxy for a neighborhood. However, individuals often leave their census tract for services or go to a neighboring area because the location may actually be closer than one within their census tract. Examining the locations that are nearest to the individuals may be a more accurate measure, particularly if the individuals can be surveyed on their shopping, dining and health care habits.

Finally, the local environment has a significant impact on public health by possibly restricting a population's food and health care choices and opportunities that affect health. In addition to previous work, this study demonstrates that the local food and health care environment may play a central role in the prevention of risk factors of diabetes complications.

9.6 TABLES

Table 9.2 Population Characteristics and Laboratory Values (N=3367)

	Males (n=1450)	Females (n=1917)	Total (N=3367)	p-value
Hypertension[1]				0.345
n(%)	1111(76.6)	1443(75.3)	2554(75.8)	
Hypercholesterolemia[2]				0.01
n(%)	801(55.2)	972(50.7)	1773(52.7)	
Overweight[3]				0.01
n(%)	962(66.3)	1351(70.4)	2313(68.7)	
Obese[4]				<0.0001
n(%)	556(38.3)	1006(52.5)	1562(46.4)	
Uncontrolled Glycemia[5]				0.02
n(%)	764(52.7)	932(48.6)	1696(50.4)	
Age				0.081
Mean [sd]	67.3[14.9]	68.3[16.5]	67.8[15.8]	
Range	19.0 - 98.3	18.4 - 101.0	18.4 - 101.0	
Ethnicity n(%)				0.845
Caucasian	1300(94.7)	1673(94.9)	2951(94.6)	
Black or African American	59(4.4)	76(4.2)	135(4.4)	
Asian	1(0.1)	4(0.2)	5(0.2)	
Hispanic/Latino	3(0.2)	2(0.1)	5(0.2)	
American Indian/Alaskan	1(0.1)	2(0.1)	3(0.1)	
Other	8(0.5)	11(0.6)	19(0.5)	
Missing = 249				
LDL				0.464
Mean [sd]	105.0 [33.6]	104.2 [33.7]	104.5 [33.7]	
Range	30.0 - 348.0	26.0 - 256.0	26.0 - 348.0	
Systolic Blood Pressure				0.773
Mean [sd]	134.5[18.1]	135.6[18.2]	135.5 [18.2]	
Range	90 - 189	90 - 192	90 - 192	
Diastolic Blood Pressure				0.163
Mean [sd]	78.5 [10.3]	77.9 [10.5]	78.2 [10.4]	
Range	40 - 104	40 - 100	40 - 104	
Body Mass Index (BMI)[6]				<0.0001
Mean [sd]	30.7 [6.8]	34.6 [8.5]	32.8 [8.1]	
Range	16.6 - 59.7	18.9 - 60.8	18.9 - 60.8	
A1c				0.0004
Mean [sd]	7.5 [1.8]	7.3 [1.7]	7.4 [1.8]	
Range	4.2 -16.2	4.3 - 18.7	4.2 - 18.7	
Duration of Diabetes (years)				0.675
Mean [sd]	5.7 [4.2]	5.8 [4.7]	5.8 [4.5]	
Range	2.2 - 43.2	2.2 - 59.2	2.2 - 59.2	

1 = SBP ≥130 or DBP ≥80 or treatment
2 = LDL > 100 mg/dL
3 = BMI ≥ 25;
4 = BMI ≥ 30;
5 =A1c > 7.0
6 = BMI = weight(kg)/height(m)^2

Table 9.3 Adjusted* Multi-Level GEE Regression Models

Supermarkets (n=45)	OR	95% CI	p-value
Hypertension	0.87	0.78, 0.97	0.002
Hypercholesterolemia	0.83	0.70, 0.89	0.002
Overweight	0.50	0.49, 1.03	0.09
Obese	1.02	0.99, 1.05	0.08
Glycemic Control	1.07	0.80, 1.31	0.49

Full-Service Restaurants (n=92)	OR	95% CI	p-value
Hypertension	0.61	0.50, 0.74	<0.0001
Hypercholesterolemia	0.97	0.82, 1.16	0.77
Overweight	0.64	0.52, 0.79	<0.0001
Obese	0.75	0.59, 0.83	<0.0001
Glycemic Control	0.92	0.78, 1.09	0.36

Grocery Stores (n=124)	OR	95% CI	p-value
Hypertension	0.95	0.79, 1.14	0.01
Hypercholesterolemia	1.29	1.07, 1.56	0.61
Overweight	0.85	0.51, 0.91	<0.0001
Obese	0.94	0.72, 0.99	0.001
Glycemic Control	1.10	0.92, 1.32	0.28

Limited-Service Restaurants (n=98)	OR	95% CI	p-value
Hypertension	0.93	0.90, 1.18	0.08
Hypercholesterolemia	1.22	1.16, 1.73	0.0007
Overweight	1.80	1.36, 2.37	<0.0001
Obese	1.43	1.17, 1.74	0.0006
Glycemic Control	0.89	0.73, 1.08	0.23

Convenience Stores (n=142)	OR	95% CI	p-value
Hypertension	1.58	1.31, 1.91	<0.0001
Hypercholesterolemia	1.19	1.00, 1.42	0.04
Overweight	1.82	1.47, 2.26	<0.0001
Obese	1.45	1.23, 1.72	<0.0001
Glycemic Control	1.19	0.99, 1.41	0.05

Fast Food Restaurants (n=187)	OR	95% CI	p-value
Hypertension	1.78	1.45, 2.19	<0.0001
Hypercholesterolemia	1.22	1.01, 1.47	0.04
Overweight	1.62	1.28, 2.06	<0.0001
Obese	1.61	1.34, 1.94	<0.0001
Glycemic Control	1.03	0.86, 1.23	0.77

Table 9.3 Continued

Pharmacies (n=166)	OR	95% CI	p-value
Hypertension	0.62	0.51, 0.76	<0.0001
Hypercholesterolemia	0.69	0.58, 0.83	<0.0001
Overweight	0.86	0.69, 1.08	0.19
Obese	0.86	0.72, 1.02	0.09
Glycemic Control	0.96	0.81, 1.15	0.66
Hospitals (n=15)	OR	95% CI	p-value
Hypertension	0.70	0.52, 0.95	0.02
Hypercholesterolemia	0.63	0.47, 0.85	0.003
Overweight	0.62	0.55, 1.06	0.07
Obese	0.99	0.74, 1.33	0.96
Glycemic Control	1.17	0.88, 1.54	0.29

Physicians' Offices (n=514)	OR	95% CI	p-value
Hypertension	0.85	0.72, 0.90	<0.0001
Hypercholesterolemia	0.75	0.65, 0.78	<0.0001
Overweight	0.66	0.53, 0.82	0.0003
Obese	0.77	0.75, 1.01	0.08
Glycemic Control	0.72	0.68, 1.03	0.07

*Adjusted for individual age, gender, race, and duration of diabetes, and census tract level % residents living below the poverty level, median income, % Black, and % residents with a high school degree or higher.

Table 9.4: Adjusted* Odds Ratios and 95% Confidence Intervals for the Associations Between the Likelihood of Risk Factors of Diabetes Complications and Specific Combinations of Food Stores

	Hypertension				Hypercholesterolemia		
All Food Stores Available	OR	95% CI	P-value		OR	95% CI	P-value
No Stores (n=33)		Reference				Reference	
Only Supermarkets (n=11)	0.40	0.28, 0.57	<0.0001		0.64	0.47, 0.86	0.001
Only Grocery (n=30)	0.71	0.51, 0.99	0.05		1.43	1.06, 1.93	0.02
Only Convenience (n=33)	1.18	0.84, 1.66	0.35		1.68	1.24, 2.27	<0.0001
All stores (n=16)	1.23	0.79, 1.92	0.35		3.79	2.49, 5.77	<0.0001
More than one type (n=45)	2.03	1.44, 2.86	<0.0001		1.08	0.80, 1.45	0.62

	Overweight				Obesity				Uncontrolled Diabetes		
All Food Stores Available	OR	95% CI	P-value		OR	95% CI	P-value		OR	95% CI	P-value
No Stores (n=33)		Reference				Reference				Reference	
Only Supermarkets (n=11)	0.80	0.67, 0.94	<0.0001		0.53	0.37, 0.75	0.0003		1.09	0.78, 1.52	0.62
Only Grocery (n=30)	0.90	0.85, 0.98	<0.0001		0.80	0.60, 1.06	0.12		1.04	0.78, 1.39	0.80
Only Convenience (n=33)	1.26	1.17, 1.94	<0.0001		1.37	1.01, 1.85	0.04		1.17	0.87, 1.58	0.29
All stores (n=16)	0.93	0.28, 0.98	0.0002		0.98	0.66, 1.45	0.90		1.31	0.89, 1.94	0.17
More than one type (n=45)	2.31	0.91, 3.52	0.61		1.59	1.19, 2.13	0.002		1.26	0.95, 1.67	0.10

*Adjusted for individual age, gender, race, and duration of diabetes, and census tract level % residents living below the poverty level, median income, % Black, and % residents with a high school degree or higher.

Table 9.5: Adjusted Odds Ratios and 95% Confidence Intervals for the Associations Between the Likelihood of Risk Factors of Diabetes Complications and Specific Combinations of Restaurants

	Hypertension			Hypercholesterolemia			Overweight		
All Available Food Service Places	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
No Restaurants		Reference			Reference			Reference	
Only Full-Service Restaurants	0.41	0.30, 0.55	<0.0001	0.98	0.96, 1.29	0.06	0.37	0.26, 0.50	<0.0001
Only Limited-Service Restaurants	1.49	0.92, 2.42	0.10	1.62	1.09, 2.40	0.02	1.85	1.02, 3.38	0.04
Only Fast Food	1.71	1.12, 2.61	0.01	1.14	1.04, 2.27	<0.0001	1.98	1.17, 3.35	0.01
All types	1.56	1.06, 2.31	0.03	3.79	1.61, 3.29	<0.0001	1.08	0.73, 1.62	0.69
More than one type	1.73	1.23, 2.44	0.002	1.01	0.75, 1.37	0.94	2.53	1.64, 3.92	<0.0001

	Obesity			Uncontrolled Diabetes		
All Available Food Service Places	OR	95% CI	P-value	OR	95% CI	P-value
No Restaurants		Reference			Reference	
Only Full-Service Restaurants	0.45	0.34, 0.60	<0.0001	0.91	0.69, 1.20	0.50
Only Limited-Service Restaurants	1.19	0.81, 1.76	0.37	0.70	0.48, 1.02	0.06
Only Fast Food	1.67	1.19 - 2.33	0.003	0.86	0.62, 1.19	0.35
All types	1.28	0.92, 1.80	0.15	1.17	0.84, 1.64	0.35
More than one type	1.50	1.12, 2.01	0.01	1.04	0.78, 1.39	0.78

*Adjusted for individual age, gender, race, and duration of diabetes, and census tract level % residents living below the poverty level, median income, % Black, and % residents with a high school degree or higher.

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10.0 MANUSCRIPT 3:

ANALYSIS OF UNCONTROLLED DIABETES IN A RURAL AREA

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10.1 ABSTRACT

Objective: To examine the association between glycemic control and improvement in individuals with type 2 diabetes, and travel burden to diabetes management centers in southwestern Pennsylvania.

Hypothesis: Individuals who have uncontrolled diabetes will be less likely to live as close to their diabetes management center as those who have controlled diabetes. Also, those who live closer to diabetes management centers will be more likely to have improved glycemic control than those who live farther from the centers.

Research Design and Methods: Addresses, demographics and risk factor and laboratory data on 3369 individuals with type 2 diabetes who receive diabetes management education at seven diabetes centers was collected. The shortest driving distance by route from the subject's home to the diabetes management center they visited was calculated. The route driving distances ($\geq$10 miles versus < 10 miles) of subjects who were in good control (HbA1c<7.0%) were compared to the distances of those who are not in control (HbA1c>7.0%) using X^2 tests. Logistic regression was also used to test the association between glycemic control (present or absent) and each marker of travel burden, adjusting for age, gender, Body Mass Index (BMI), and duration of diabetes. To investigate improvement in HbA1c values over time and the association with travel burden, the differences between the first visit HbA1c and last visit HbA1c value was calculated. Similar X^2, t-tests and logistic regression analysis was conducted to find associations between improvement in HbA1c levels and travel burden, adjusting for individual and community level factors.

Results: The analysis included 3,369 individuals with diabetes from seven diabetes centers in Southwestern Pennsylvania. They were predominantly older (mean age = 67.9), female (57.6%), and Caucasian (94.6%). 50.6% individuals were categorized as having uncontrolled diabetes. The mean distance by route subjects traveled to visit their diabetes management center were 13.3 miles. Fifty-five percent of the subjects lived less than 10 miles from their diabetes center. The associations between the dichotomous distance subjects traveled to their center and the glycemic control were modeled. Those who lived more than 10 miles from their diabetes management center were 91% more likely to have an HbA1c level greater than 7.0% compared to those who lived less than 10 miles from their center, adjusted for individual-level factors such as age, sex, race, duration of diabetes, and BMI as well as community level factors such as percent of residents with a high school degree or higher, median household income and percent of residents living below the poverty level. The association between the numbers of miles from the center as a continuous variable and glycemic control was also modeled. For every mile the subjects lived from their diabetes management center, they are 2% more likely to have an HbA1c level greater than 7.0%, adjusted for individual and community level factors. In addition, those who lived within 10 miles from their center, were 2.24 times more likely to have improved their HbA1c values between their first and last office visits, adjusted for individual and community level factors.

Conclusions: Specialists who provide diabetes care should be aware of travel burden as a potential barrier to proper management of diabetes. In the future, it may be useful to minimize driving distance for individuals with diabetes, perhaps by improved public transportation, more diabetes center locations in rural areas, telemedicine, or home visits. Additional research should focus on more effective ways to connect diabetes care providers and patients in rural areas. In

addition to previous work, this study demonstrates that the travel burden may play a central role in glycemic control and improvement in those with type 2 diabetes.

10.2 INTRODUCTION

Diabetes is a group of diseases marked by high levels of blood glucose resulting from defects in insulin production, insulin action, or both. Diabetes can lead to serious complications and premature death, but people with diabetes can take steps to control the disease and lower the risk of complications (1). Diabetes is a major public health challenge due to the enormous impact on the affected individual, their families and the health care system. However, recent research has shown that diabetes related mortality and morbidity can be prevented or delayed by controlling risk factors (2).

Glycemic control refers to the typical levels of blood sugar (glucose) in an individual with diabetes (1). There is much evidence to suggest that many of the long-term complications of diabetes, especially the microvascular complications, result from many years of hyperglycemia (elevated levels of glucose in the blood). Good glycemic control, in the sense of a "target" for treatment, has become an important goal of diabetes care (2). Because blood sugar levels fluctuate throughout the day and glucose records are imperfect indicators of these changes, the percentage of hemoglobin which is glycosylated is used as a proxy measure of long-term glycemic control (2). This test, the hemoglobin HbA1c reflects average glucoses over the preceding 2-3 months. In those with normal glucose metabolism, the glycosylated hemoglobin level is usually 4-6%. Accepted "target levels" of HbA1c for those with diabetes is less than 7% (1).

Certain environmental aspects play an important role in the prevention and treatment of chronic diseases such as diabetes. Studies have shown that access to health care, diet, physical activity, housing, income, and environmental exposures contribute to diabetes, which are all part

an individual's environment or community (4). While there are many ways to define community, geographic location is one important way to understand the context in which people live. Until recently, there has not been a valid method for defining and analyzing geographic areas that make up a community where these risk factors and chronic diseases may cluster. Geographical modeling may allow for better identification of the geographic area of communities that provide risk for diabetes. There is great variability in the health and well being of residents depending upon where they live. Health-promotion interventions may need to be designed to target the geographic areas that represent clusters of health problems and unhealthy lifestyles.

The seven diabetes centers included in this study provide diabetes prevention and treatment classes, diabetes self-management education, meal planning and nutrition counseling, and insulin and medication therapies. Diabetes management education has been shown to reduce the severity of diabetes and risk factors for diabetes complications. Along with pharamacological interventions, several recent controlled trials on diabetes prevention have confirmed that lifestyle changes targeting diet, activity patterns, and weight regulation (7, 8, 10). Traditionally, diabetes education has emphasized increasing knowledge about diabetes, risk factors, and diabetes self-care. In spite of the availability of these services, adequate management of diabetes remains an indefinable goal.

Because diabetes self-management education has been shown to be effective at improving short-term behavioral and physiologic outcomes for patients with diabetes, decreased access to education is an important barrier in rural settings. In addition, busy rural primary care practices often lack the organizational support and computerized tracking systems to initiate practical interventions to improve diabetes care (8). For rural communities, one of the key areas

in which change is needed may be improving access to diabetes education. This could be accomplished through distance communication strategies, such as telemedicine, or through the provision of educational support and resources to assist health professional to improve their diabetes education skills and their ability to develop quality education programs (8).

Geographical Information Systems (GIS) may allow investigators to conduct analysis that can to be used to increase comprehension of chronic disease pathogenesis. First, geographical studies may suggest possible causal factors based on geography and play an important role in the understanding of the development and control of diabetes (3). Associations between disease and place imply that the population living there possesses inherent traits that make it more susceptible to disease. However, it has been shown that there are certain risk factors that cluster in these areas that cause increased risk for disease. Second, spatial analysis can help identify how populations adapt and relate to their environment (3).

Diabetes is preventable and can be controlled with intervention. However, some areas may not have resources that would enable its residents to lead a healthy lifestyle. Geospatial mapping techniques can be used to show areas with higher prevalence of diabetes and where funds need to be targeted. Geospatial analysis tools can be used to discover and analyze cause and affect relationships based on geographic proximities. The use of GIS is a relatively inexpensive way to determine the most direct driving route between two addresses (5). For rural areas, where the routes are often circuitous, driving distance have been shown to be a more accurate measure of travel burden than straight-line Euclidean measures (6). In this study, the relationship between glycemic control and the driving distance from a patient's home to the diabetes management center they visited was examined.

10.3 METHODS

10.3.1 Study Population

In an effort to improve diabetes education and care, the University of Pittsburgh Diabetes Institute started a regional health care collaboration, the Pittsburgh Regional Initiative for Diabetes Education (PRIDE). Data on individuals with type 2 diabetes was collected from seven diabetes management centers who are PRIDE partners, using a data management system, Delphi. This system was used by the University of Pittsburgh Diabetes Institute in order to collect data on individuals with diabetes attending these diabetes centers throughout southwestern Pennsylvania. The participating centers include: The Center for Diabetes Care at the Indiana Regional Medical Center, Community Medical Services, Centerville Clinics, Inc., Conemaugh Diabetes Institute, The Diabetes Center at Uniontown Hospital, Highlands Hospital Diabetes Center and the Washington Hospital Diabetes Education & Management Program. The Delphi Data Management System allowed the staff of these centers to enter patient data into an organized system. Individual-level data such as home street addresses, demographics, lab test data, medications, health indicators, co-morbid conditions, and complications were entered into this data system from June 2005 to January 2007. The variable list is included in Table 9.6, Appendix B. All of the individuals 18 years and older that were entered into the Delphi system (n=3369) were diagnosed by their physician with diabetes prior to be being referred to the diabetes center.

10.3.2 Measurement of Travel Burden and Definitions of Outcomes

The home addresses of the subjects and the location of PRIDE Diabetes Centers they attend were geocoded to the street address level using ArcGIS software (ESRI, Redlands, CA). The ESRI street centerline datasets for each county in the study area was used to geocode the location data and was used for the network analysis. The driving distance from each subject's house to the diabetes centers was calculated using the Network Analyst tool. This tool uses the centerline street data to calculate the shortest route driving distance based on the street segment distance of the route. The route distances the subjects lived from the diabetes management centers were also measured and dichotomized as living less than or greater than ten miles from the center they visit. A ten mile distance was chosen because several examples in the literature also used ten miles based on recommendations from the Rural Health Association (30, 31, 32). In addition, the South Carolina Rural Health Research Center took advantage of a highly detailed, nationally representative survey of travel conducted by the U.S. Department of Transportation, the 2001 National Household Travel Survey (NHTS), to explore the potential for disparities in access associated with rural residence. The researchers found that nationally, the average distance traveled for medical/dental care was 10.2 miles (35). Rural trips averaged 17.5 miles, versus 8.3 miles for urban residents. Several state health departments have proposed a standard in which rural residents should not have to travel more than 30 minutes to see a physician (30).

Using Network Analyst, an origin-destination (OD) cost matrix was created for the homes of subjects to each diabetes centers they visited. The parameters for the OD cost matrix were specified and paths from each home to the particular center they visit.

Laboratory values of the patients who were entered into the Delphi Data Management System were used to define the risk factor values. The first lab values that were entered for each

patient were used in the analysis. Glycemic control was measured by the glycosolated hemoglobin HbA1c assay. Subjects were classified as having hyperglycemia if they had an HbA1c level > 7.0%. A dichotomous variable for glycemic control was created and used as the main outcome of interest. Subjects visited the management several times during the study period. The difference between the first visit HbA1c values and the last visit HbA1c values were calculated to determine if the subjects HbA1c improved over time. Body Mass Index (BMI) was calculated as [weight in kilograms/height in meters^2]. Individuals with a BMI ≥25 were classified as overweight and those with a BMI ≥30 as obese. Individuals were categorized as having hypercholesterolemia if they had a LDL >100 mg/dL, and/or who reported taking cholesterol lowering medications in the system. Patients were considered to have hypertension if they had a systolic blood pressure (SBP) measurement ≥130 mmHg, a diastolic (DBP) measurement ≥80 mmHg and/or if they reported taking anti-hypertensive medications.

10.3.3 Statistical Analysis

To estimate odds ratios (OR) of having uncontrolled glycemia and the association with the distance to diabetes management centers, generalized estimating equations (GEE) logistic regression was performed using the PROC GENMOD program in SAS 9.1. This is a multilevel test that takes census tract and individual-level data into account and the repeated measures option was used to account for the clustering of subjects within the census tracts. Logistic regression was performed using the PROC LOGISTIC program in SAS 9.1 when census track data was not included in the model. Each of the risk factors of age, gender, race, duration of diabetes, and BMI was modeled separately for each marker of travel burden (distance as a continuous variable and as a dichotomous variable). Since individual-level socioeconomic status

(SES) information was not available, census tract information was used in the model to control for these factors. The percentage of residents living below the poverty level, percentage of residents reporting Black as their race, median household income, and percentage of residents with a high school education or higher for each census tract were also considered in the regression models. Descriptive analysis was conducted to calculate the mean and percentages of laboratory values, age, gender, duration of diabetes, co-morbidities and complications of diabetes. Descriptive analysis was conducted to calculate the mean and percentages of laboratory values, age, gender, duration of diabetes, co-morbidities and complications of diabetes. Univariate analysis was conducted to find significant difference between glycemic control and population characteristics as described above.

To investigate improvement in HbA1c values over time and the association with travel burden, the differences between the first visit HbA1c and last visit HbA1c value was calculated. Similar X^2, t-tests and logistic regression analysis was conducted to find associations between improvement in HbA1c levels and travel burden, adjusting for individual and community level factors.

10.4 RESULTS

10.4.1 Description of the Population

The analysis included 3,369 individuals with diabetes from seven diabetes centers in Southwestern Pennsylvania. They were predominantly older (mean age = 67.9), female (57.6%), and Caucasian (94.6%). Approximately fifty percent (n=1704) of individuals were categorized as having uncontrolled diabetes (HbA1c > 7.0). Seventy-two percent of the individuals had

hypertension (mean SBP = 135.4; mean DBP = 78.1), 52.7% had hypercholesterolemia (mean HDL = 40.3; mean LDL = 104.6; mean triglycerides = 181.3), 68.7% were overweight (mean BMI = 32.9), and 46.4% were obese. The mean duration of diabetes was 5.8 years and those with uncontrolled glycemia had significantly longer diabetes duration than those who were in control (6.1 and 5.4 years, respectively). Of those who reported insurance information (n=2116), 24.9% use Medicare, 1.6% self-paid, and 73.4 % used commercial or government health insurance. The mean distance subjects traveled to visit their diabetes management center were 13.3 miles (range 0.06 – 85.1 miles). Approximately 55% of the subjects lived less than ten miles from their diabetes center.

10.4.2 GEE Regression

The associations between the distance subjects traveled to their diabetes management centers and the glycemic control are presented in Table 10.2. The associations were adjusted for individual-level factors such as age, duration of diabetes, race, and gender. Since individual-level SES variables were unavailable, census track information for the percentage of residents living below the poverty level, median household income, percentage of residents with a high school education or higher, and percentage of residents reporting Black as their race were included in the model adjustment.

Table 10.2: Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Likelihood of Having Uncontrolled Diabetes Associated with Travel Burden (Dichotomous)

Parameter	OR	95% CI	p-value
Diabetes Center ≥10 miles	1.91	1.59, 2.30	<0.0001
Age (Years)	0.99	0.98, 0.99	0.00015
Sex (Male)	1.12	0.94, 1.34	0.22
Race (White)	1.05	0.69, 1.59	0.80
Duration of Diabetes (Years)	1.03	1.01, 1.06	0.0007
BMI	0.99	0.98, 1.01	0.83
% High School Degree	0.99	0.97, 1.01	0.31
Median Income (2000 US Dollars)	0.99	0.99, 1.00	0.11
% Living Below Poverty Level	0.97	0.95, 0.99	0.03
% Black (County)	1.01	0.99, 1.03	0.19

The results indicated that residing more than ten miles from the diabetes management center (OR = 1.88, p = <0.0001), being younger (OR = 0.99, p = 0.001), and having a longer duration of diabetes (OR = 1.03, p = 0.0009) were significant contributors to the model. Therefore, those who live more than ten miles from their diabetes management center are 91% more likely to have an HbA1c level greater than 7.0% compared to those who live less than 10 miles from their center, adjusted for individual-level factors such as age, sex, race, duration of diabetes, and BMI as well as community level factors such as percent of residents with a high school degree or higher, median household income and percent of residents living below the poverty level.

The association between the numbers of miles from the diabetes center as a continuous variable and glycemic control was also modeled (Table 10.3). The results indicated that greater driving distance from diabetes management center (OR = 1.02, p = <0.0001), being younger (OR = 0.99, p = 0.007), having a longer duration of diabetes (OR = 1.03, p = 0.004), and living in a census tract with a higher percent of residents living below the poverty level (OR = 0.98, p = 0.05) were significant contributors to the model. Therefore, for every mile the subjects live from

their diabetes management center, they are 2% more likely to have an HbA1c level greater than 7.0%, adjusted for individual-level factors such as age, sex, race, duration of diabetes, and BMI as well as community level factors such as percent of residents with a high school degree or higher, median household income and percent of residents living below the poverty level.

Table 10.3: Odds Ratios (OR) and 95% Confidence Intervals (CI) for Likelihood of Having Uncontrolled Diabetes Associated with Travel Burden (Continuous)

Parameter	OR	95% CI	p-value
Miles to the Diabetes Center	1.02	1.01, 1.03	<0.0001
Age (Years)	0.99	0.98, 0.99	0.007
Sex (Male)	1.10	0.92, 1.31	0.31
Race (White)	1.06	0.71, 1.61	0.77
Duration of Diabetes (Years)	1.03	1.01, 1.05	0.004
BMI	0.998	0.98, 1.01	0.72
% High School Degree	0.99	0.97, 1.01	0.34
Median Income (2000 US Dollars)	0.99	0.99, 1.00	0.08
% Living Below Poverty Level	0.97	0.95, 0.99	0.04
% Black (County)	1.01	0.98, 1.03	0.39

Subjects visited the diabetes management center more than one time during the study period (mean = 1.86 visits). The first visit was defined as the first HbA1c laboratory value that was collected on the office visit date. The last visit was defined as the last HbA1c value that was entered into the Delphi system on the last office visit date. The office visit date was in the definition to control for those laboratory values that were historical values entered into the system from medical records. The difference between the first visit HbA1c values and the last visit HbA1c values were calculated to determine if the subjects' HbA1c improved over time. If the subject only had one office visit, they were removed from the analysis (n=230). The mean time between visits was 0.36 years (range =0.3 – 1.7 years) and mean difference between HbA1c values was an improvement of -0.01 (Table 10.4). There was a significant difference between travel burden and the number of visits (p= 0.0003). Those who lived less than ten miles from their center had a mean of 2.0 office visits while those who lived greater than ten miles from the

center had a mean of 1.6 visits. There was also significant difference between travel burden and change in HbA1c values over time (p< 0.0001). Individuals who resided less than ten miles from their diabetes center, had a mean improvement in HbA1c value of -0.19; indicating that their mean HbA1c values decreased 0.19. Those who lived greater than ten miles from their diabetes center had a mean increase in HbA1c values of 0.12. Furthermore, 85.1% of those living more than ten miles from their center were able to improve their HbA1c values between their first and last visits while 91.9% were able to improve their HbA1c values (p<0.0001) if they lived less than or equal to 10 miles from the center.

Table 10.4: Characteristics of A1c Values

	Center ≤ 10 mi (n=1737)	Center > 10 mi (n=1402)	Total (N=3139)	p-value
Difference between first and last A1c values				<0.0001
Mean [sd]	-0.19[1.0]	0.12[1.1]	-0.01[1.09]	
Range	-7.6 - 9.0	-7.7 - 9.0	-7.6 - 9.0	
Time Between Visits (years)				<0.0001
Mean [sd]	0.26[0.65]	0.43[0.97]	0.36[0.86]	
Range	0.1 - 3.2	0.1 – 3.1	0.1 – 3.2	
Improved A1c Values				<0.0001
n(%)	1719(91.9)	1276(85.1)	2967(88.2)	
Number of Office Visits				0.0003
Mean [sd]	2.0[2.1]	1.7[2.0]	1.8[2.1]	
Range	2 - 15	2 - 19	2 - 19	

The association between living less than or greater than ten miles from the diabetes center and improvement in HbA1c values over time was also modeled (Table 10.5). The results indicated that those who lived within ten miles of their diabetes management center (OR = 2.48, p = <0.0001), being older (OR = 1.01, p = 0.004), having a shorter duration of diabetes (OR = 0.95, p = 0.0001), and having more office visits (OR = 1.47, p= <0.0001) were significant contributors to the model. Therefore, those who lived less than ten miles from their diabetes management center, were than 2.49 times more likely to have improved their HbA1c values

between their first and last office visits, adjusted for individual and community level factors. Additionally, those who live less than ten miles from their center had a significantly shorter time between visits compared to those who lived ten or more miles from the center (0.26 years and 0.43 years, respectively).

Table 10.5: Odds Ratios (OR) and 95% Confidence Intervals (CI) for Likelihood of Having Improved HbA1c Values Associated with Travel Burden (Dichotomous)

Parameter	OR	95% CI	p-value
Diabetes Center <10 miles	2.48	1.65, 3.71	<0.0001
Age (Years)	1.01	1.00, 1.02	0.004
Sex (Male)	1.01	0.73, 1.41	0.94
Race (White)	1.74	0.91, 3.33	0.09
Duration of Diabetes (Years)	0.95	0.93, 0.98	0.001
BMI	1.00	0.98, 1.02	0.83
% High School Degree	0.99	0.95, 1.03	0.57
Median Income (US Dollars, 2000)	1.00	0.99, 1.00	0.63
% Living Below Poverty Level	1.00	0.95, 1.05	0.99
Number of Office Visits	1.47	1.38, 1.57	<0.0001
% Black (County)	0.99	0.96, 1.03	0.86

A sub-analysis of those who reported health insurance information (n = 2116) indicated that type of insurance coverage was not significantly associated with glycemic control and travel burden (dichotomous or continuous) in this study.

10.5 CONCLUSION

Results from this study indicated that the distance patients live from their diabetes management center has an affect of glycemic control. There is a clear association between travel burden and glycemic control among individuals with type 2 diabetes. Many of the subjects are from rural areas of Southwestern Pennsylvania, where it has become apparent that there is less access to health care. Those who live more than ten miles from their diabetes management center are 88%

more likely to have an HbA1c level greater than 7.0% compared to those who live less than 10 miles from their center, adjusted for both individual and community level factors. Additionally, for every mile the subjects live from their diabetes management center, they are 2% more likely to have an HbA1c level greater than 7.0, adjusted for individual and community level factors. In addition, those who lived ten miles or less from their diabetes management center, were than 2.24 times more likely to have improved their HbA1c values between their first and last office visits, adjusted for individual and community level factors.

Patients in rural areas may use less medical care than those living in urban areas (10). This difference in access to health care in rural areas may be dependent on a number of variables. These include patient-specific factors such as age, race, ethnicity, and perceptions of quality, as well as extrinsic factors such as insurance coverage and health care costs (10). Age and duration of diabetes were significant factors in the association between travel burden and glycemic control in this study. A sub-analysis of those who reported health insurance information indicated that type of insurance coverage was not significantly associated with glycemic control and travel burden in this study indicating that health insurance coverage was not a factor in glycemic control. However, there may have been a reporting bias since only two centers reported the information. Another potential factor related to health care utilization is travel time and distance (11, 12). Research has suggested that utilization is adversely affected by long travel times. One study found that patients may forgo free care if it is greater than 20 miles away (11). Several state health departments have proposed a standard in which rural residents should not have to travel more than 30 minutes to see a physician (10).

Our current framework of the rural-urban hierarchy of care is one in which rural areas are very dependent on urban ones for health care, in particular specialty care that is integral to

diabetes care. In this "hub-and-spoke model," rural patients must travel long distances for their care. It also has been found that rural residents have fewer overall visits and see fewer medical specialists and more generalists for their care than their urban counterparts (133). In addition, they found residents of small and isolated rural areas have greater travel distance and time compared to those living in urban areas. Median one-way travel time was less than 30 minutes for all patients, including those living in isolated small rural areas. However, some patients with specific diagnoses or undergoing specific procedures needed to travel much farther. Less than 30% of those living in all rural areas traveled to urban areas for their care. The vast majority were seen in their area or traveled to a larger rural location (10). Although this study concentrated only on rural residents, 45% of the subjects lived more than ten miles from their diabetes center. It should also be noted that ten miles in rural areas may take more travel time due to lower speed limits, more mountainous terrain, and less highways (9).

Rural areas are frequently characterized by poorly developed and fragile economic infrastructures, resulting in fewer available per capita hospital beds, doctors, nurses, and other health care services (31). In addition to socioeconomic hardships rural residents face substantial physical barriers, including a lack of public transportation, difficult terrain, and long distances to services (32, 33). It still remains unclear how rural elders perceive barriers to health care access and how they cope with those perceived barriers. Researchers Goins, Williams, Carter, Spencer, and Solovieva (30) examined what barriers rural elders report experiencing when accessing needed health care. In response to the questions posed to focus group participants, five categories of barriers to health care emerged from the discussions: transportation difficulties, limited health care supply, lack of quality health care, social isolation, and financial constraints (30).

Social isolation reflected some aspects of rural norms and values, such as the strong sense of self-reliance and reluctance to use formal services. Some participants were unaware of or did not have accurate information about available services. Participants also suggested that it would be helpful if older adults had information on services that might help meet their needs (30).

Financial constraints posed considerable barriers to accessing needed health care among study participants, including issues related to health care expense, inadequate health care coverage, income ineligibility to Medicaid, and the high cost of prescription medications. Participants commented they were not poor enough to qualify for Medicaid but did not have enough financial resources to afford health care (30). Rural areas have significant gaps in the continuum of care since home-based and community-based long-term care services are often unavailable (32). Beyond having a limited supply of health care providers, rural respondents also reported physicians are inadequate and lack professionalism. In rural areas, local physicians are often perceived as having poor interpersonal skills and/or lower quality care than what is available in more populated areas (34).

The findings of this study expand on those of Littenberg, Strauss, MacLean, and Troy (5) who conducted Wilcoxon rank-sum tests assess the role of travel burden as a barrier to the use of insulin in adults with diabetes. The researchers recruited 781 adults receiving primary care for type 2 diabetes. Travel burden was estimated as the shortest driving distance from the patient's home to the site of primary care. Medication use, age, sex, race, martial status, education, health insurance duration of diabetes, and frequency of care were self-reported. The researchers found that driving distance was significantly associated with insulin use, controlling for the covariates and potential cofounders. The odds ratio for using insulin associated with each kilometer of driving distance was 0.97. They concluded that adults with type 2 diabetes who live farther from

their source of primary care are significantly less likely to use insulin. The researchers hypothesize that this may be because patients and physicians are concerned about the risks of insulin and are reluctant to use it if they feel the patient lives too far way from care for rescue in the event of hypoglycemia. However, they had no direct data on the attitudes of these decision makers in this regard. Although our study focused on glycemic control and travel burden, and Littenberg et al. focused on insulin use in smaller population, the results strengthen the associations between the travel burden and glycemic control in those with diabetes.

Despite the availability of effective treatments, many patients with diabetes do not receive optimal glycemic control. Travel burden may be one of many obstacles for diabetes patients, especially in rural areas. Travel burden often also includes arranging transportation, the time required to travel, arranging child care, the cost of missing work, and the cost of the transportation. Driving distance is one aspect of travel burden, and may serve as a marker for at least some of the burden of obtaining diabetes care. Strauss et al. (13) examined the relationship between glycemic control and the driving distance from a patient's home to the site of primary care. The authors found that driving distance was significantly associated with glycemic control in their population of older, rural subjects. Each 22 miles of driving distance was associated with a 0.25% increase in HbA1c. Although our study focused on subjects who visited diabetes management centers, and Strauss et al focused primary care offices, the results support the associations between the travel burden and health care in those with diabetes. Our subjects received separate diabetes prevention classes, diabetes self-management education, meal planning and nutrition counseling, and insulin and medication therapies at the diabetes centers. The type of care received at a primary care office may not be as specialized as that received at the diabetes centers. Strauss et al. did not collect data on those who may have visited diabetes

specialists and recruited patients only from primary care offices, and therefore who would be less likely to use insulin.

This study demonstrates the need for more strategically located health care centers in rural areas. Only increasing the number of facilities without conducting location analyses would not be as effective as including these analyses. Including information on where the majority of residents' live, road connectivity, and geography will allow for the deliberate placement of needed health care locations.

There were some limitations in the study. Since the study was conducted in rural southwestern Pennsylvania, the population was mostly white and older so these results may not be generalized to urban or more diverse populations. Also, driving distance from the subject's home to the center may not be a perfect measurement of travel burden. Some subjects may take public transportation or have a friend or family member to drive them to the diabetes center.

This study is unique to the literature because it is the only study, to our knowledge, that examines the association between diabetes outcomes and diabetes management services that the subjects actually received. Having data on the number of visits, time between the visits and laboratory values is very distinctive and enabled us to find relationships between how the subjects are self-managing their diabetes and travel burden to a care site. Furthermore, results from this study demonstrate that travel burden is a potential barrier to proper management of diabetes. In the future, it may be useful to minimize driving distance for individuals with diabetes, perhaps by improved public transportation, more diabetes center locations in rural areas, telemedicine, or home visits. Additional research should focus on more effective ways to connect diabetes care providers and patients in rural areas. In addition to previous work, this

study demonstrates that the travel burden may play a central role in glycemic control and improvement in those with type 2 diabetes.

TABLES 10.6

Table 10.1: Population Characteristics

	Uncontrolled (n=1704)	Controlled (n=1665)	Total (n=3369)	p-value
Miles traveled to diabetes center				<0.0001
Mean [sd]	14.9[16.4]	11.7[15.3]	13.3[15.9]	
Range	0.06 - 78.4	0.06 - 85.1	0.06 - 85.1	
Subjects within 10 miles of diabetes center				<0.0001
n(%)	830(48.7)	1037(51.3)	1867(55.4)	
Gender n(%)				0.24
Male	738(43.4)	688(41.3)	1943(57.6)	
Female	965(56.6)	978(58.7)	1426(42.4)	
Age (Years)				<0.0001
Mean [sd]	66.7[15.7]	69.1[15.9]	67.9[15.9]	
Range	18.4 - 101.0	18.4 - 100.9	18.4 - 101.0	
Ethnicity n(%)				0.56
Caucasian/White	1439(94.9)	1474(94.3)	2913(94.6)	
Black/African American	63(4.2)	72(4.6)	135(4.3)	
Asian	2(0.1)	3(0.2)	5(0.2)	
American Indian/Alaskan	3(0.2)	0(0.0)	3(0.1)	
Hispanic/Latino	2(0.1)	3(0.2)	5(0.2)	
Other	7(0.5)	10(0.7)	17(0.6)	
Missing=291				
HbA1c (%)				<0.0001
Mean [sd]	8.6[1.6]	6.1[0.5]	7.4[1.7]	
Range	7.0 - 18.7	4.2 - 6.9	4.2 - 18.7	
Body Mass Index*				0.99
Mean [sd]	32.8[8.1]	32.9[8.1]	32.9[8.1]	
Range	16.6 - 56.6	18.9 - 56.7	16.6 - 56.7	
Duration of Diabetes (Years)				0.0004
Mean [sd]	6.1[5.2]	5.4[3.6]	5.8[4.5]	
Range	2.2 - 59.2	2.2 - 43.2	2.2 - 59.2	
Systolic Blood Pressure (mmHg)				0.44
Mean[sd]	135.7[18.2]	135.2[18.2]	135.4[18.2]	
Range	90 - 189	90 - 192	90 - 192	

* BMI = [weight in kilograms/height in meters^2]

Table 10.1: Population Characteristics Continued

	Uncontrolled (n=1704)	Controlled (n=1665)	Total (n=3369)	p-value
Diastolic Blood Pressure (mmHg)				0.27
Mean[sd]	78.3[10.4]	77.9[10.4]	78.1[10.4]	
Range	40 - 104	40 - 100	40 - 104	
HDL (mg/dL)				0.04
Mean[sd]	39.8[11.4]	40.7[11.7]	40.3[11.6]	
Range	10.0 - 89.0	10.0 - 94.0	10.0 - 94.0	
LDL (mg/dL)				0.99
Mean[sd]	104.6[33.7]	104.6[34.0]	104.6[33.9]	
Range	28 - 348	26 - 235	26 - 348	
Triglycerides (mg/dL)				0.17
Mean[sd]	183.9 [114.6]	178.6[110.9]	181.3[112.9]	
Range	46 - 605	43 - 438	43 - 605	
% Living Below the Poverty Level				0.09
Mean [sd]	13.1[7.9]	13.6[9.3]	13.4[8.6]	
Range	3.8 - 57.1	3.8 - 59.6	3.8 - 59.6	
Median Income				0.57
Mean [sd]	29434.5[6709.2]	29572.0[7402.2]	29502.4[7095.5]	
Range	10490 - 53580	10490 - 65540	10490 - 65540	

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11.0 CONCLUSIONS

Diabetes mellitus is a serious chronic disease with rates increasing substantially over the past decade and is expected to grow drastically over the next several years (1). It is a significant public health problem as it places a serious burden on patients, the health care system, and society. Diabetes has always been difficult to manage because of the complexity of the disease. It is more than a disease of abnormal glucose metabolism due to the related macro and microvascular complications. Management of diabetes involves clinical, behavioral, psychosocial and environmental factors. Despite many advances in the understanding of its pathophysiology (5), factors that affect its care (5), and improved treatment options (5), diabetes remains a complex and challenging chronic condition. Often, diabetes management falls below recommended standards regardless of patient related factors, emphasizing the necessity for changes in the built environment.

The built environment is defined as human-modified places such as homes, schools, workplaces, parks, industrial areas, farms, roads, and highways (154). The built environment encompasses all buildings, spaces and products that are created or modified by people. It impacts the indoor and outdoor environments such as indoor/outdoor air quality, as well as social environments such as community participation and investment, and subsequently our health and quality of life (154). Much discussion of the built environment has focused on the challenges of providing adequate transportation, urban sprawl, air pollution and the diminishing natural environment. However, new research increasingly recognizes that the places we live and work clearly affect our health (155,156). Access to green open space can increase physical activity and mental wellbeing; because evidence demonstrates that the most sustained exercise is incorporated into daily routine activities (163). Recent research also explores the effect the built

environment on physical activity (157), asthma (158), obesity (159), cardiovascular disease, lung cancer mortality (160), and mental health (161,162). The growing health burdens and rising economic costs associated with higher chronic disease incidence require such research efforts. These complex diseases are attributable to an interaction of genetic and environmental influences, and many of the latter can be directly connected to the built environment. Research investigating the association between public health and quality-of-life benefits of sustainable communities is necessary.

Certain environmental aspects play an important role in the prevention and treatment of chronic diseases such as diabetes. Studies have shown that access to health care, diet, and physical activity contribute to diabetes, which are all part an individual's environment or community (4). While there are many ways to define community, geographic location is one important way to understand the context in which people live. Until recently, there has not been a valid method for defining and analyzing geographic areas that make up a community where these risk factors and chronic diseases may cluster. Geographical modeling may allow for better identification of the geographic area of communities that provide risk for diabetes or diabetes complications. There is great variability in the health and well being of residents depending upon where they live. Health-promotion interventions may need to be designed to target the geographic areas that represent areas of health problems and unhealthy lifestyles.

Diabetes is preventable and can be controlled with intervention. However, some areas may not have resources that would enable its residents to lead a healthy lifestyle. Geospatial mapping techniques can be used to show areas with higher likelihood of diabetes, risk factors for diabetes complications, or unmanaged diabetes and where funds need to be targeted. This type

of analysis can provide important clues about the geographic variability of risk factors, disease states and clinical services utilization.

11.1 SUMMARY OF FINDINGS

This dissertation examined geographical patterns of diabetes hospitalizations, risk factors for diabetes complications and glycemic control among individuals with type 2 diabetes in rural regions. The aims were to: 1.) identify an association between county rurality hospitalization rates for uncontrolled diabetes; 2.) determine if there is an association between the availability of disease prevention and health care facilities, the local food environment and risk factors for complications of diabetes; 3.) examine the association between glycemic control and improvement in individuals with type 2 diabetes, and travel burden to diabetes management centers in southwestern Pennsylvania.

In the first aim, we sought to determine if individuals who reside in counties with increased rurality will be more likely to be hospitalized for uncontrolled diabetes than counties that are more urbanized. We found that during 2007 calendar year, diabetes was the principal diagnosis upon admission in 14.5 per 10,000 adult residents, and for any-listed diagnosis in 246.8 per 10,000 adult residents for the entire study area. Hospitalization rates for uncontrolled diabetes as any-listed diagnoses upon admission were also calculated for the study area. The rate was 8.2 per 10,000 adult residents. Results of this study indicate an association between the rurality of a county and the diabetes hospitalization rates of the county's residents. Residents of more rural counties are 11% more likely to be hospitalized for uncontrolled diabetes compared to those living in areas that are less rural for every increase in rurality ranking.

In specific aim two, the association between the presence of supermarkets, full-service restaurants, physicians' offices, hospitals and pharmacies and risk factors for diabetes complications in individuals with type 2 diabetes was explored. We found that nearly 57% of the individuals lived in census tracts with convenience stores, while only 24.3% lived in census tracts with large supermarkets. Sixty-percent of individuals lived in census tracts with fast food restaurants while only 41.0% lived in areas with full-service restaurants. Approximately 57% of the population lived in census tracts with a physician's office, 56.7% lived in an area with a pharmacy and only 8.0% lived near a hospital.

Furthermore, we demonstrated that while supermarkets and grocery stores were associated with a decrease in the likelihood of hypertension, hypercholesterolemia, being overweight and obese, the presence of convenience stores was associated with an increase in the likelihood of individuals having hypertension, hypercholesterolemia, being overweight, obese, and hyperglycemia, after adjusting for individual and community level factors.

A similar trend was found in food service places. The presence of full-service and limited-service restaurants was associated with a decrease in the likelihood of having hypertension, being overweight and obese while the existence of fast food restaurants was associated with an increased likelihood of having in these factors. The presence of any of the health care locations was associated with a decrease in the likelihood of having these factors. Results from this study indicate that the local food and health care environment at the neighborhood level is a possible ecological determinant of health. There is a clear association between the presence of food stores and service places, and health care locations with risk factors for diabetes complications among individuals with diabetes. The local environment has a

significant impact on public health by possibly restricting a population's food and health care choices and opportunities that affect health.

In specific aim three, we sought to explore the relationship between travel burden to a diabetes management center and glycemic control and improvement. Approximately 50.6% (n=1704) individuals were categorized as having uncontrolled diabetes (HbA1c > 7.0). We found that the mean distance subjects traveled to visit their diabetes management center were 13.3 miles (range 0.06 – 85.1 miles). Fifty-five percent of the subjects lived less than ten miles from their diabetes center. The associations between the distance subjects traveled to their diabetes management centers and the glycemic control were modeled. Those who live more than ten miles from their diabetes management center are 88% more likely to have an HbA1c level greater than 7.0% compared to those who live less than ten miles from their center, adjusted for individual-level factors such as age, sex, race, duration of diabetes, and BMI as well as community level factors such as percent of residents with a high school degree or higher, median household income and percent of residents living below the poverty level. The association between the numbers of miles from the diabetes center as a continuous variable and glycemic control was also modeled. For every mile the subjects live from their diabetes management center, they are 2% more likely to have an HbA1c level greater than 7.0%, adjusted for individual and community level factors. In addition, those who lived within ten miles from their diabetes management center, were 2.24 times more likely to have improved their HbA1c values between their first and last office visits, adjusted for individual and community level factors. This study demonstrates that the travel burden may play a central role in glycemic control and improvement in those with type 2 diabetes.

11.2 CONTRIBUTION TO THE LITERATURE

The findings of this dissertation are significant and help to fill the gap in the literature by examining associations between diabetes and the built environment. There is a paucity of literature on geographic studies in diabetes research. The first manuscript incorporated into this report provides supporting evidence that there is a need for more services in rural areas. This current study adds to the existing literature by describing a population at the individual-level for a small geographic area. Most of the data collected for diabetes rates are extrapolated from larger random surveys and exact rates are not available at the county-level for many states. This study uses individual-level data to calculate both county-level and individual-level rates. It also focuses on hospitalizations for uncontrolled diabetes which can be an indication of how well the health care system in an area is performing. Hospitalizations for diabetes, particularly for uncontrolled diabetes, may be preventable because appropriate care can generally be provided on an outpatient basis (7). If a patient reaches the point where hospitalization for diabetes is required, a breakdown in care, or access to care, may have already occurred. The majority of the literature on the geographic variation of chronic diseases and diabetes examines urban areas and does not focus on rural populations. This is the first study, to our knowledge, to look at diabetes hospitalization rates at the geographic scale of the county-level and links it to the rurality of the county.

The second manuscript that is incorporated into this dissertation adds significantly to the literature, as little is known about the how the local food and health care environment is associated with the health of a population. The literature demonstrates that diabetes encompasses behavioral, environmental, social, and clinical factors, all which play an important role in the management of the disease. It is assumed that behavioral characteristics of

individuals with diabetes are affected by their access to health care and disease prevention facilities, a healthy local food environment and physical activity locations. Furthermore, it is believed that those living in more rural areas have less access to these locations and therefore will have higher rates of disease. We believe that our work in this manuscript will provide further evidence for this theory.

These findings expand on those of Moreland, Roux, and Wing (192) who conducted multilevel modeling in order to calculate prevalence ratios of the associations between the presence of specific types of food stores and cardiovascular disease risk factors. This analysis demonstrated that the presence of supermarkets was associated with a lower prevalence of obesity and overweight (obesity prevalence ratio [PR] = 0.83, 95% CI=0.75-0.92; overweight PR=0.94, 95% CI=0.90-0.98), and the presence of convenience stores was associated with a higher prevalence of obesity and overweight (obesity PR=1.16, 95% CI=1.05-1.27; overweight PR=1.06, 95% CI=1.02-1.10). The results from this study suggest that characteristics of local food environments may play a role in the prevention of overweight and obesity (192). Although our study focused on those with diabetes and risk factors of complications, and Moreland et al. used a cross-sectional population from major metropolitan areas, the results strengthen the associations between the local food environment and health.

Inagami et al. (206) found residents in poor neighborhoods have a higher body mass index (BMI) and eat less healthfully. One possible reason might be the quality of available foods in their area. The researchers examined the location of grocery stores where individuals shop and its association with BMI. Inagami and colleagues aimed to estimate the associations between BMI and socioeconomic characteristics of grocery store locations after adjustment for individual-level factors and socioeconomic characteristics of residential neighborhoods. They

were able to conclude that where people shop for groceries and distance traveled to grocery stores are independently associated with BMI. Our study also demonstrated that after controlling for SES factors of the census tract, the significant associations between food stores, food service places, and health care locations and risk factors for complications remained.

Our study also investigated the associations between health care locations and risk factors for diabetes complications. There have been few studies focusing on associations between risk factors and health care locations. Dabney and Gosschalk found that rural residence is a significant risk factor for never receiving an ophthalmic examination, which can detect early signs of complications such as diabetic retinopathy (178). However, this study only focused on ophthalmic offices. It is also important to note that the results from our study demonstrate that the food environmental factors were more significant in contributing to risk factors of diabetes complications that the health care locations. However, even after adjusting for age, gender and race, the controllable environmental factors still had a significant association with risk factors. This is evidence that the environment can play a role in the health of residents and should be changed in order to control important risk factors. This is first study to our knowledge that shows a difference in the role of food environmental factors and health care locations.

The third manuscript also adds to the existing literature by demonstrating that the travel burden may play a central role in glycemic control and improvement in those with type 2 diabetes. The majority of the literature on this subject does not focus on travel burden and visits to a diabetes management center. It is also unique that the particular center that the subjects visited, the number of office visits, and the time between the visits was recorded and included as a part of the dataset.

The findings of this manuscript expand on those of Littenberg, Strauss, MacLean, and Troy (150) who conducted Wilcoxon rank-sum tests assess the role of travel burden as a barrier to the use of insulin in adults with diabetes. They concluded that adults with type 2 diabetes who live farther from their source of primary care are significantly less likely to use insulin. Although our study focused on glycemic control and travel burden, and Littenberg et al. focused on insulin use in smaller population, the results strengthen the associations between the travel burden and glycemic control in those with diabetes. Strauss et al. (149) examined the relationship between glycemic control and the driving distance from a patient's home to the site of primary care. The authors found that driving distance was significantly associated with glycemic control in their population of older, rural subjects. Each 22 miles of driving distance was associated with a 0.25% increase in HbA1c. Although our study focused on subjects who visited diabetes management centers, and Strauss et al focused primary care offices, the results support the associations between the travel burden and health care in those with diabetes. Our subjects received separate diabetes prevention classes, diabetes self-management education, meal planning and nutrition counseling, and insulin and medication therapies at the diabetes centers. The type of care received at a primary care office may not be as specialized as that received at the diabetes centers. Strauss and colleagues did not collect data on those who may have visited diabetes specialists and recruited patients only from primary care offices, and therefore would be more likely to using insulin.

11.3 STUDY LIMITATIONS

In conducting geographical-based ecological studies, all circumstances are not "controllable"; therefore, limitations exist. First, due to the Health Information Protection and Portability Act

(HIPPA), and the Institutional Review Board (IRB) at the university associated with this research, the subjects could not be depicted geographically at a reasonable scale. There are also issues and limitations with geographic data. The subjects' home addresses were entered into the data management system as mailing addresses. Approximately 5% of the home addresses could not geocoded because PO Boxes were given as the address. An attempt was made to match some of the PO Boxes (n=12) with street addresses using 9-1-1 emergency data. A limitation in the first manuscript is that the number of total hospitalizations for 2007 in the study area from the PHC4 dataset was unavailable. This did not allow for the calculation of rates based on all hospitalizations and allow for comparisons of age, gender, and race for those who were not hospitalized for diabetes. Although a number of potential confounders were controlled for in the multivariate analyses, residual confounding by unmeasured variables such as health care insurance cannot be ruled out. In the second manuscript, the subjects from the Delphi Data Management System were not surveyed on where they shopped, the restaurants in which they ate, or where they went for health care, so misclassification may have occurred if the census tract did not represent the area where the subjects patronage. Also, market research has an impact on where food stores, food service and health care places are located (192). Businesses may be located in more populated areas or areas with a higher SES. Since the study was conducted in rural southwestern Pennsylvania, the population was mostly white and older so these results may be able to be generalized to urban or more diverse populations. Another possible limitation to our study is that nearly all of our data are self-reported, with the exception of the laboratory data, which inherently biases the results toward the null. Lastly, in the third manuscript, driving distance from the subject's home to the center may be a perfect measurement of travel burden.

Some subjects may take public transportation or have a friend or family member to drive them to the diabetes center.

11.4 PUBLIC HEALTH SIGNIFICANCE

Diabetes is a complex chronic disease with many causes, complications and management needs. It affects a large proportion of people of varying ages, income levels, races/ethnicities and geographic areas. Diabetes is becoming more common in the United States and shifts in the patterns of disease have occurred. There are no longer epidemics of acute illnesses. Instead they have been replaced by epidemics of chronic diseases such as diabetes (7). From 1980 through 2007, the number of Americans with diabetes increased from 5.6 million to 17.9 million (2). It is estimated that another 5.7 million Americans are undiagnosed (2). Approximately 762,000 or 7.0% of Pennsylvanians have been diagnosed with diabetes and is responsible for nearly 4,000 deaths in Pennsylvania (6). Diabetes is a major public health challenge due to the enormous impact on the affected individual, their families and the health care system. However, recent research has shown that diabetes related mortality and morbidity can be prevented or delayed by controlling risk factors (7).

Certain environmental aspects play an important role in the prevention and treatment of chronic diseases such as diabetes. There is great variability in the health and well being of residents depending upon where they live. Health-promotion interventions may need to be designed to target the geographic areas that represent clusters of health problems and unhealthy lifestyles. More research is needed to study how the built environment relates geographically to chronic diseases such as diabetes in order to develop public health prevention programs and improve diabetes management and outcomes.

Based on the findings of the first manuscript, residents of rural counties have higher rates of uncontrolled diabetes hospitalizations compared to all diabetes hospitalizations. This is significant to public health because diabetes is a serious, costly disease, in which hospitalizations continue to rise. It is responsible for $174 billion in direct medical costs and indirect (work loss, disability, premature death) medical expenditures every year. Diabetes also has an enormous impact on the affected individual, their families, and the health care system. Understanding where gaps in health care and diabetes educations exist may lead to changes in policy and the local neighborhood environment to increase the access of rural patients. It is important to further investigate the access residents of these counties have to health care facilities, other disease prevention facilities, and the local food and physical activity environments. This will shed more light on how the environment of individuals with diabetes affects their overall health and their ability to control their diabetes.

Given the considerable public health burden of diabetes, improving care for individuals with diabetes should be a priority in the majority of communities. In selecting and improving access within the built environment to improve care and management for diabetes, communities should strive to develop comprehensive strategies to promote healthy lifestyles and to assist people with diabetes improve glycemic control, decrease diabetes complications, and improve quality of life, just as we did in this research. Choosing interventions based on geographically targeted areas and that are well matched to local neighborhood needs are vital steps toward improving outcomes for people with diabetes.

Results from the second manuscript indicate that the local environment has a significant impact on public health by possibly restricting a population's food and health care choices and opportunities that affect health. In addition to previous work, this study demonstrates that the

local food and health care environment may play a central role in the prevention of risk factors of diabetes complications. Furthermore, results from the third manuscript demonstrate that travel burden is a potential barrier to proper management of diabetes. In the future, it may be useful to minimize driving distance for individuals with diabetes, perhaps by improved public transportation, more diabetes center locations in rural areas, telemedicine, or home visits. Additional research should focus on more effective ways to connect diabetes care providers and patients in rural areas. In addition to previous work, this study demonstrates that the travel burden may play a central role in glycemic control and improvement in those with type 2 diabetes.

There is a growing recognition that the built environment has an impact on health. For example, one may expect more physical activity and healthier diets among persons in communities with convenient, safe walking paths and accessible sources of fresh fruits and vegetables. On the other hand, poorer health indicators may be expected among residents of communities with high crime rates, few parks or walking paths, numerous alcohol and tobacco outlets, and little access to fresh food. Low-income and/or rural communities are more likely to be sites of hazards and less likely to be conducive to physical activity and healthy eating.

11.5 FUTURE RESEARCH

Important decisions about the built environment have traditionally been made without active inclusion of public health. It is clear from the results of this dissertation that the built environment is associated with the health of a population and should be considered in community planning and policy making. Future research should focus on the connections between the built environment and health, focusing on access to health care, healthy food,

physical activity locations, transportation and neighborhood characteristics such as sidewalk conditions, and lighting. More research should be focused on the issues of the built environment in rural areas, lower socioeconomic strata, and minority populations. Studies on sustainable communities exploring the planning that is needed to create an environment that is conducive to the mental and physical well-being of residents should be conducted. There is also limited research on measures and methods to quantify the health benefits of improved community planning. Multidisciplinary research investigating the positive and negative health impacts of planned communities is needed to develop models to incorporate programs that improve health for community development in less desirable areas. The available evidence lends itself to the argument that a combination of urban design, land use patterns, and transportation systems that promote access to healthy lifestyle factors will help create more active, healthier, and more livable communities. Collaborative research efforts that build on the research models of the fields of both public health and community planning are essential to making further progress in the effort to build healthier and more livable communities.

12.0 RECOMMENDATIONS

In this research, the associations between the environment and diabetes, risk factors for diabetes complications and glycemic control were investigated. As the burden of diabetes continues to escalate, new approaches for diabetes care and self-management education are needed if we are to advance care at the patient, provider, community, and health care systems levels. Chronic diseases, such as diabetes, are leading health concerns which are influenced by the built environment. Decisions about zoning, transportation, land use and community design influence

the distances people travel to health care facilities, the convenience of purchasing healthy foods, and the safety and attractiveness of neighborhoods for walking. It is clear from the health implications of these decisions that public health should be a strong ally to ensure that decisions about neighborhood design are made with the health of community members at the forefront. Future location analysis should be conducted to find the most strategic places to build new health care facilities, physicians' offices, supermarkets, and farmer's markets.

However, decisions about the built environment have traditionally been made without active inclusion of public health. To facilitate public health's participation, this project provides a concrete example that demonstrates the importance of the built environment for chronic diseases and illustrates potential roles for public health. A greater understanding of opportunities to improve health outcomes through altering the built environment will strengthen linkages between public health and community planners.

APPENDIX A: TABLES AND FIGURES

Table 8.5: 2003 Rural-Urban Continuum Codes	
Code	**Description**
Metro counties:	
1	Counties in metro areas of 1 million population or more
2	Counties in metro areas of 250,000 to 1 million population
3	Counties in metro areas of fewer than 250,000 population
Nonmetro counties:	
4	Urban population of 20,000 or more, adjacent to a metro area
5	Urban population of 20,000 or more, not adjacent to a metro area
6	Urban population of 2,500 to 19,999, adjacent to a metro area
7	Urban population of 2,500 to 19,999, not adjacent to a metro area
8	Completely rural or less than 2,500 urban population, adjacent to a metro area
9	Completely rural or less than 2,500 urban population, not adjacent to a metro area

Table 8.6: Rural-Urban Continuum Codes for Counties in the Study Area		
County Name	2003 Rural-Urban Continuum Code	2000 Population
Cambria County	3	152,598
Allegheny County	1	1,281,666
Armstrong County	1	72,392
Fayette County	1	148,644
Greene County	6	40,672
Indiana County	4	89,605
Somerset County	4	80,023
Westmoreland County	1	369,993
Washington County	1	202,897

Table 8.7 International Classification of Diseases, 9th Revision, Clinical Modification Codes (ICD-9)

250.0 Diabetes mellitus without mention of complication

-250.00 Diabetes mellitus without complication type ii or unspecified type not stated as uncontrolled

-250.01 Diabetes mellitus without complication type i not stated as uncontrolled

-250.02 Diabetes mellitus with complication type ii or unspecified type uncontrolled

-250.03 Diabetes mellitus with complication type i uncontrolled

250.1 Diabetes with ketoacidosis (*A complication of diabetes mellitus, primarily with Type 1 with sever insulin deficiency and extreme hyperglycemia)*

-250.10 Diabetes mellitus with ketoacidosis type ii or unspecified type not stated as uncontrolled

-250.11 Diabetes mellitus with ketoacidosis type i not stated as uncontrolled

-250.12 Diabetes mellitus with ketoacidosis type ii or unspecified type uncontrolled

-250.13 Diabetes mellitus with ketoacidosis type i uncontrolled

250.2 Diabetes with hyperosmolarity (*A complication of Type 2 Diabetes characterized by extreme hyperglycemia and dehydration)*

-250.20 Diabetes mellitus with hyperosmolarity type ii or unspecified type not stated as uncontrolled

-250.21 Diabetes mellitus with hyperosmolarity type i not stated as uncontrolled

-250.22 Diabetes mellitus with hyperosmolarity type ii or unspecified type uncontrolled

-250.23 Diabetes mellitus with hyperosmolarity type i uncontrolled

250.3 Diabetes with other coma (*A state of unconsciousness as a complication of diabetes)*

-250.30 Diabetes mellitus with other coma type ii or unspecified type not stated as uncontrolled

-250.31 Diabetes mellitus with other coma type i not stated as uncontrolled

-250.32 Diabetes mellitus with other coma type ii or unspecified type uncontrolled

-250.33 Diabetes mellitus with other coma type i uncontrolled

250.4 Diabetes with renal manifestations (*Kidney injuries associated with diabetes and affecting kidney glomerulus; arterioles; kidney tubules)*

-250.40 Diabetes mellitus with renal manifestations type ii or unspecified type not stated as uncontrolled

-250.41 Diabetes mellitus with renal manifestations type i not stated as uncontrolled

-250.42 Diabetes mellitus with renal manifestations type ii or unspecified type uncontrolled

-250.43 Diabetes mellitus with renal manifestations type i uncontrolled

250.5 Diabetes with ophthalmic manifestations

-250.50 Diabetes mellitus with ophthalmic manifestations type ii or unspecified type not stated as uncontrolled

-250.51 Diabetes mellitus with ophthalmic manifestations type i not stated as uncontrolled

-250.52 Diabetes mellitus with ophthalmic manifestations type ii or unspecified type uncontrolled

-250.53 Diabetes mellitus with ophthalmic manifestations type i uncontrolled

250.6 Diabetes with neurological manifestations (*Peripheral, autonomic, and cranial nerve disorders that are associated with diabetes)*

-250.60 Diabetes mellitus with neurological manifestations type ii or unspecified type not stated as uncontrolled

-250.61 Diabetes mellitus with neurological manifestations type i not stated as uncontrolled

-250.62 Diabetes mellitus with neurological manifestations type ii or unspecified type uncontrolled

-250.63 Diabetes mellitus with neurological manifestations type i uncontrolled

250.7 Diabetes with peripheral circulatory disorders

-250.70 Diabetes mellitus with peripheral circulatory disorders type ii or unspecified type not stated as uncontrolled

-250.71 Diabetes mellitus with peripheral circulatory disorders type i not stated as uncontrolled

-250.72 Diabetes mellitus with peripheral circulatory disorders type ii or unspecified type uncontrolled

-250.73 Diabetes mellitus with peripheral circulatory disorders type i uncontrolled

250.8 Diabetes with other specified manifestations

-250.80 Diabetes mellitus with other specified manifestations type ii or unspecified type not stated as uncontrolled

-250.81 Diabetes mellitus with other specified manifestations type i not stated as uncontrolled

-250.82 Diabetes mellitus with other specified manifestations type ii or unspecified type uncontrolled

-250.83 Diabetes mellitus with other specified manifestations type i uncontrolled

250.9 Diabetes with unspecified complication (*Conditions or pathological processes associated with diabetes. Due to the impaired control of blood glucose level in diabetic patients, pathological processes develop in numerous tissues and organs including the eye, the kidney, the blood vessels, and the nerve tissue.*)

-250.90 Diabetes mellitus with unspecified complication type ii or unspecified type not stated as uncontrolled

-250.91 Diabetes mellitus with unspecified complication type i not stated as uncontrolled

-250.92 Diabetes mellitus with unspecified complication type ii or unspecified type uncontrolled

-250.93 Diabetes mellitus with unspecified complication type i uncontrolled

585 Chronic Kidney Disease
586 Renal failure unspecified
V420 Kidney replaced by transplant
V560 Aftercare involving extracorporeal dialysis
V568 Aftercare involving other dialysis
996.62 Infection and inflammatory reaction due to vascular device, implant and graft
996.73 Other complications due to renal dialysis device implant and graft
996.81 Complications of transplanted kidney

Table 8.8: Pennsylvania Health Care Cost Containment Council Data File Variables

Field Name	Data Description	Notes
	Record Identification	
SYSID	System assigned unique record sequence number	Unique code for each quarter
YEAR	Processing year	
QUARTER	Processing Quarter	
	Facility Identification	
PAF	PA Facility Number	PHC4 assigned code
HREGION	Facility Region Code	PHC4 assigned code
	Patient Data	
PTSEX	Patient Sex Code	Gender
ETHNIC	Hispanic/Latino Origin	Ethnic descent
RACE	Race Code	Race
PSEUDOID	Pseudo Patient Identifier	PHC4 assigned unique patient code
AGE	Patient Age in Years	Age of patient; Zero if less than 1 year or unknown
County	Patient Home County Code	PA county code (1-67)
STATE	Patient State Code	USPS standard state code
	Admission Date	
ADTYPE	Priority (Type of Visit)	Defines urgency level of admission
ADSOURCE	Point of Origin for Admission	Defines point of origin for admission
ADMDX	Admitting Diagnosis	Defines diagnosis at admission
ADHOUR	Admission Hour	Military time
	Discharge Data	
DCSTATUS	Patient Discharge Status	Defines discharge destination
LOS	Length of Stay	Number of hospitalization days
DCHOUR	Discharge Hour	Military time
	Diagnosis Codes	
PDX	Principal Diagnosis Code	Defines diagnosis at discharge
SDX1-SDX8	Secondary Diagnosis Code (1)-(8)	Defines additional diagnosis conditions
	Payer Identification	
PAYTYPE1	Primary Payer	Defines primary payer
PAYTYPE2	Secondary Payer	Defines secondary payer
PAYTYPE3	Tertiary Payer	Defines tertiary payer
HEALTHPALNID1	Health Plan Identification Number (NAIC/NPI)	Primary health plan

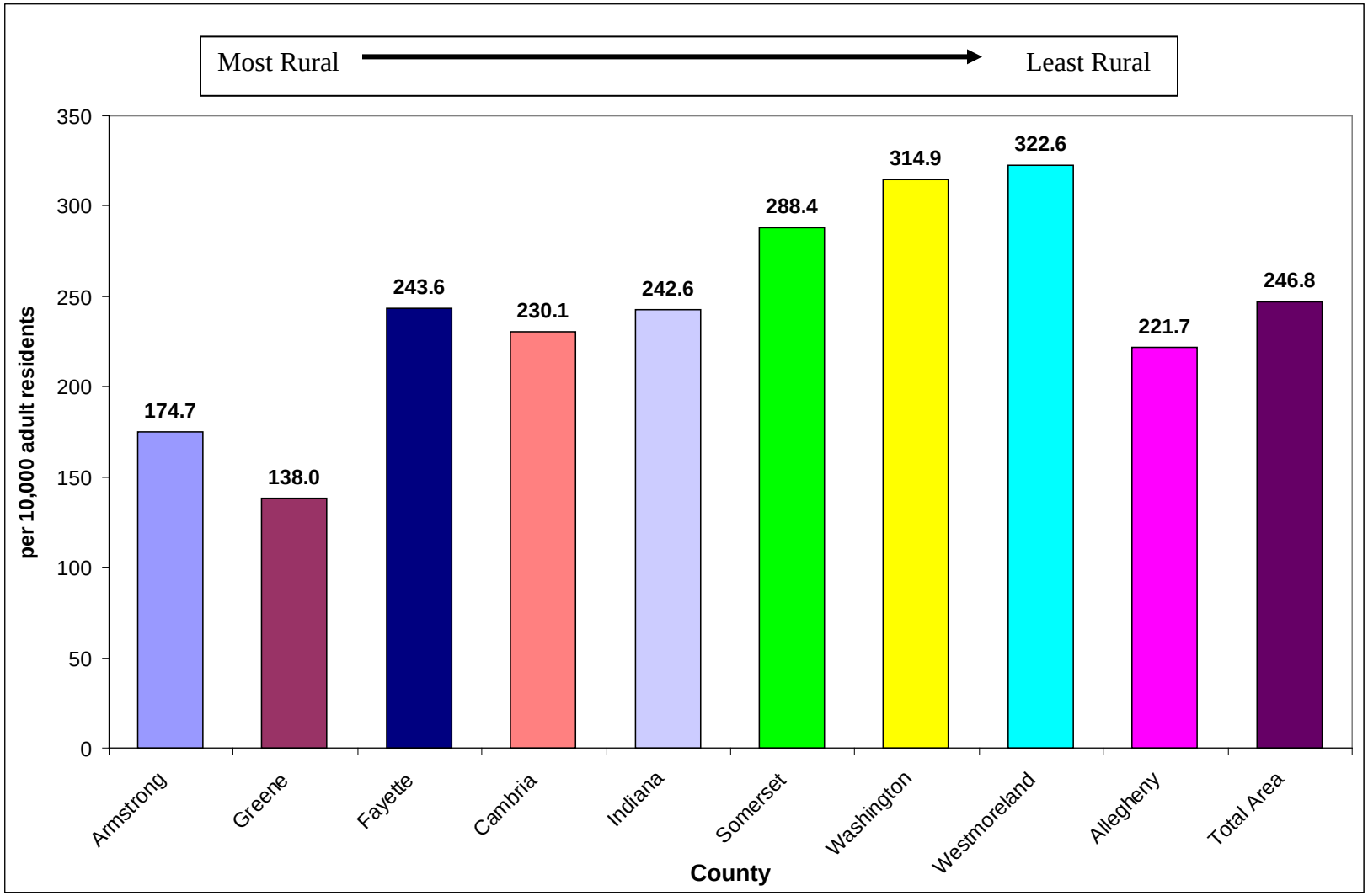


Figure 8.0 Age-Adjusted Diabetes Hospitalization Rates*, Any-Listed Diagnosis, by County, 2007
**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes (Pennsylvania Health Cost Containment Council (PHC4)*

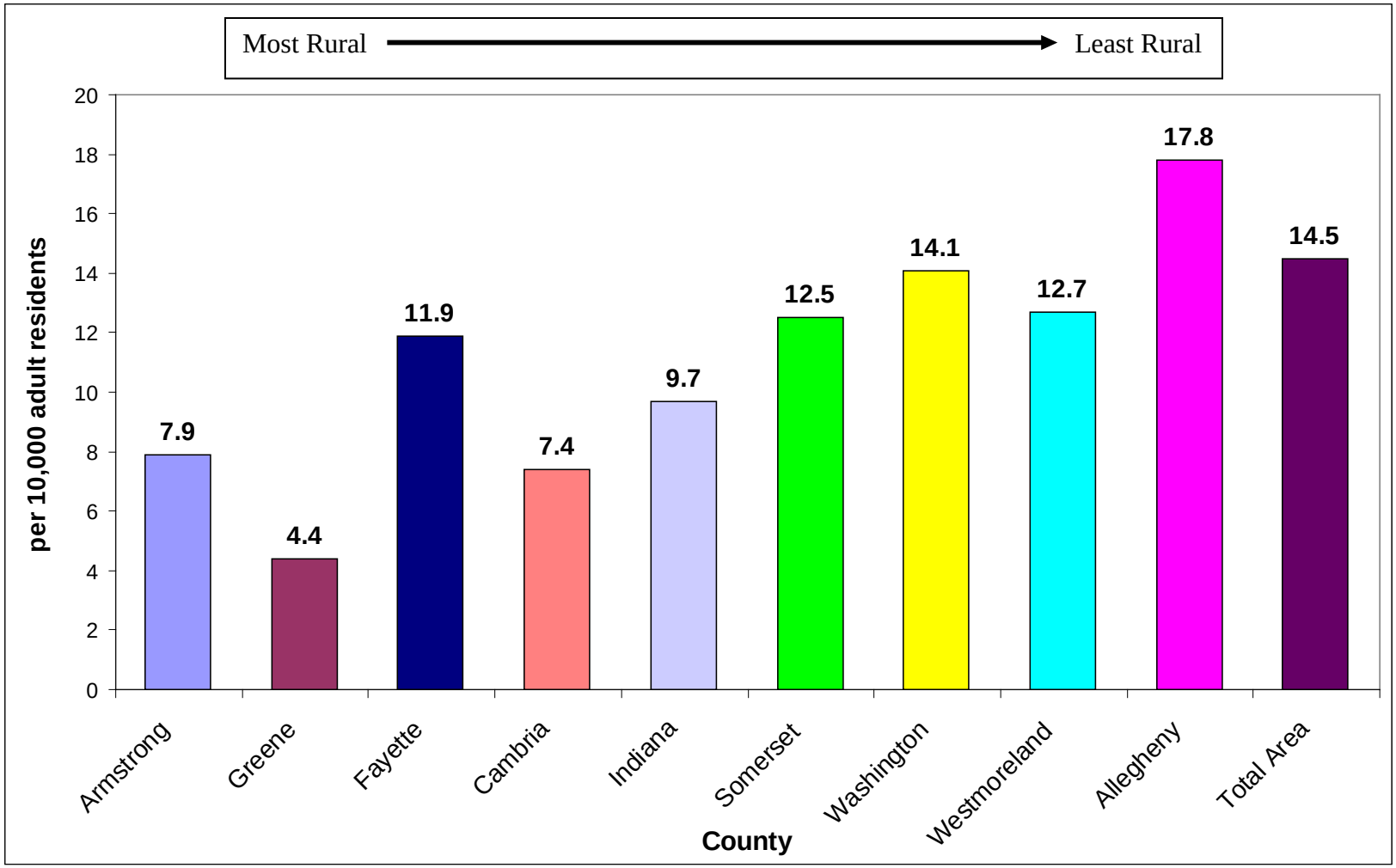


Figure 8.1: Age-Adjusted Diabetes Hospitalization Rates*, Principal Diagnosis, by County, 2007
**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes, PHC4*

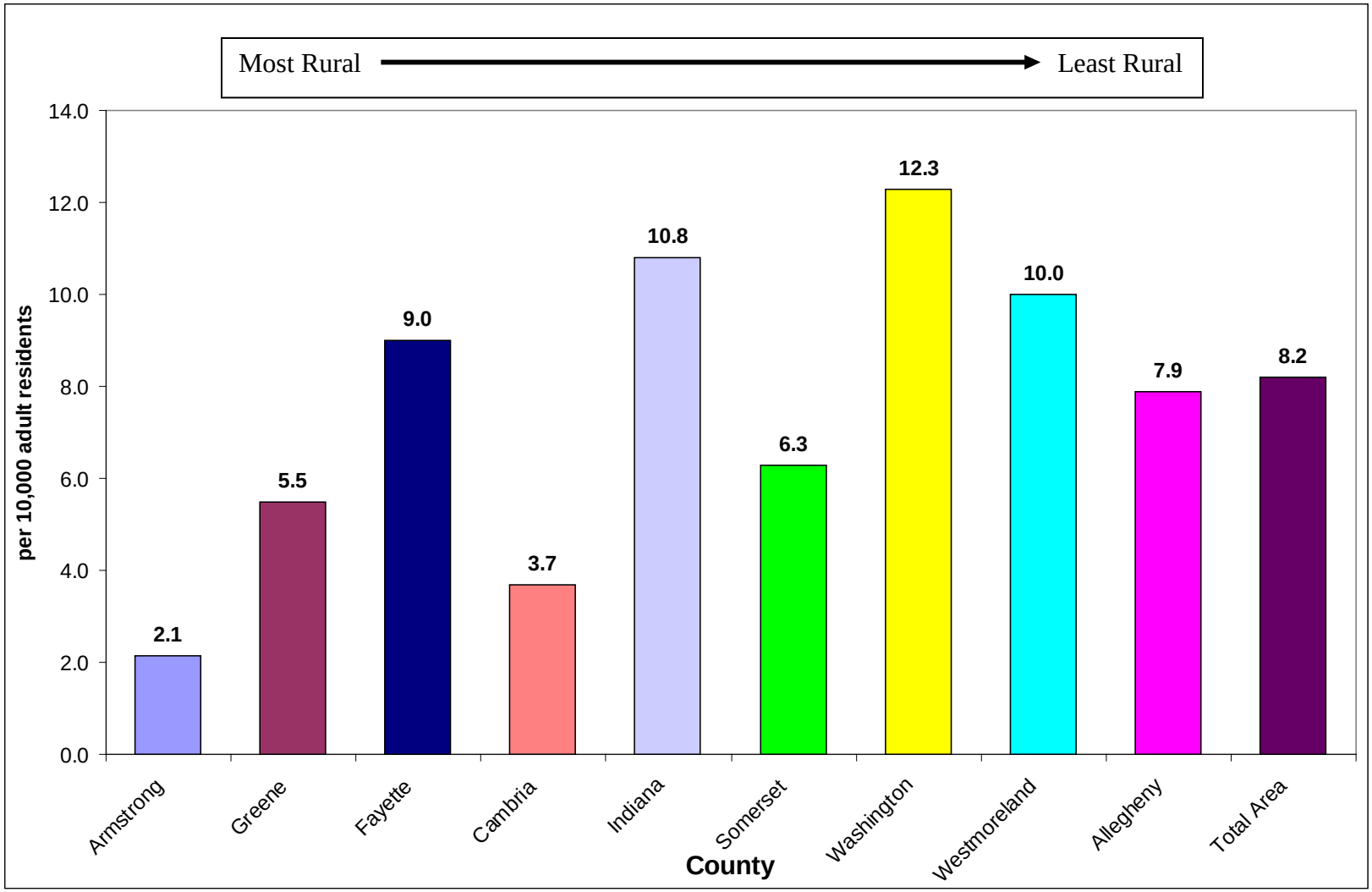


Figure 8.2: Age-Adjusted Uncontrolled Diabetes Hospitalization Rates, Any-Listed Diagnosis, by County, 2007

**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes, PHC4*

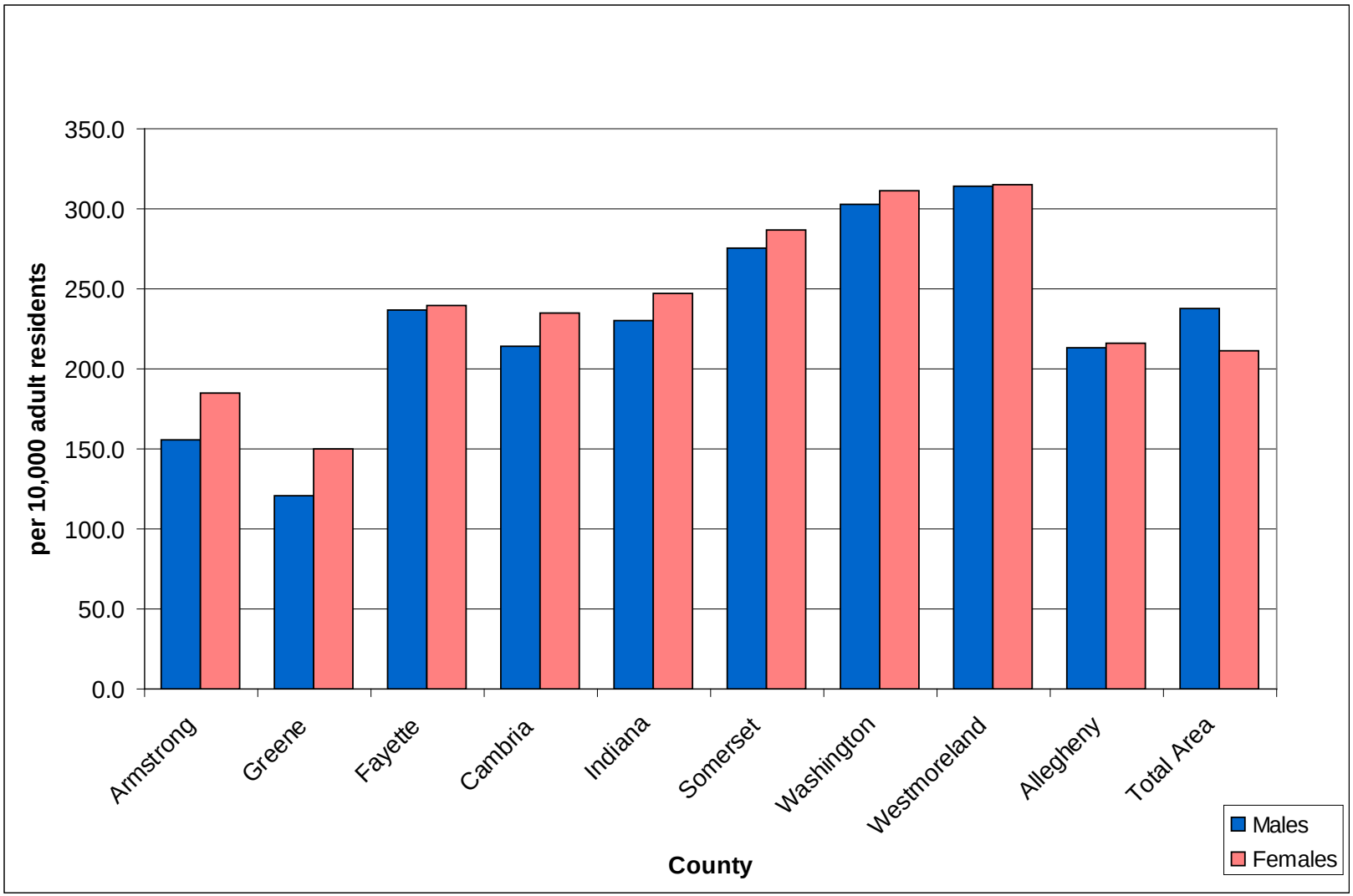


Figure 8.3: Age and Sex-Adjusted Diabetes Hospitalization Rates, Any-Listed Diagnosis, by County, 2007

**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes, PHC4*

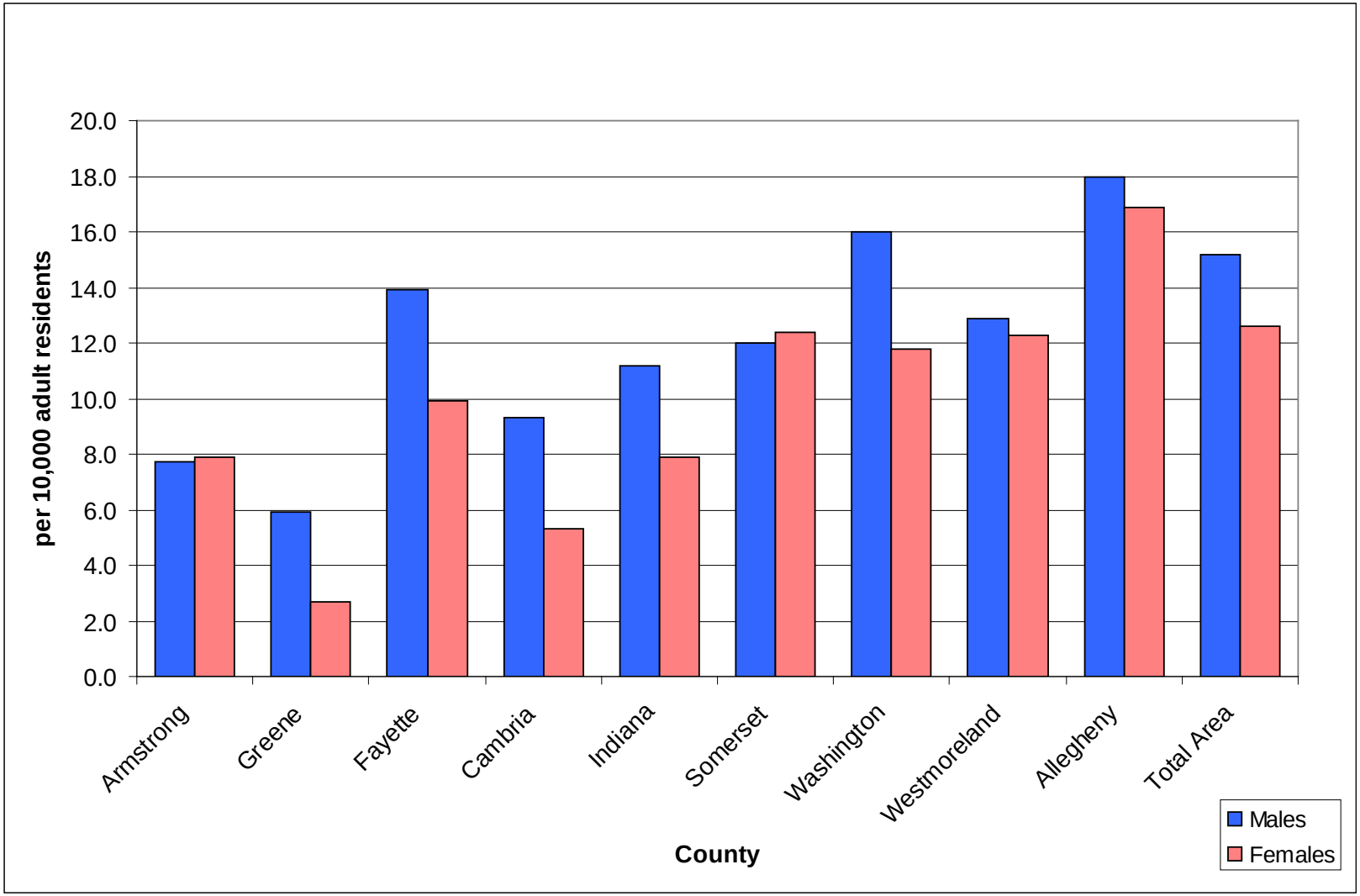


Figure 8.4: Age and Sex-Adjusted Diabetes Hospitalization Rates, Principal Diagnosis, by County, 2007

**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes, PHC4*

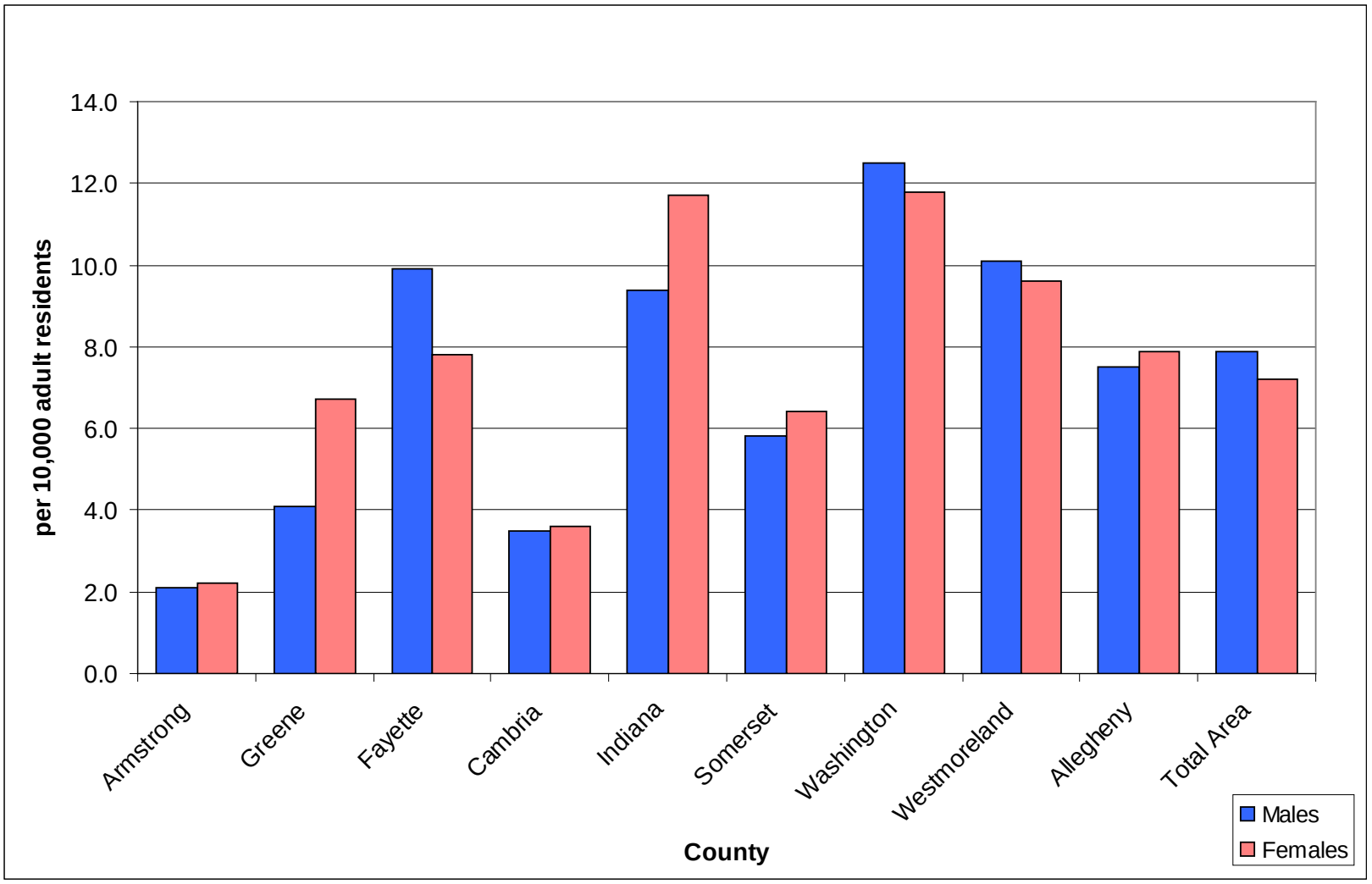


Figure 8.5: Age and Sex-Adjusted Uncontrolled Diabetes Hospitalization Rates, Any-Listed Diagnosis, by County, 2007

**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes, PHC4*

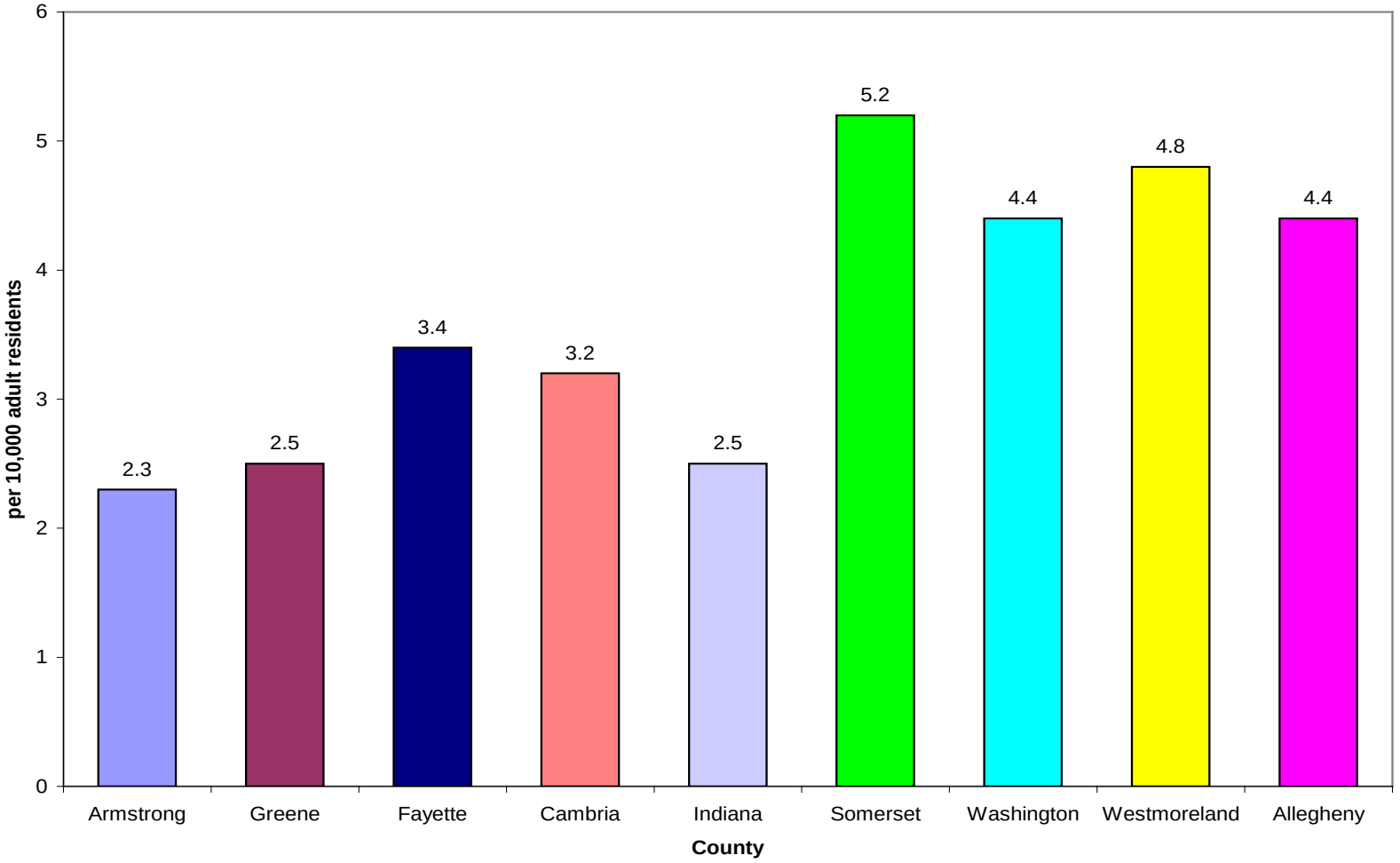


Figure 8.6: Age-Adjusted Hospitalization Rates, Short-Term Complications of Diabetes, Any-Listed Diagnosis, by County, 2007

*Short-term complications of diabetes include diabetic coma and diabetic ketoacidosis (ICD.9 250.xy; where, x = 1,2,3 and y = 0,1,2,3). Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes

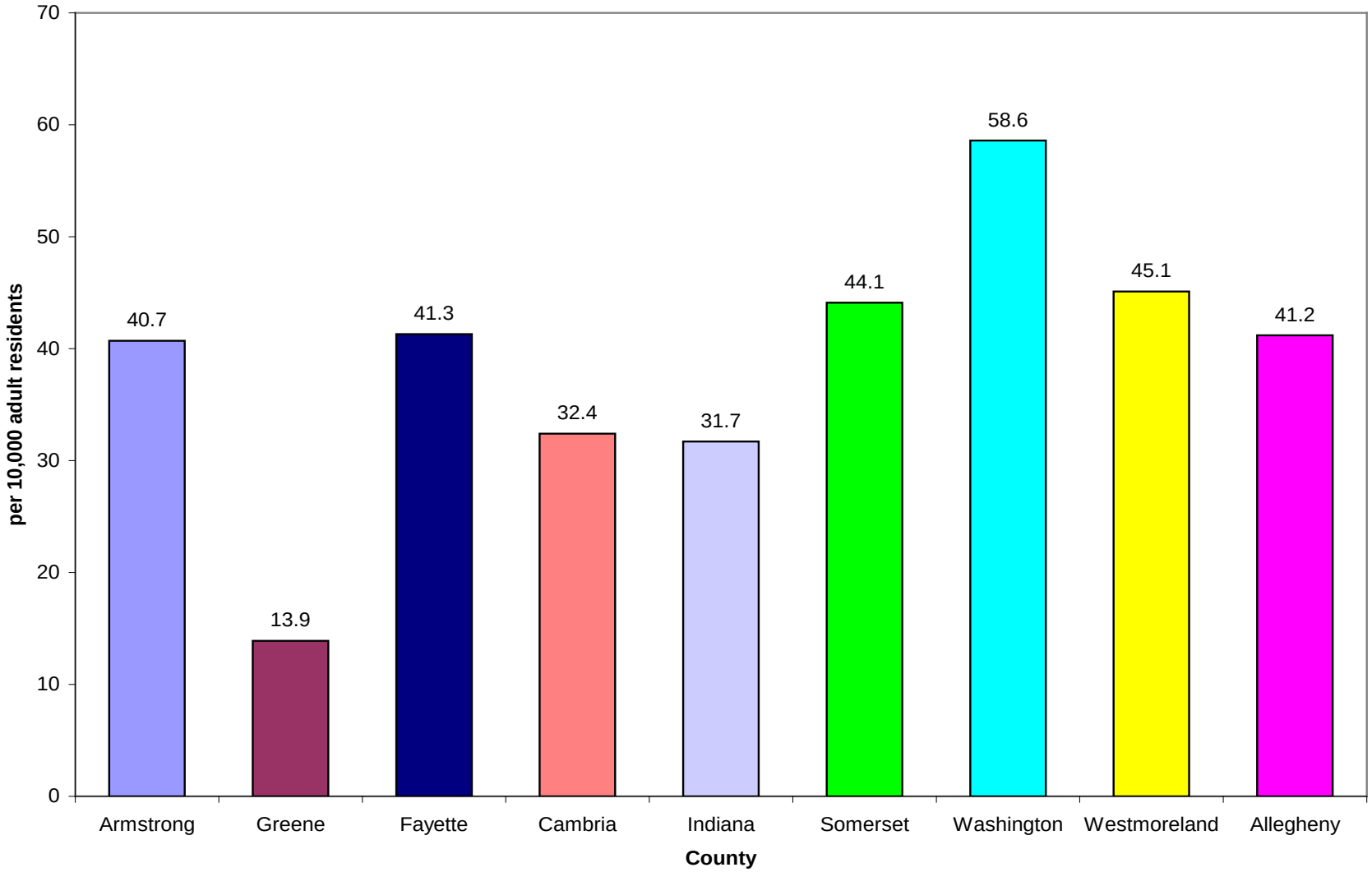


Figure 8.7: Age-Adjusted Hospitalization Rates, Long-Term Complications of Diabetes, Any-Listed Diagnosis, 2007
*Long-term complications of diabetes include chronic problems such as stroke, kidney disease, neurological complications (ICD.9 250.xy; where, x = 4,5,6,7,8,9 and y = 0,1,2,3). Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes

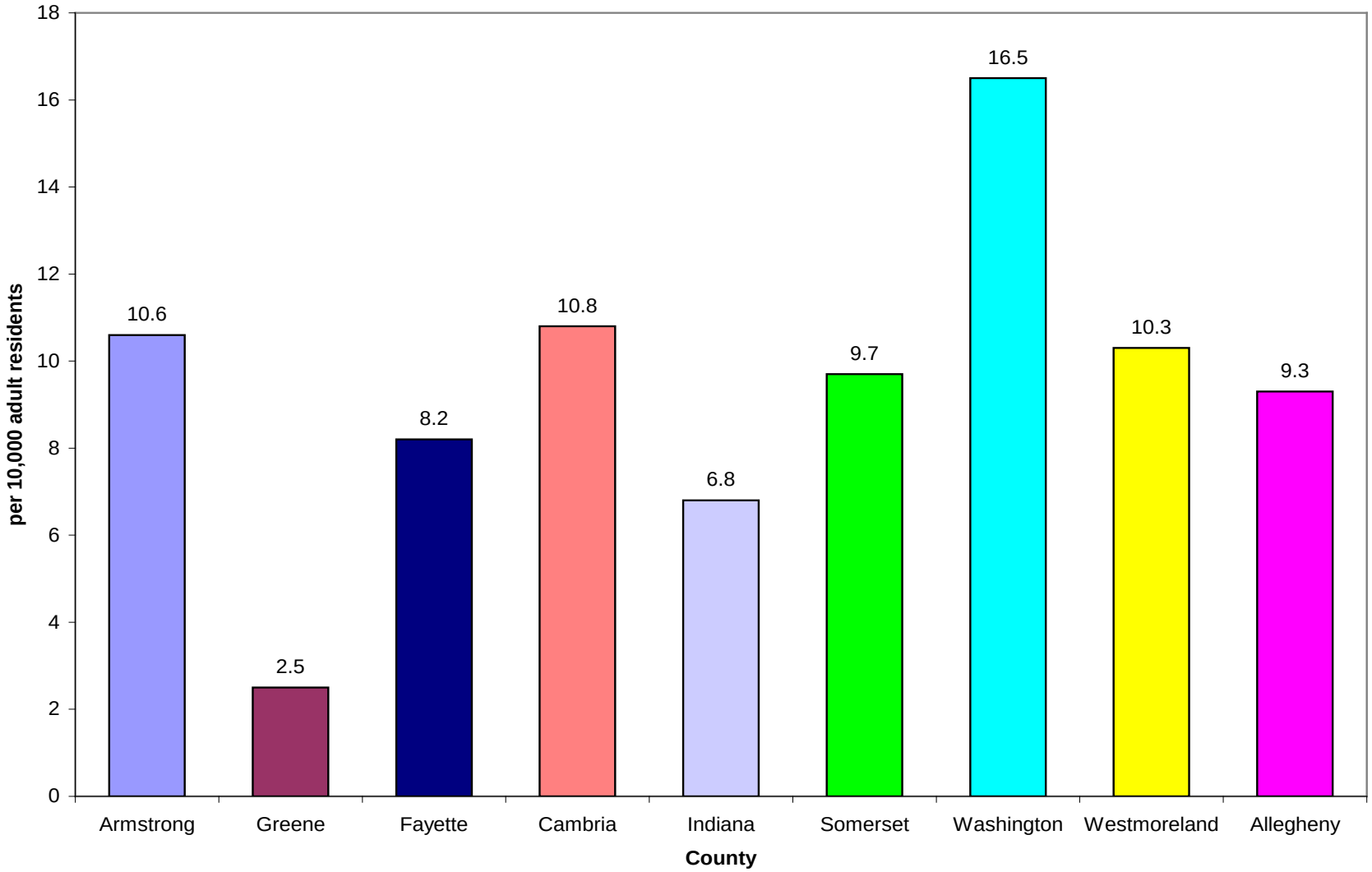


Figure 8.8: Age-Adjusted Hospitalization Rates, ESRD, Any-Listed Diagnosis, by County, 2007
**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes, PHC4*

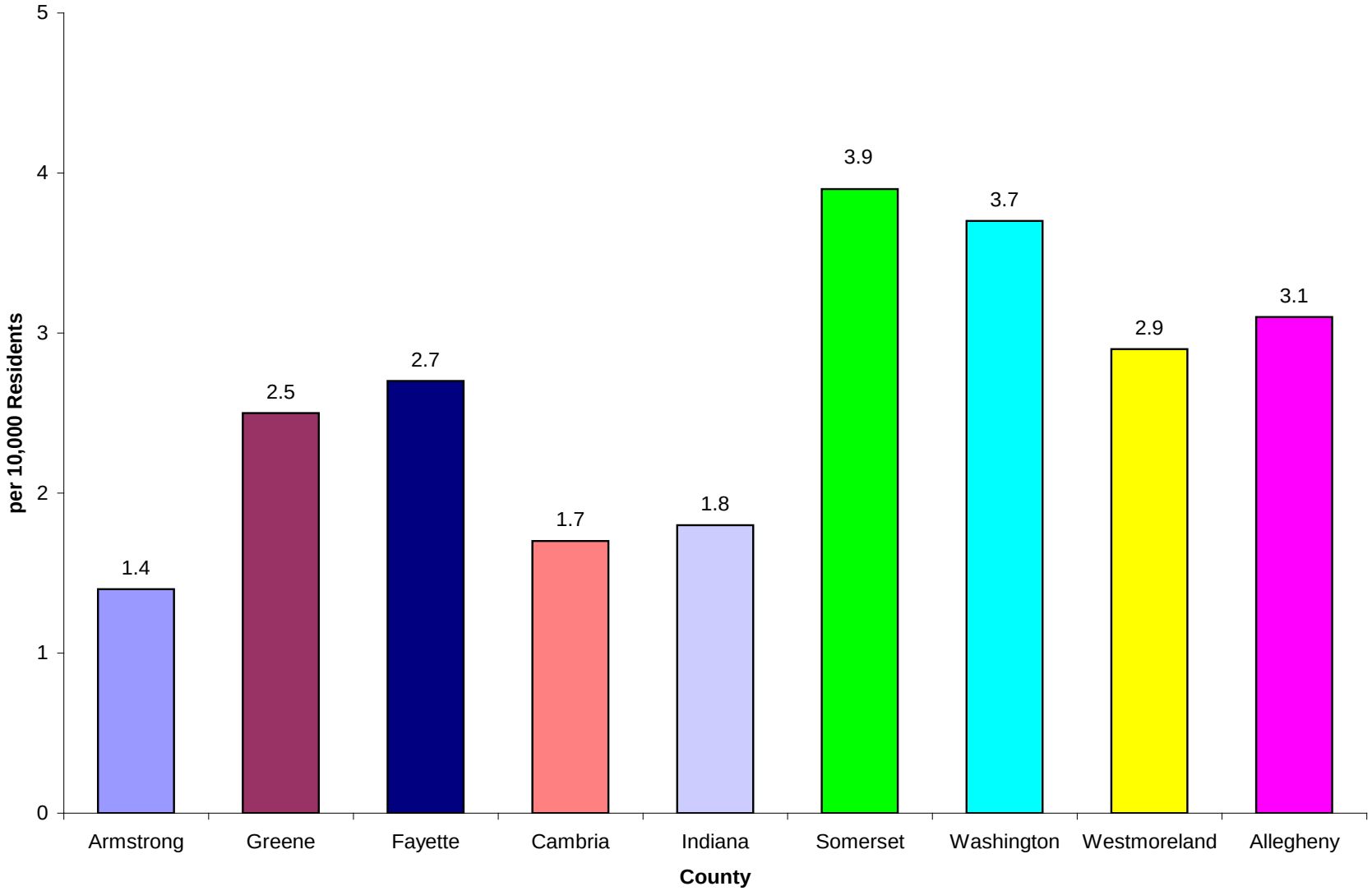


Figure 8.9: Age-Adjusted Hospitalization Rates, Short-Term Complications of Diabetes, Principal Diagnosis, 2007
*Short-term complications of diabetes include diabetic coma and diabetic ketoacidosis (ICD.9 (250.xy; where, x = 1,2,3 and y = 0,1,2,3). *Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes*

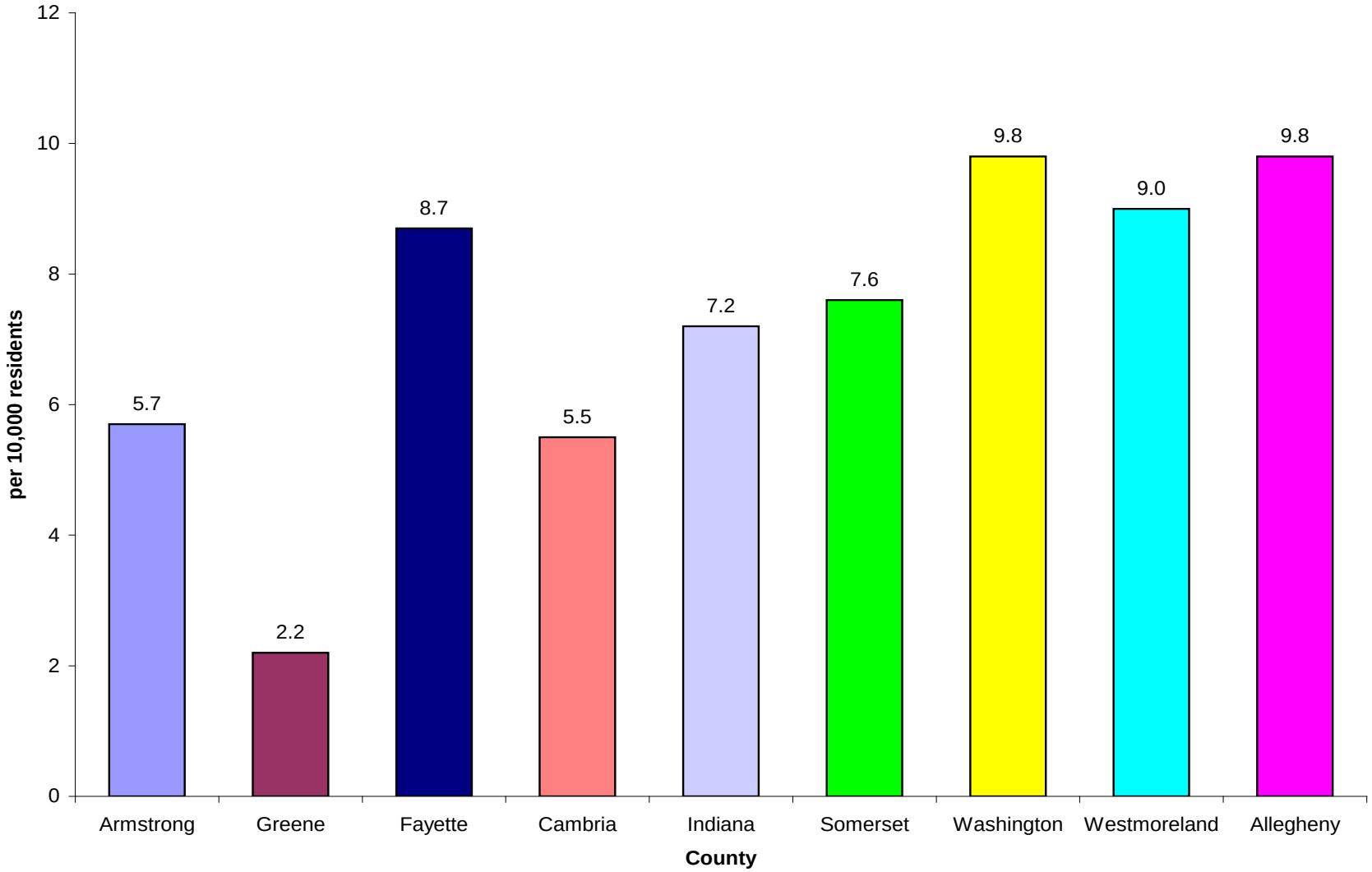


Figure 8.10: Age-Adjusted Hospitalization Rates, Long-Term Complications of Diabetes, Principal Diagnosis, 2007
*Long-term complications of diabetes include chronic problems such as stroke, kidney disease, neurological complications (ICD.9 250.xy; where, x = 4,5,6,7,8,9 and y = 0,1,2,3). *Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes*

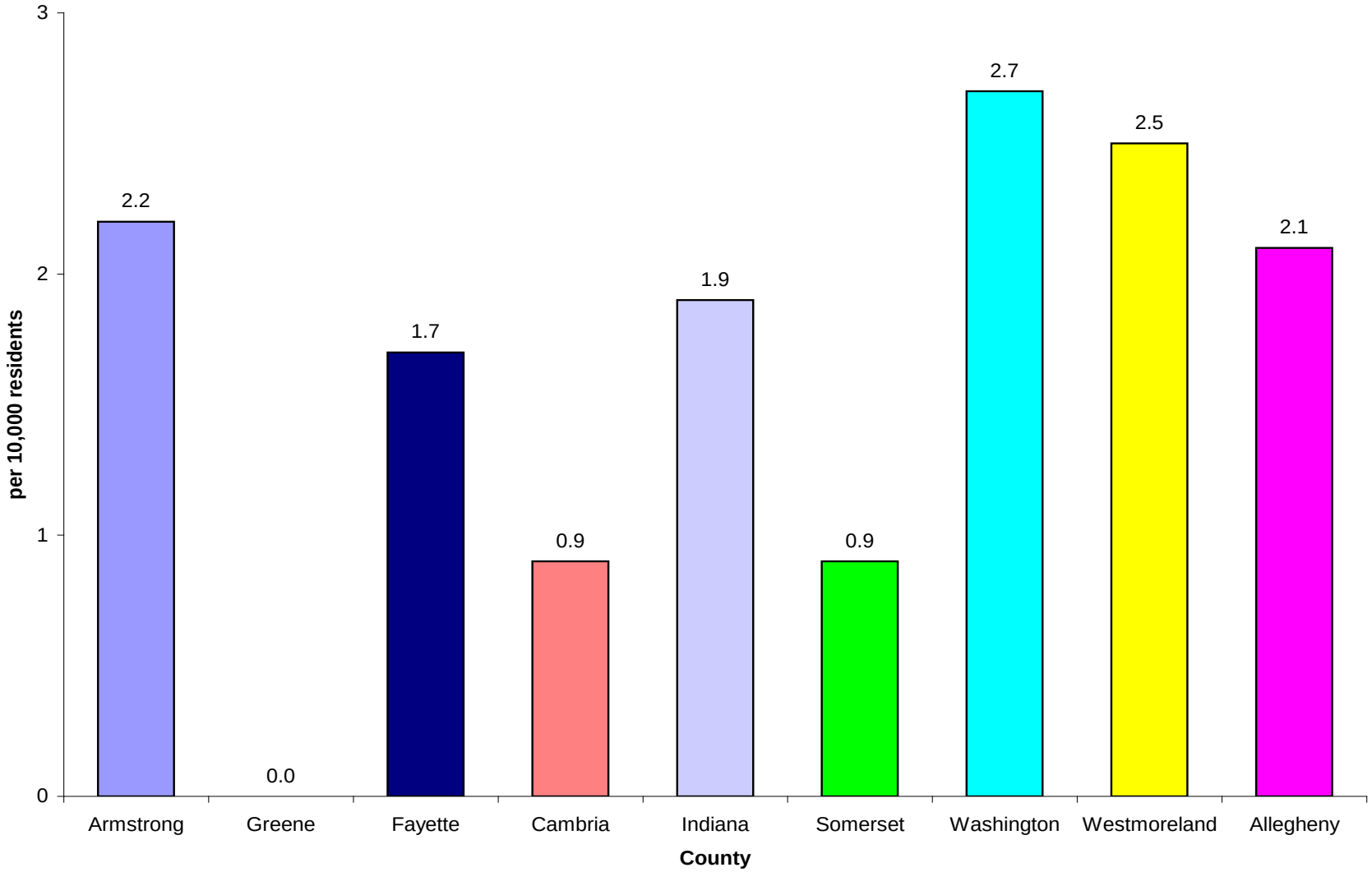


Figure 8.11: Adjusted Hospitalization Rates, ESRD, Any-Listed Diagnosis, by County, 2007
**Rates are based on individual-level hospitalization data among those who were hospitalized for diabetes, PHC4*

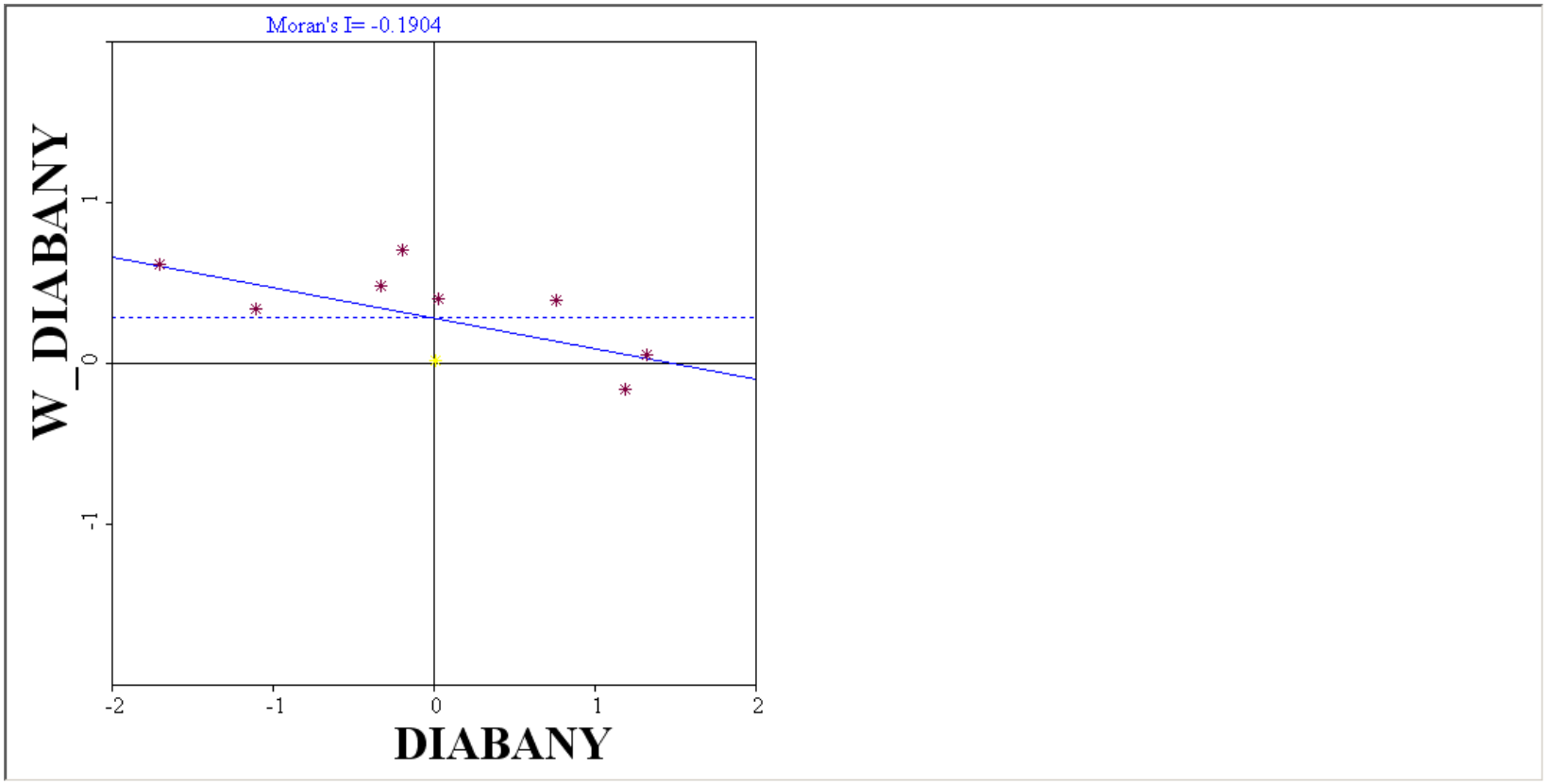


Figure 8.12: Moran's I Spatial Autocorrelation, Hospitalization Rates for Diabetes, Any-Listed Diagnosis

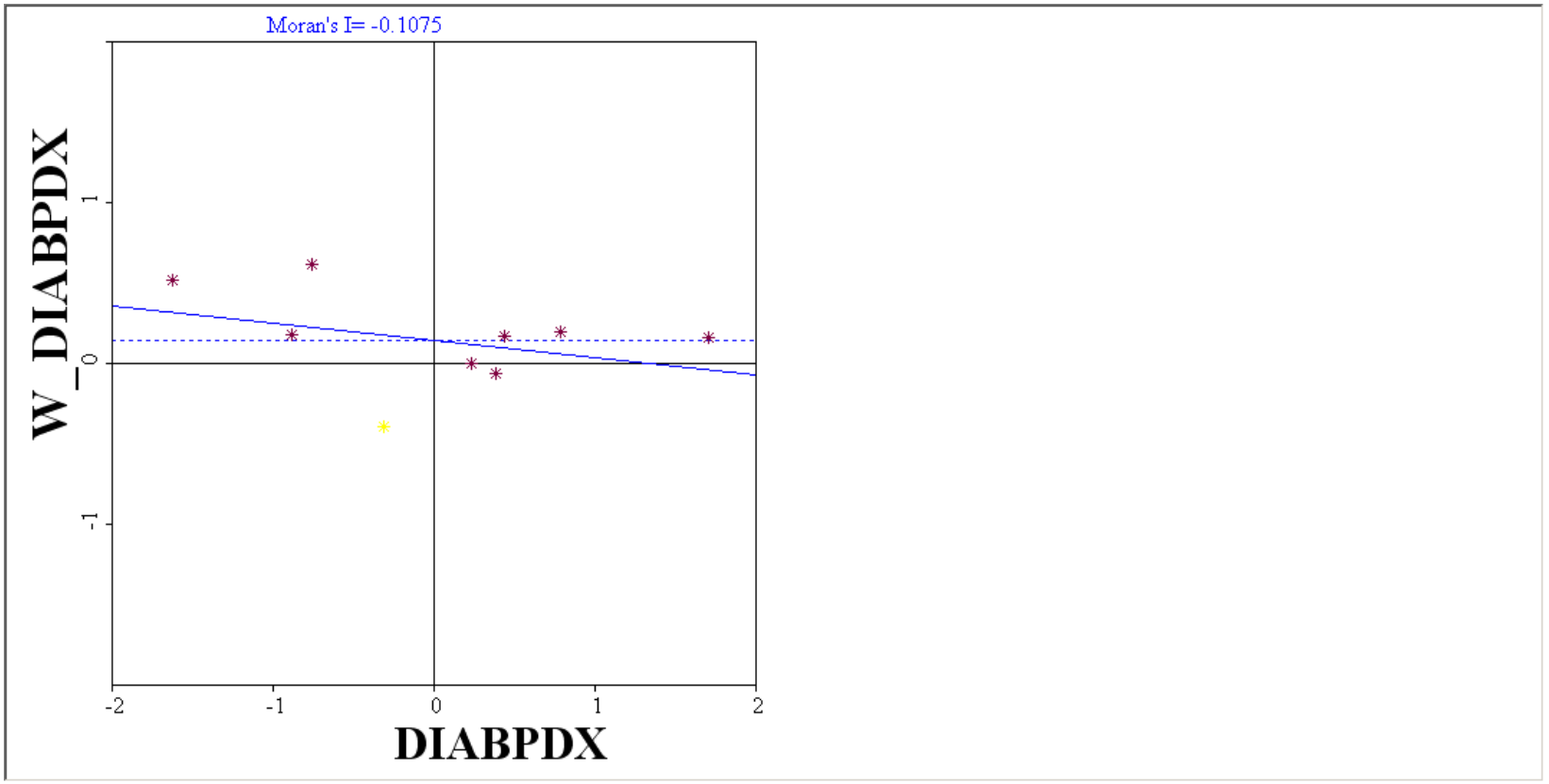


Figure 8.13: Moran's I Spatial Autocorrelation, Hospitalization Rates for Diabetes, Principal Diagnosis

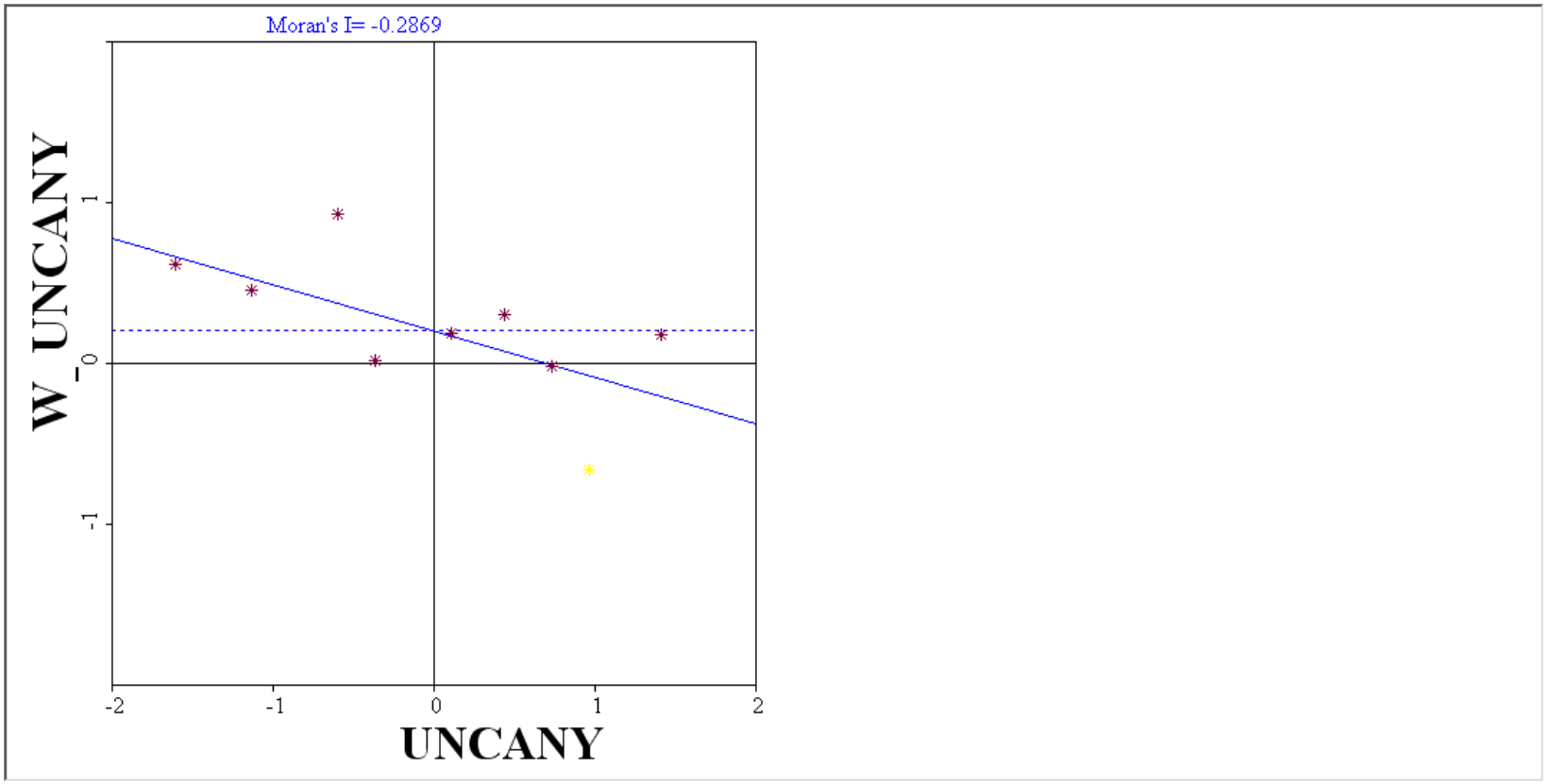


Figure 8.14: Moran's I Spatial Autocorrelation, Hospitalization Rates for Uncontrolled Diabetes

Figure 8.15: Age-Adjusted Hospitalization Rates for Uncontrolled Diabetes, per 10,000 Adult Residents by County, 2007

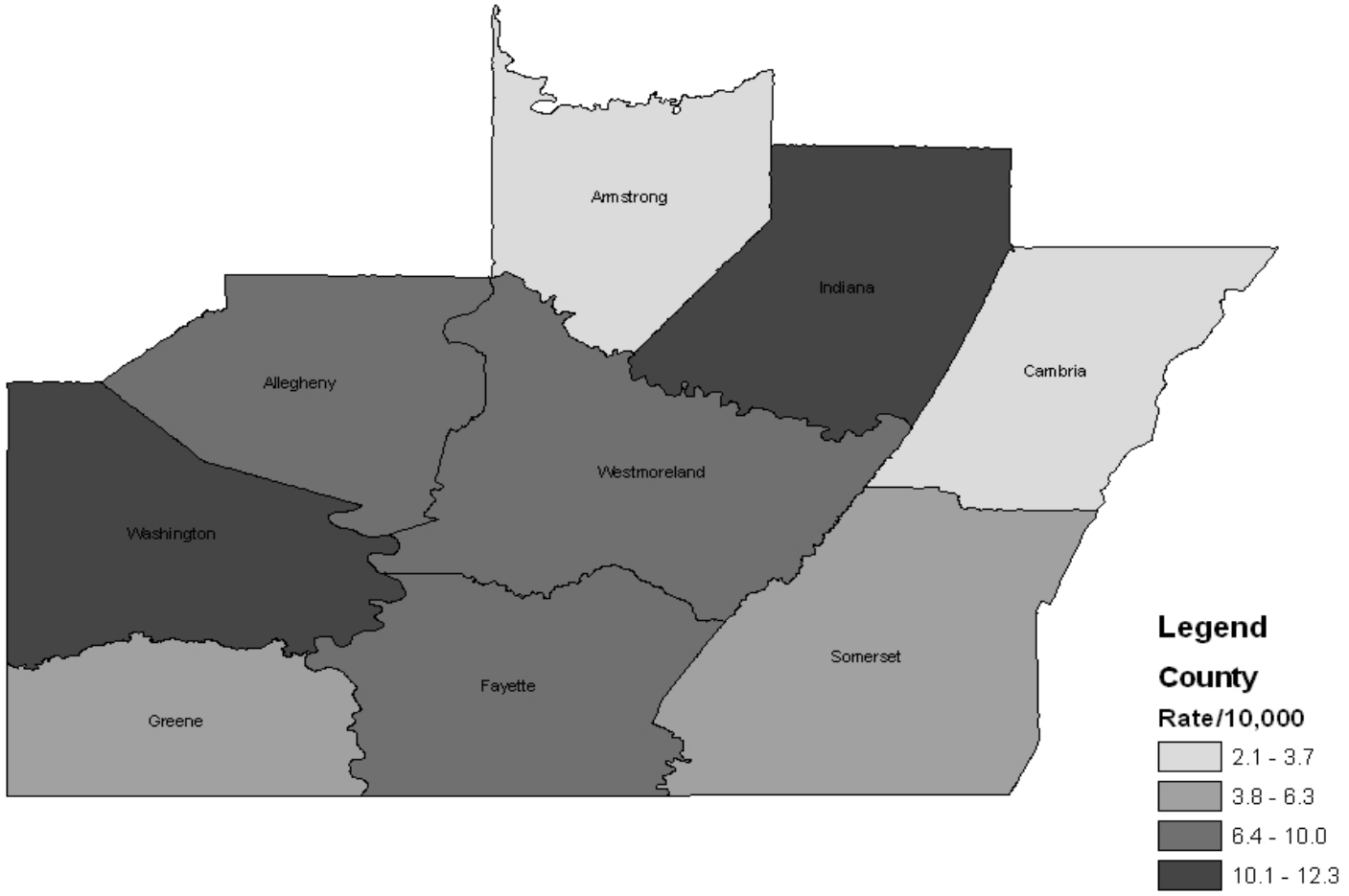


Figure 8.16: Age-Adjusted Hospitalization Rates for Diabetes as Principal Diagnosis, per 10,000 Adult Residents, by County, 2007

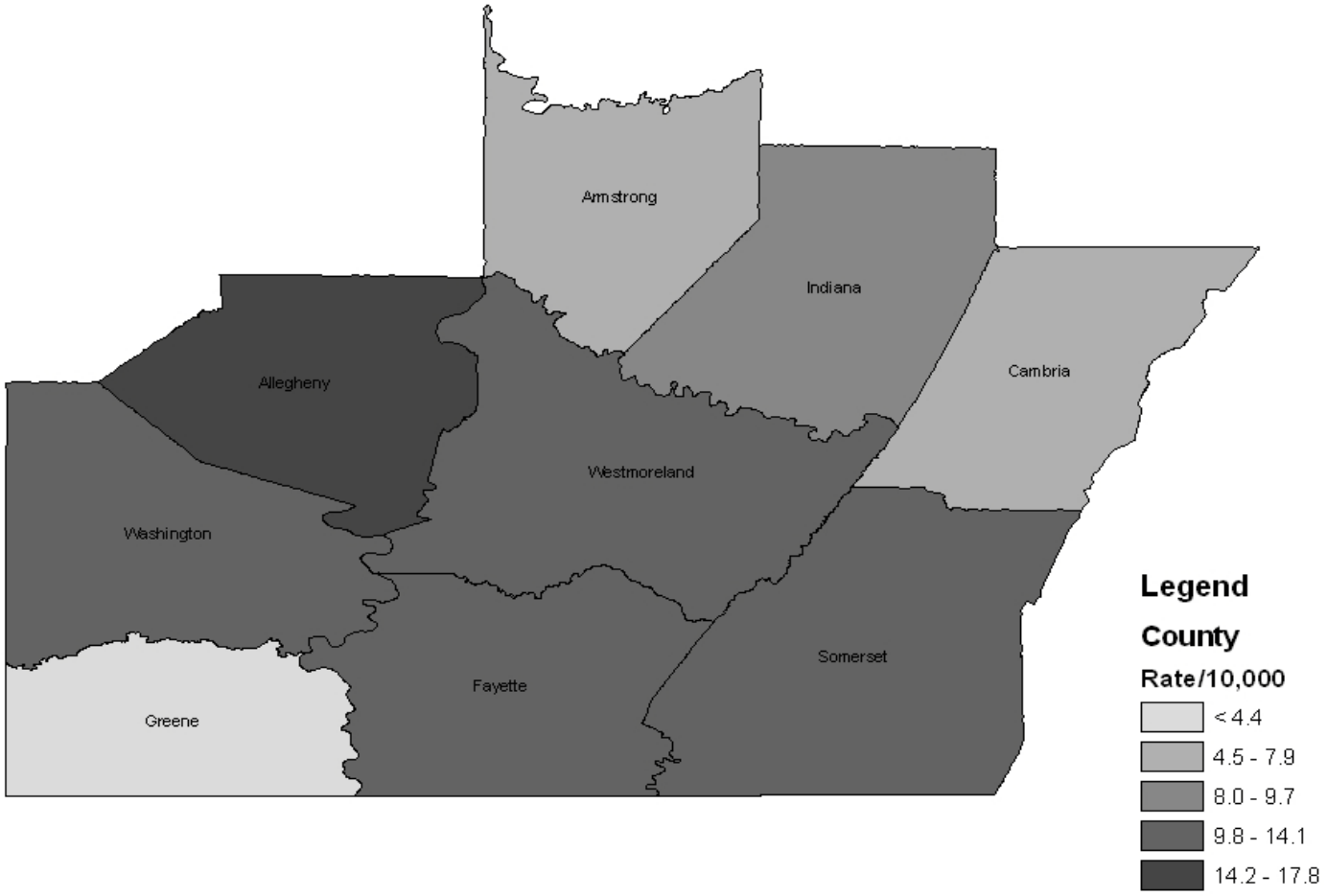


Figure 8.17: Age-Adjusted Hospitalization Rates for Diabetes as Any-Listed Diagnosis, per 10,000 Adult Residents, by County, 2007

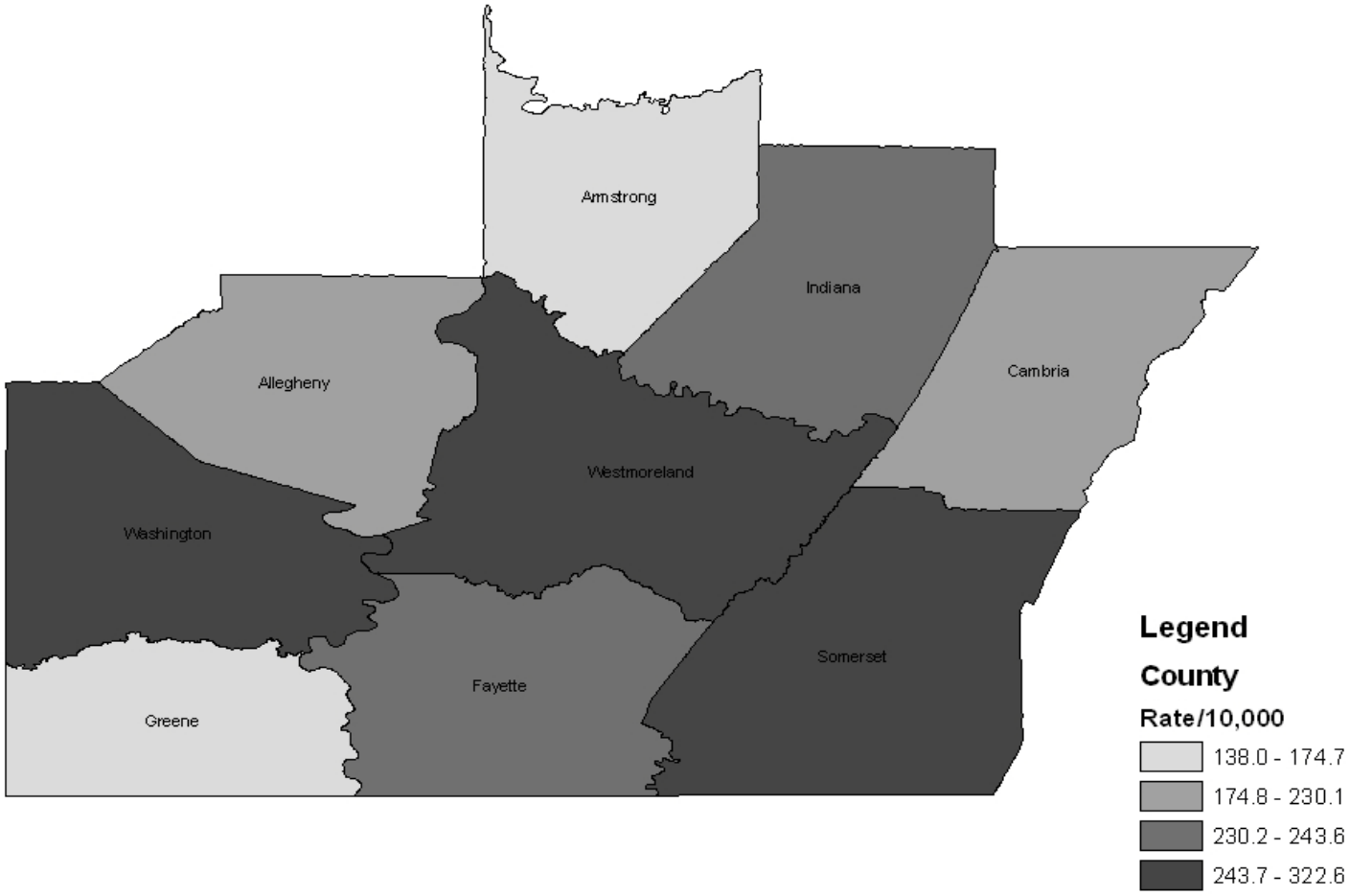


Figure 8.18: Percent of Residents Living Below the Poverty Level, by County, 2007

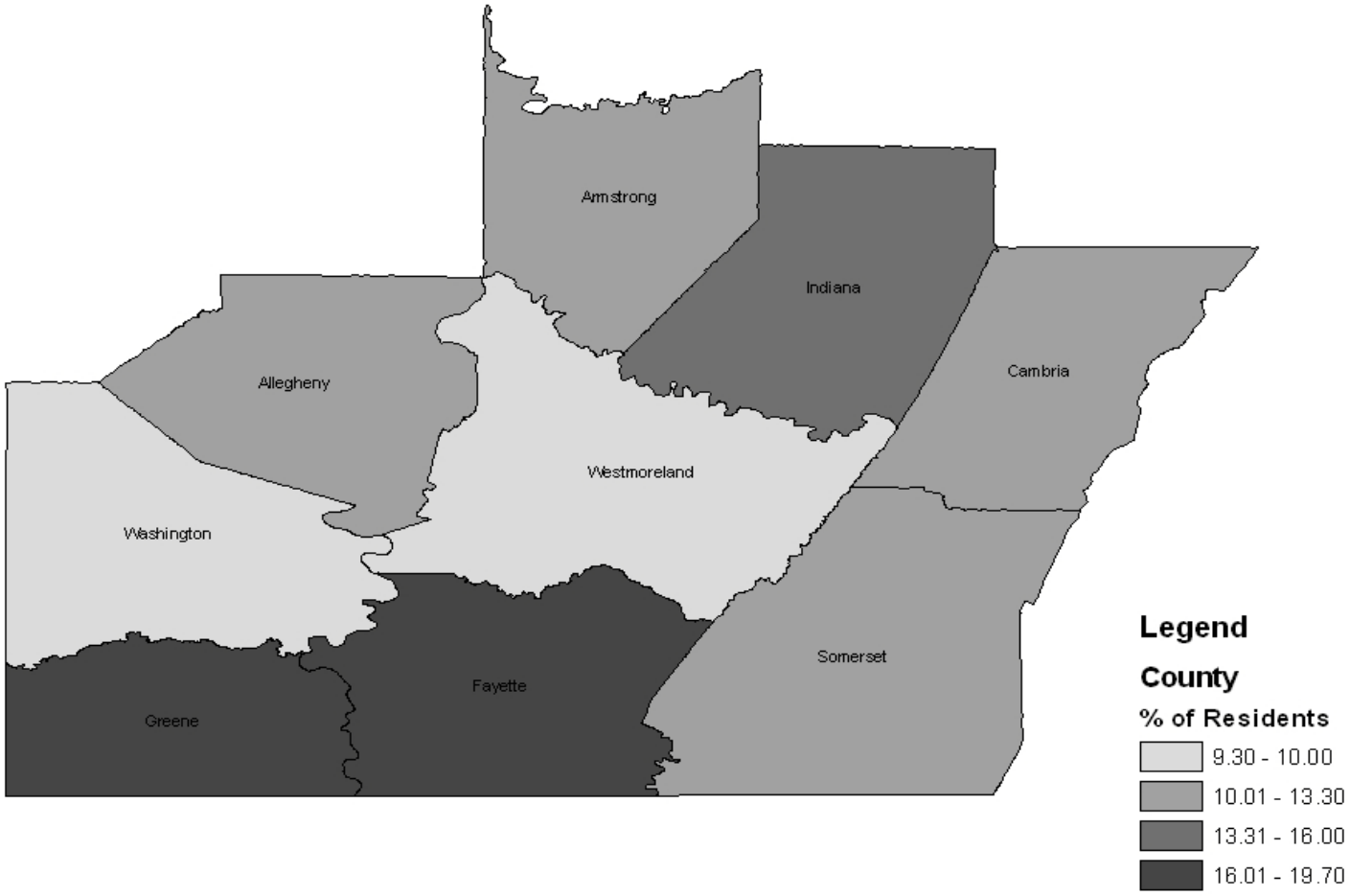


Figure 8.19: Percent of Black Residents
Hospitalized for Diabetes, PHC4, by County, 2007

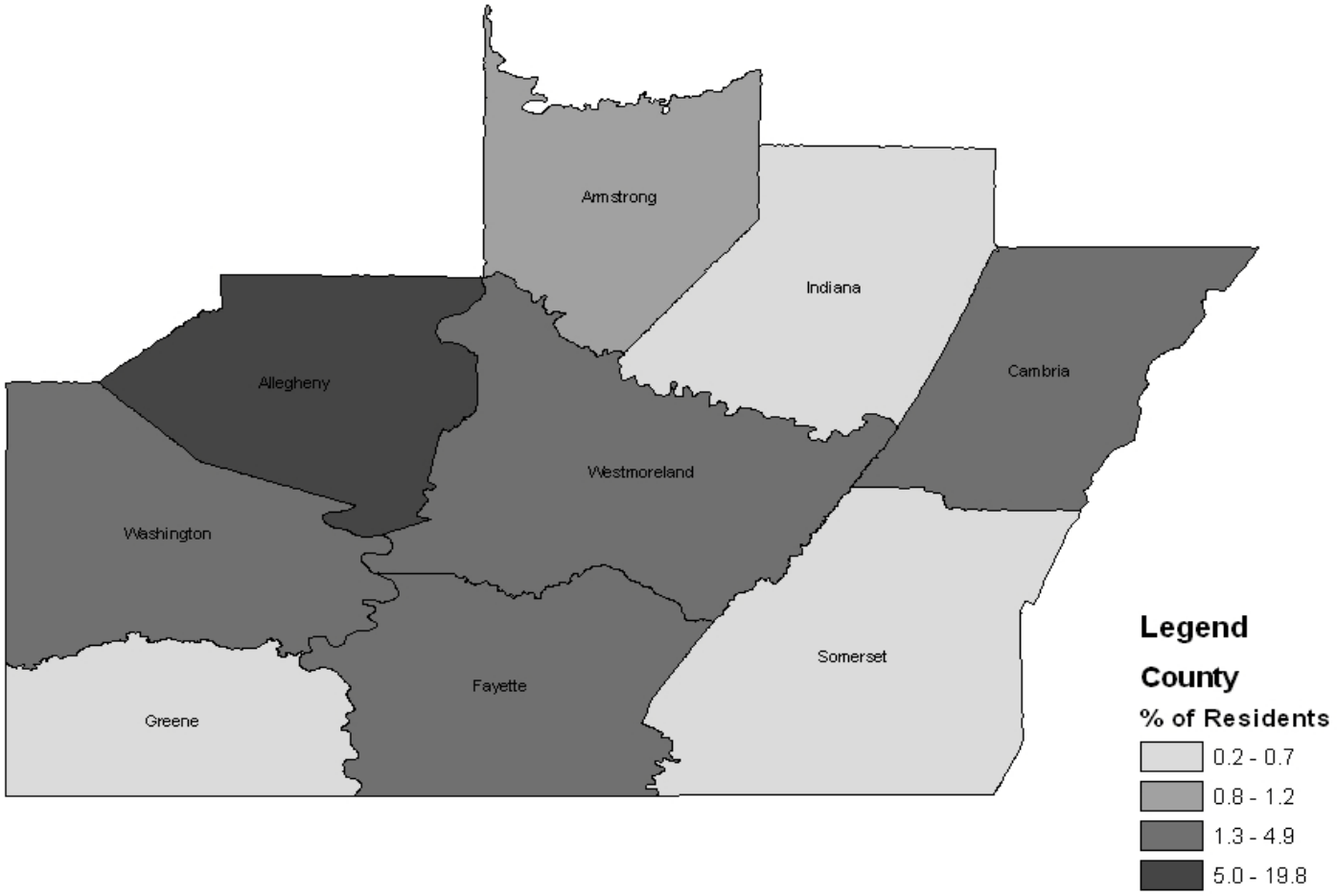
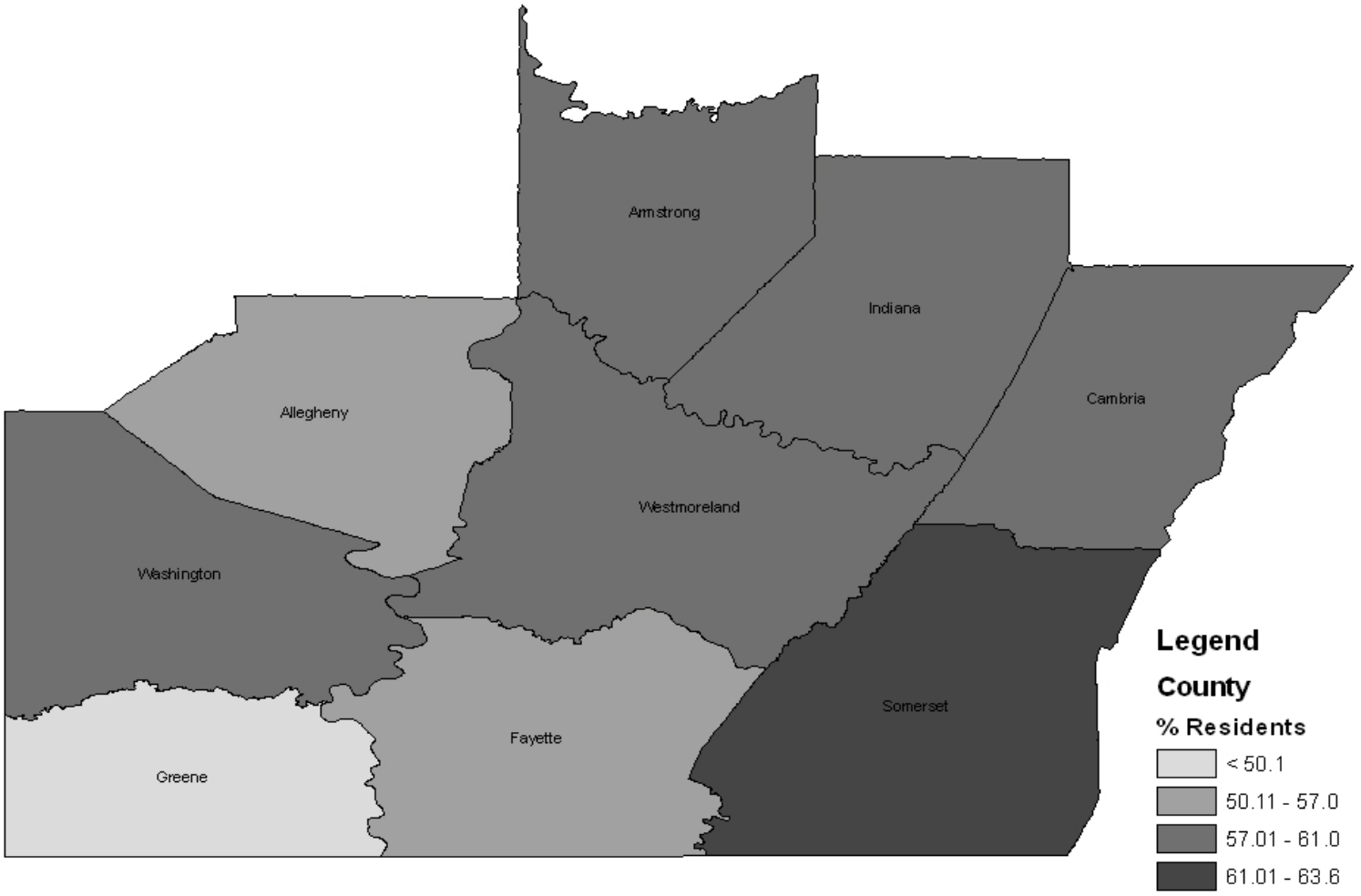


Figure 8.20: Percent of Residents over 65 Years of Age Hospitalized for Diabetes, PHC4, by County, 2007



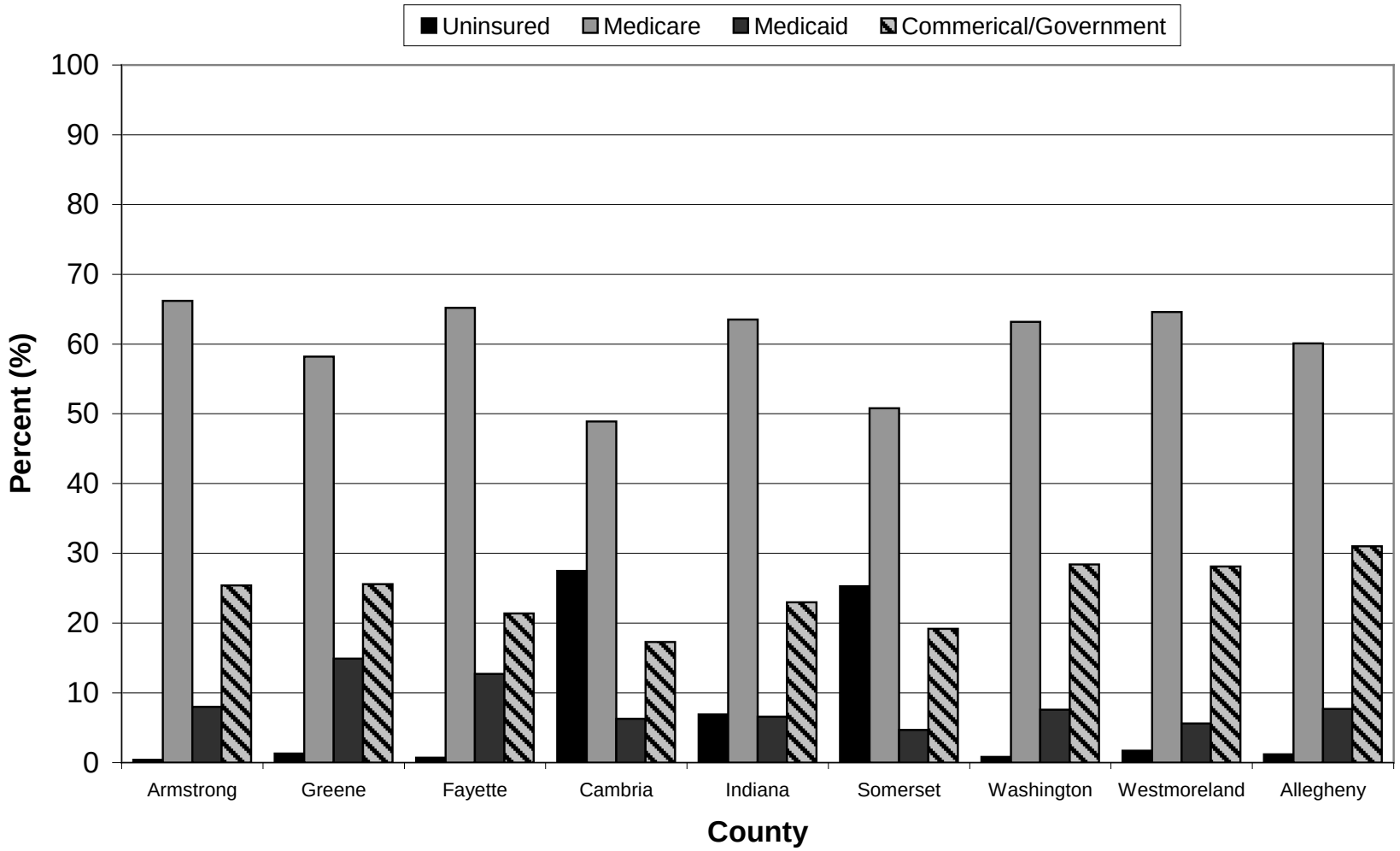


Figure 8.21: Proportion of Diabetes Hospitalizations by Insurance Type, 2007

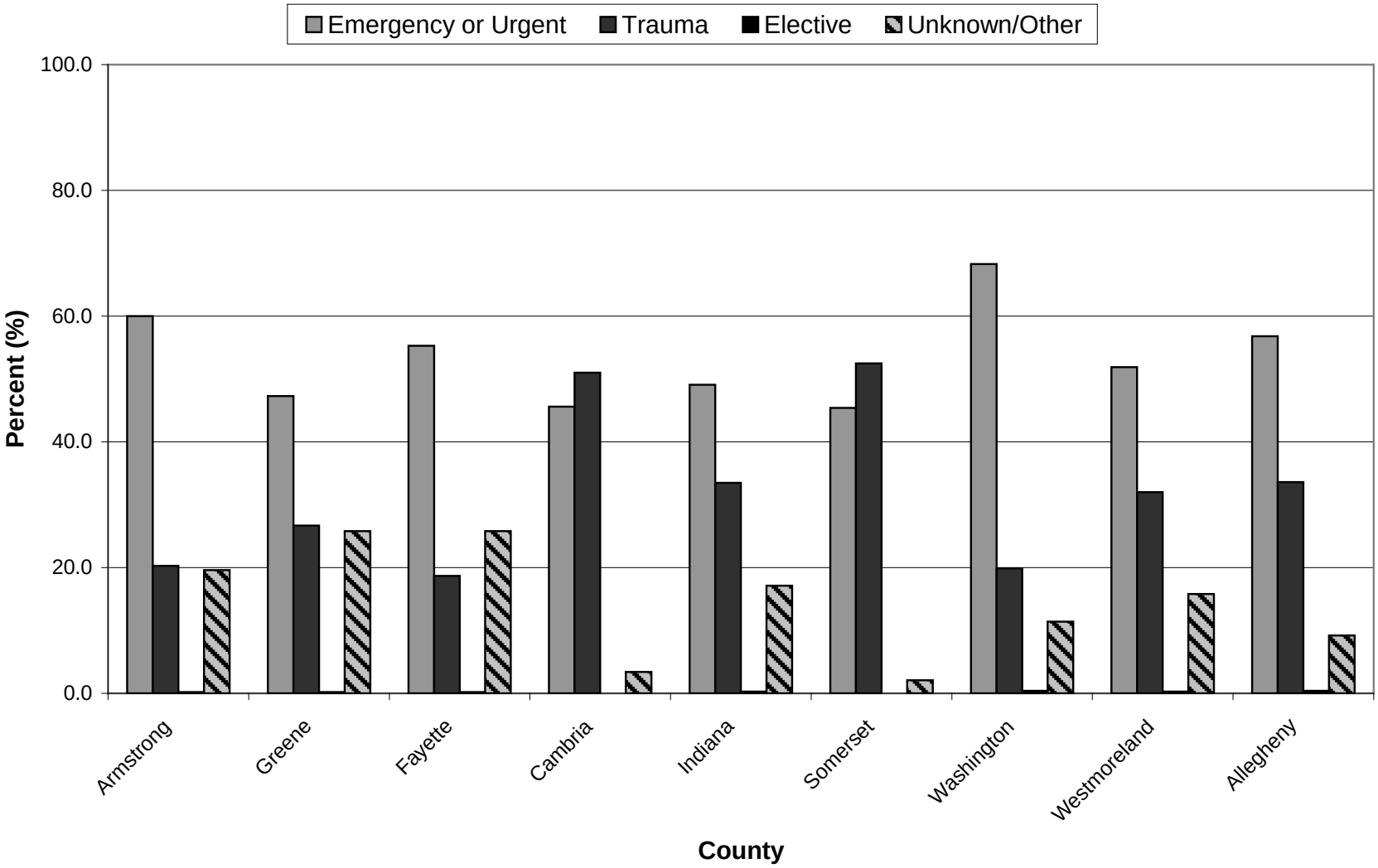


Figure 8.22: Proportion of Diabetes Hospitalizations by Admission Type, 2007

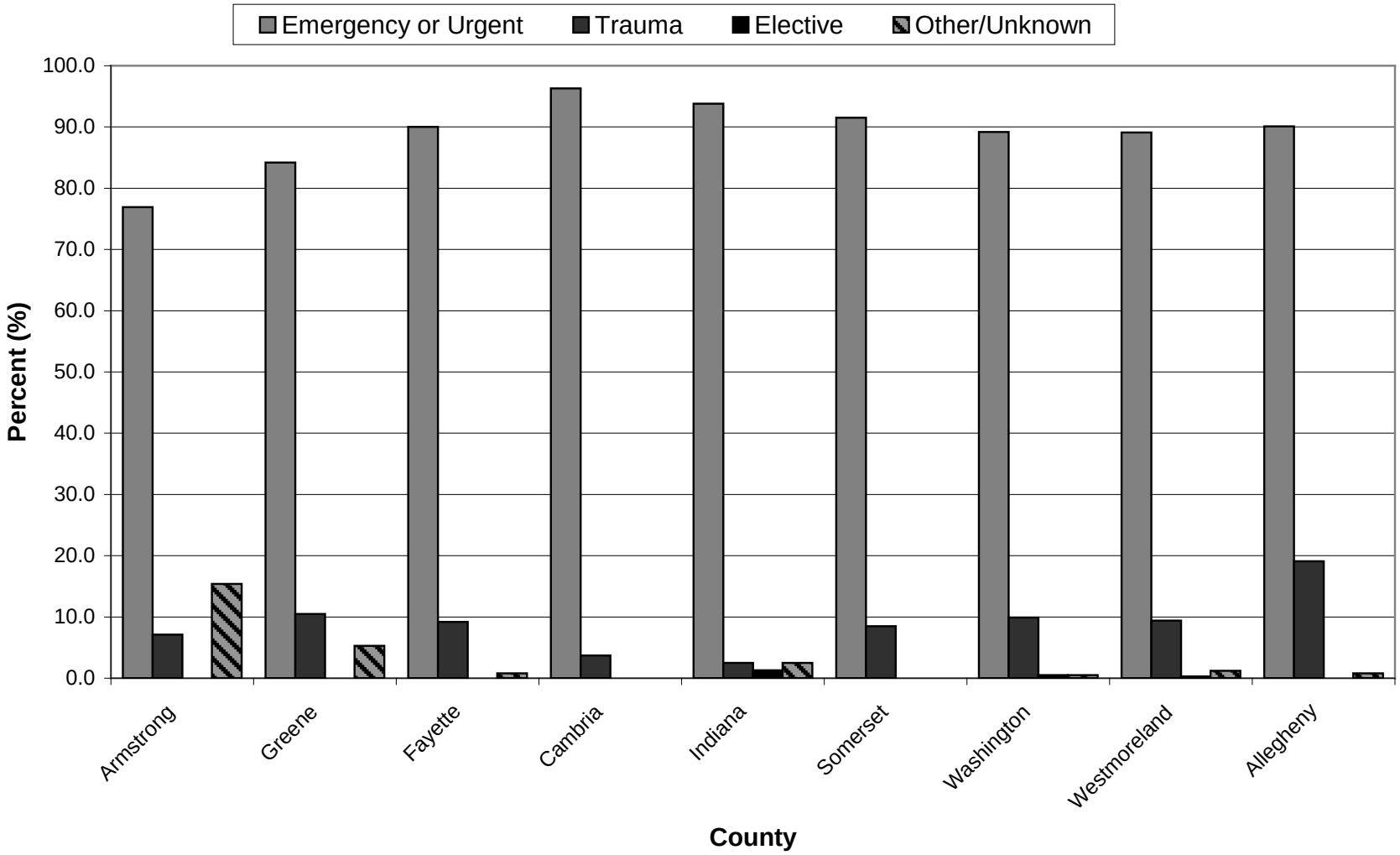


Figure 18.23: Proportion of Uncontrolled Diabetes Hospitalizations by Admissions Type, 2007

APPENDIX B: TABLES

Table 9.6: Delphi Data Management System Data File Variable Descriptions
Patient Demographics

Patient ID
Gender: (Male or Female)
Ethnicity: (White, Black, Hispanic, Native American, Asian or Pacific Islander, Arabic, Other)
Type of Diabetes: (Type 1, Type 2, Gestational, Pre-Diabetes)
Year of Diabetes Diagnosis
Health Insurance (Yes/No)
Health Plan ID/Health Plan Name
Date of Birth
First Visit Date (Initiation of Care)
Date of Death
Street Address, including zip code
Employment Status: (Working full-time, Working part-time, Unemployed and looking for work, Unemployed and not looking for work, Homemaker, In school, Retired, Disabled, Not able to work, Other)

Clinical Lab Information and Standards of Care

HbAlc: (Date and Values)
Lipid Profile: (Date and Total Cholesterol, Triglycerides, LDL, HDL values)
Urinalysis: For proteinuria/microalbuminuria; (Date and Values)
Serum Creatinine: (Date and Values)
Blood Pressure: Systolic and Diastolic (Date and Values)
Body Mass Index
Weight
Height
Co-morbid Conditions: (Patient reported - Coronary Heart Disease, Congestive Heart Failure, Cerebrovascular Disease, Depression)
Complications: (Patient reported – Coronary Artery Disease, TIA, Peripheral Vascular Disease, Retinopathy, Neuropathy, Nephropathy, Gastroparesis, Erectile Dysfunction, Other)
Medications: (Patient reported- Insulin; Oral Diabetes Medications; Other Medications)
Smoking Status: (Non-smoker, Ex-smoker (Quit Date), Current smoker)

Exams in the Previous Year

Dilated Eye Exam: (Yes/No)
Foot Exam: (Yes/No)
Flu Vaccine: (Yes/No)
Pneumonia Vaccine: (Yes/No)

Table 9.7 North America Industry Classification System (NAICS) codes[8]

Industry Group	1997 NAICS definitions	NAICS Index
Supermarkets	445110 Supermarkets	445110 Supermarkets
Grocery stores	445110 Other grocery (excluding convenience) stores	44511013 Grocery Stores 44511014 Food stores
Convenience stores	445120 Convenience Stores	445120 Convenience Stores
Convenience stores with gas stations	447110 Gasoline stations with convenience stores	447110 Gasoline stations with convenience stores
Full-service restaurants	722110 Full-service restaurants	722110 Restaurants, full-service 722110 Steak houses 722110 Pizzerias, full-service 722110 Fine dining 722110 Family restaurants 722110 Diners, full-service 722212 Cafeterias
Fast-food restaurants Carryout eating places	722211 Limited-service restaurants	722211 Fast-food restaurants 722211 Pizza parlor, limited service 722211 Pizza delivery shops 722211 Sandwich shops 722110 Bagel shops, full-service
Carryout specialty places	722213 Snack and nonalcoholic beverage bars	722213 Beverage bars 722213 Doughnuts shops 722213 Ice cream shops 722213 Pretzel shops
Health care and Social Assistance	621111 Offices of Physicians	621111 Offices of Physicians (except mental health specialists) 621320 Offices of Optometrists 621391 Offices of Podiatrists
	62 Other Health care	621492 Kidney Dialysis Centers
Retail Trade	4461 Pharmacies and Other	446110 Pharmacies and Drug Stores 446199 All Other Health And Personal Care Stores 446191 Food (Health) Supplement Stores

APPENDIX C: DATA USE AGREEMENT AND DISCLAIMER

This research was sponsored by funding from the United States Air Force administered by the U.S. Army Medical Research Acquisition Activity, Fort Detrick, Maryland, and Award Number W81XWH-04-2-003. Review of material does not imply Department of the Air Force endorsement of factual accuracy or opinion.

The Pennsylvania Health Care Cost Containment Council (PHC4) is an independent state agency responsible for addressing the problem of escalating health costs, ensuring the quality of health care, and increasing access to health care for all citizens regardless of ability to pay. PHC4 has provided data to this entity in an effort to further PHC4's mission of educating the public and containing health care costs in Pennsylvania. PHC4, its agents, and staff, have made no representation, guarantee, or warranty, express or implied, that the data -- financial, patient, payor, and physician specific information -- provided to this entity, are error-free, or that the use of the data will avoid differences of opinion or interpretation. This analysis was not prepared by PHC4. This analysis was done by Laura Bettencourt, MPH. PHC4, its agents and staff, bear no responsibility or liability for the results of the analysis, which are solely the opinion of this entity.

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