Geographic Disparities and Temporal Patterns of Diabetes-Related Deaths in Florida

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DEDICATION

This dissertation is dedicated to my loving parents for their unconditional love and constant support so that I could pursue my dream; to my elder brother and sisters who guided me in making all the important decisions of my life.

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ABSTRACT

Diabetes-related mortality is an important public health concern in Florida. However, little is known about geographic disparities, predictors, temporal trends, and future burden of diabetes-related mortality risks (DRMR), and yet this information is important for health planning and disease control efforts. Therefore, the objectives of this study were to identify: (a) geographic disparities and temporal changes; (b) county-level socioeconomic and demographic predictors; and (c) temporal patterns and future DRMR in Florida. This information is useful for guiding resource allocation aimed at reducing burden and health disparities associated with diabetes.

Retrospective mortality data from 1999 to 2023 were obtained from the Florida Department of Health and the Centers for Disease Control and Prevention WONDER database. The 10th International Classification of Disease codes E10-E14 were used to identify diabetes-related deaths which were aggregated to the county-level. County-level DRMRs were then computed and presented as number of deaths per 100,000 persons. Significant high-risk spatial clusters of DRMR were identified using Tango's flexible spatial scan statistics and their geographic distribution displayed in choropleth maps. Ordinary least squares regression model was used to identify county-level predictors of DRMR. Time series analysis and forecasting of DRMR were performed using Seasonal Autoregressive Integrated Moving Average with Exogenous variable (SARIMAX) and Neural Network Autoregressive model with Exogenous variable (NNARX) time series models.

County-level DRMR varied by geographic location, ranging from 12.6 to 81.1 deaths per 100,000 persons. High DRMR clusters were identified in the northern and central counties of Florida. Counties with high percentages of population that were: 65 years and older ($p<0.001$), current smokers ($p=0.032$), population with diabetes ($p<0.001$), households without vehicles ($p=0.022$), and insufficiently physically active ($p=0.036$) tended to have high risks of DRMR. There were seasonal patterns of DRMR in Florida with the highest mortality risks recorded during the winter months. The DRMR forecast indicated a gradual increase for the next four years.

The study identified geographic disparities, predictors, seasonal patterns, and increasing temporal trends of DRMR in Florida. The findings are useful in guiding health planning and future intervention programs to reduce DRMR burden and disparities in Florida.

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LIST OF ABBREVIATIONS

ACS: American Community Survey

ADA: American Diabetes Association

AIC: Akaike Information Criterion

BMI: Body Mass Index

BRFSS: Behavioral Risk Factor Surveillance System

CDC: Centers for Disease Control and Prevention

CHHR: County Health Rankings and Roadmap

CI: Confidence Interval

COVID 19: Corona Virus Disease 2019

DFITS: Difference in Fits

DM: Diabetes Mellitus

DRMR: Diabetes-Related Mortality Risk

DSME: Diabetes Self-management Education

FDOH: Florida Department of Health

FPG: Fasting Plasma Glucose

FSSS: Flexible Spatial Scan Statistics

GD: Gestation Diabetes

GIS: Geographic Information System

HDL: High Density Lipoprotein

HHS: Department of Health and Human Services

ICD: International Classification of Diseases

IGT: Impaired Glucose Tolerance

KW: Kruskal-Wallis

LDL: Low Density Lipoprotein

LLR: Log Likelihood Ratio

MAE: Mean Absolute Error

MAPE: Mean Absolute Percent Error

MASE: Mean Absolute Scaled Error

NIH: National Institutes of Health

NNARX: Neural Network Auto Regressive Integrated Moving Average with Exogenous Variable

GTT: Glucose Tolerance Test

OLS: Ordinary Least Square

QS: Q-statistic Test for Seasonal Autocorrelations

RMSE: Root Mean Squared Error

RR: Relative Risk

SARIMAX: Seasonal Auto Regressive Integrated Moving Average with Exogenous Variable

SE: Standard Error

SEB: Spatial Empirical Bayes Smoothing

TG: Triglyceride

TIGER: Topologically Integrated Geographic Encoding and Referencing

US: United States

VIF: Variance Inflation Factor

WHO: World Health Organization

CHAPTER 1

Introduction and Literature Review

1.1 Introduction

The prevalence of diabetes mellitus in the United States (US) has been increasing over the last two decades (Centers for Disease Control and Prevention, 2024a). The condition has a significant impact on overall public health with about 1.2 million new cases every year (American Diabetes Association, 2024a). Although the mortality rate of diabetes has decreased in the last ten years, it remains one of the leading causes of death in the US. (Centers for Disease Control and Prevention, 2024a). Data from the Centers for Disease Control and Prevention indicate that diabetes is responsible for 103,294 deaths, representing approximately 3.0% of the total annual mortality (Centers for Disease Control and Prevention, 2025a). The risk of diabetes-associated mortality is notably higher in southeastern states, including Florida, than in the other states of the country. The American Diabetes Association reports that approximately 11.6% of the adults in Florida have diabetes. The age-adjusted mortality risk of the condition in the state is estimated at 21.0 deaths per 100,000 persons (American Diabetes Association, 2025). This growing burden reflects the interplay of various demographic, socioeconomic, health behavioral, and lifestyle factors (Gonzalez-Zacarias et al., 2016; Hill-Briggs et al., 2021; Richards, Wijeweera & Wijeweera, 2022).

Despite the advancement in diabetes management and treatment, the burden of the condition varies significantly among population subgroups defined by geography, socioeconomic status, and demographic factors. Florida's distinctive population, characterized by a high percentage of elderly (≥65 years) and Hispanic residents (United States Census Bureau, 2024a), increases its diabetes mortality risks compared to other states (Boersma, Black & Ward, 2020). Additionally, nearly half of the counties of Florida are located in rural areas with limited access to healthcare facilities, contributing to higher risk of death from a number of conditions including diabetes (United States Department of Health and Human Services, 2024a). Therefore, addressing geographic disparities and characterizing populations with disproportionately high mortality risks is essential to reducing the burden of diabetes. In addition, investigating socioeconomic and demographic factors responsible for the high diabetes mortality risks at the county level is important for the development of evidence-based policies and intervention programs to reduce diabetes mortality and improve population health. Unfortunately, little is known about the geographic distribution and determinants of diabetes-related mortality risks at the county level in Florida.

Following national trends, the prevalence of diabetes among Florida adults has more than doubled over the past 20 years. Time series analysis is a crucial statistical tool for modeling these temporal changes as it helps to identify disease trends and seasonality as well as predict future risk. Accurate prediction of future diabetes risk and mortality trends is important for planning and development of effective intervention programs. However, no such studies have been conducted to predict the future risk of diabetes mortality in Florida.

With the above issues in mind, the objectives of this study were to identify: (i) county-level geographic disparities and temporal changes; (ii) county-level socioeconomic and demographic predictors; and (iii) temporal patterns and future diabetes-related mortality risk (DRMR) in Florida. Addressing geographic disparities, and socioeconomic and demographic factors responsible for high DRMR is important for the development of evidence-based policies and intervention programs to reduce diabetes burden and improve population health. Additionally, forecasting DRMR from historical data is crucial for early prediction of future risks and can guide health planning and service provision.

This dissertation is divided into five chapters. The first chapter includes an introduction and literature review. Chapters 2, 3, and 4 describe the methods and findings of studies addressing objectives 1, 2, and 3, respectively. Lastly, chapter 5 provides a summary of the conclusions and recommendations of this study.

1.2 Literature review

1.2.1 Etiology

Diabetes mellitus is a chronic metabolic non-communicable disease characterized by high levels of fasting plasma glucose (≥126 mg/dl) resulting from defects in insulin secretion, its action, or both (American Diabetes Association, 2009, 2024a). Insulin, a hormone produced by pancreatic β-cells, helps in regulating blood sugar levels (Fu et al., 2012; Mziaut et al., 2006). When insulin function is impaired, glucose accumulates in the bloodstream, leading to diabetes. Several pathogenic mechanisms contribute to the development of diabetes. These include autoimmune destruction of the pancreatic β-cells, leading to insulin deficiency, as well as abnormalities that cause resistance to insulin action (Cnop et al., 2005). In addition, insufficient action of insulin on target tissues also causes abnormalities in carbohydrate, fat, and protein metabolism and increases the risk of diabetes (American Diabetes Association, 2024a). Insufficient insulin action arises from either inadequate insulin secretion and/or reduced tissue responsiveness to insulin in the complex pathways of hormone action (American Diabetes Association, 2024a). Impaired insulin secretion and defects in insulin action often co-exist in the same patient, making it difficult to determine which abnormality is the primary cause of hyperglycemia. Understanding the etiology of diabetes is crucial for prevention, early diagnosis, and targeted treatment strategies.

1.2.2 Types of diabetes

There are several types of diabetes, each with distinct causes, mechanisms, and management approaches: type 1, type 2, gestational, and other specific types of diabetes.

1.2.2.1 Type 1 (immune-mediated or insulin-dependent) diabetes

Type 1 diabetes results from cellular-mediated autoimmune destruction of the pancreatic β-cells, leading to little or no insulin production (Cnop et al., 2005; Centers for Disease Control and Prevention, 2025a). Type 1 diabetes usually develops during childhood or adolescence, but can occur at any age, including individuals in their 80 and 90 years of age (Cnop et al., 2005). About 2 million or 0.6% of the total population in the US have type 1 diabetes, including 304,000 children and adolescents (American Diabetes Association, 2025). Autoimmune destruction of pancreatic β-cells occurs due to genetic predisposition and environmental factors (American Diabetes Association, 2024a). The risk of developing type 1 diabetes can frequently be identified through serological evidence of an autoimmune process targeting the pancreatic islets, as well as the presence of specific genetic markers. Indicators of the immune-mediated destruction of β-cells include the presence of islet cell autoantibodies, insulin autoantibodies, glutamic acid decarboxylase (GAD65) autoantibodies, and autoantibodies to the tyrosine phosphatases IA-2 and IA-2β (Cnop et al., 2005; Mziaut et al., 2006; Fu, R. Gilbert & Liu, 2012; American Diabetes Association, 2024a). One or more of these autoantibodies are detectable during the initial stage of type 1 diabetes. Additionally, it is strongly associated with Human Leukocyte Antigen genes, particularly linked to the DQA and DQB genes, and is influenced by the DRB genes (American Diabetes Association, 2024a).

1.2.2.2 Type 2 (non-insulin dependent) diabetes

Type 2 diabetes (T2D) develops gradually over many years and is most commonly diagnosed in adults (Centers for Disease Control and Prevention, 2025a). However, it is increasingly being identified in children, teenagers, and young adults. Approximately 36.4 million or 10.9% of the US population have T2D (American Diabetes Association, 2025). Type 2 diabetes results from a combination of two factors: defective insulin secretion from pancreatic β-cells and reduced responsiveness of insulin-sensitive tissues to insulin (Festa et al., 2000; Mulder, 2017; Galicia-garcia et al., 2020). Inflammation, ectopic lipid accumulation, endoplasmic reticulum stress, and oxidative stress contribute to the development and progression of T2D by reducing insulin sensitivity and causing pancreatic β-cell dysfunction (Lu et al., 2024). Normally, insulin binds to insulin receptors on cell membranes, triggering signaling pathways, particularly the phosphoinositide 3-kinase (PI3K)/protein kinase B (Akt)/PI3K/Akt pathway, which promotes the translocation of glucose transporter-4 (GLUT4) to the cell surface, thereby facilitating glucose uptake (Jaldin-Fincati et al., 2017). However, during insulin resistance, these signaling pathways become impaired, reducing GLUT4 movement to the membrane and consequently decreasing glucose entry into cells, ultimately leading to hyperglycemia (Jaldin-Fincati et al., 2017). Additionally, in the insulin-resistant state, insulin becomes less effective and induces the pancreas to produce higher levels of insulin (hyperinsulinemia), and chronic insulin resistance places sustained stress on pancreatic β-cells (James, Stöckli & Birnbaum, 2021). This ongoing stress, inflammation, and glucotoxicity leads to β-cell apoptosis, decreased β-cell mass, and impaired insulin secretion. Additionally, lipotoxicity resulting from persistently elevated levels of free fatty acids further contributes to β-cell injury and dysfunction (Jaldin-Fincati et al., 2017; James, Stöckli & Birnbaum, 2021). As hyperglycemia gradually develops, numerous cellular and molecular changes occur, driving the progression of T2D and leading to severe macrovascular complications, such as cardiovascular and cerebrovascular diseases, as well as microvascular complications, including retinopathy, neuropathy, and renal diseases (James, Stöckli & Birnbaum, 2021).

1.2.2.3 Gestational diabetes

Gestational diabetes (GD) mellitus is a metabolic complication in which spontaneous hyperglycemia develops during the second or third trimester of pregnancy (Alberti & Zimmet, 1998; Elsayed et al., 2023a). The condition significantly affects both maternal and fetal health, contributing to both short-term and long-term complications. According to the International Diabetes Federation, in 2021, about 16.7% of women had high blood glucose during pregnancy worldwide (International Diabetes Federation, 2021). This condition is more prevalent in low- and middle-income countries where access to maternal care is limited.

Although the exact cause of GD is unknown, several mechanisms suggest possible explanations contributing to its development. During pregnancy, the placenta produces hormones to support fetal development and supplies essential nutrients and water to maintain an adequate energy supply for the growing fetus (Stern et al., 2021; John Hopkins University, 2024). Certain hormones, such as estrogen, cortisol, and human placental lactogen, disrupt insulin function, resulting in the contra-insulin effect, which emerges between 20 and 24 weeks of pregnancy (Rassie et al., 2022). As the placenta continues to grow, the production of these insulin-blocking hormones increases, and thereby enhancing the risk of insulin resistance (Shao et al., 2002; Plows et al., 2018). In most cases, the pancreas can produce additional insulin to counteract this insulin resistance. However, when insulin production is insufficient to overcome the hormonal effects, gestational diabetes develops. Additionally, factors such as obesity, family history of diabetes, ethnicity, advanced maternal age, and prediabetes play a critical role in the progression of GD (Elsayed et al., 2023). In most cases, gestational diabetes resolves after pregnancy, but there is a 50% higher risk of developing type 2 diabetes later in life (Plows et al., 2018).

1.2.2.4 Other specific types of diabetes

Diabetes due to other causes develops as a result of underlying medical conditions, genetic mutations, autoimmune destruction, hormonal disorders, and external factors that impair insulin production or function (Elsayed et al., 2023). In addition, monogenic diabetes syndromes (neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (glucocorticoid use in the treatment of HIV/AIDS) are contributors to development of diabetes mellitus. Proper prevention and management are important to reduce diabetes. These may include lifestyle modifications, oral medications, or insulin therapy, depending on the underlying cause.

1.2.3 Risk factors of diabetes

1.2.3.1 Modifiable risk factors

1.2.3.1.1 Obesity

Approximately 100 million or 40.3% of the adult population in the US are classified as obese (BMI ≥30) (Emmerich et al., 2024). Obesity, particularly abdominal adiposity, is a key factor in the early onset of type 2 diabetes. The risk of developing diabetes increases significantly when obesity is compounded by physical inactivity (Emmerich et al., 2024). In addition, excess abdominal fat worsens insulin resistance and increases the risk of both high blood pressure and diabetes, creating a cycle of metabolic dysfunction (Serné et al., 2007). Weight loss can enhance insulin sensitivity in individuals with both obesity and insulin resistance (McLaughlin et al., 2019). It is estimated that losing 5-10% of body weight, combined with regular physical activity, can significantly lower the risk of developing diabetes (American Heart Association, 2024a).

1.2.3.1.2 Physical activity

Physical inactivity is a key modifiable risk factor for prediabetes and T2D. Regular physical activity helps lower insulin resistance and improves effectiveness of insulin. Even a 30-minute walk for five days a week can help reduce the risk of diabetes. However, about 75% of US adults do not follow the recommended 30 minutes of moderate exercise a day and walk only 15-20 minutes daily. (Elgaddal, Kramarow & Reuben, 2022; American Heart Association, 2024b). These sedentary habits, combined with an aging population, contribute to the rising prevalence of diabetes in the country.

1.2.3.1.3 Blood pressure

Hypertension increases the risk of diabetes through insulin resistance, vascular dysfunction, chronic inflammation, and metabolic imbalances (American Heart Association, 2024a). High blood pressure can impair microvascular function and reduce blood flow to insulin-sensitive tissues (such as muscle), which results in decreasing glucose uptake and leads to insulin resistance (Serné et al., 2007; Petrie, Guzik & Touyz, 2018). It also damages the endothelial cells lining blood vessels, reducing the availability of nitric oxide, a key molecule for proper insulin signaling (Jia & Sowers, 2021). Additionally, hypertension is linked to increased levels of inflammatory markers like TNF-α and IL-6, which disrupt insulin function and increase the risk of developing insulin resistance and diabetes (Petrie, Guzik & Touyz, 2018; Jia & Sowers, 2021). Hypertension is also associated with obesity, a major risk factor for type 2 diabetes. Managing blood pressure with lifestyle changes and appropriate medications can help reduce the risk of developing diabetes and its associated complications.

1.2.3.1.4 Smoking

Smoking contributes to the development of diabetes by disrupting normal cellular function. Nicotine from smoking triggers inflammation throughout the body, reducing insulin effectiveness and increasing the risk of insulin resistance (United States Department of Health and Human Services, 2014). Additionally, when nicotine interacts with oxygen in the body, it generates oxidative stress, which damages cells and further contributes to diabetes risk. Both oxidative stress and chronic inflammation play a significant role in the onset of insulin resistance and T2D (United States Department of Health and Human Services, 2014). Research shows that smokers are 30-40% more likely to develop T2D compared to non-smokers (United States Department of Health and Human Services, 2024b). In addition, for individuals with diabetes, smoking can lead to other serious complications, including heart disease, kidney disease, nerve damage, poor circulation, and even amputation (Sliwinska-Mosson & Milnerowicz, 2017). An estimated 9,000 people die annually in the US due to diabetes caused by cigarette smoking (United States Department of Health and Human Services, 2024b).

1.2.3.1.5 Unhealthy diet

Unhealthy diet is significantly associated with the risk of developing T2D through weight gain, chronic inflammation, and insulin resistance (Mirabelli, Russo & Brunetti, 2020). High amounts of refined carbohydrates, added sugars, and unhealthy fats in diet produce excess glucose which over time causes stress in the pancreas and impairs the ability of the body to use insulin effectively (Gadgil et al., 2013; Mirabelli, Russo & Brunetti, 2020; Magalhães et al., 2022). In addition, excess calories from processed food contribute to obesity and increase risk of insulin resistance (Almarshad et al., 2022). Low intake of fiber and essential nutrients further disrupts blood sugar regulation and negatively affects gut health (Fu et al., 2022). Together, these dietary patterns create metabolic imbalances that increase the likelihood of developing diabetes.

1.2.3.1.6 Excessive alcohol consumption

Excessive alcohol consumption has toxic effects on pancreas and damages the pancreatic beta-cells by disrupting insulin signaling, which ultimately leads to reduced insulin secretion (Wang et al., 2014; Federico, Cotticelli & Schiumerini, 2015; Li et al., 2022). Alcohol induces beta-cell apoptosis through mitochondrial dysfunction, characterized by increased production of reactive oxygen and decreased adenosine triphosphate levels (Federico, Cotticelli & Schiumerini, 2015). Alcohol also inhibits insulin-induced phosphatidylinositol 3-kinase activity and reduces the expression of glucose transporter 4 in skeletal muscle, contributing to insulin resistance (Dembele et al., 2009). Additionally, alcohol is calorie-dense and often leads to weight gain—particularly the accumulation of abdominal fat—which further elevates the risk of developing type 2 diabetes (Traversy & Chaput, 2015; Martínez-Urbistondo et al., 2024).

1.2.3.1.7 Income

Income is significantly associated with diabetes and associated mortality in the US (Turi & Grigsby-Toussaint, 2017; Nassereldine et al., 2025). Populations with low median household income often experience a high risk of diabetes due to limited access to healthcare facilities, low diabetes management resources, high rates of obesity, food insecurity, and physical inactivity (Nassereldine et al., 2025). In addition, economically disadvantaged communities lack sufficient healthcare infrastructure, diabetes self-management education, and healthy lifestyle. These contribute to higher diabetes risk and associated mortality compared to more affluent communities (Turi & Grigsby-Toussaint, 2017). A recent study conducted by Turi et al. reported that there are significant income inequalities in the southern parts of the US and high percentages of diabetes and associated mortality (Turi & Grigsby-Toussaint, 2017). Therefore, addressing income inequalities is important for public health interventions and resource allocation to reduce DRMR in low-income communities.

1.2.3.1.8 Education

In the US, diabetes risk differs substantially based to educational attainment. People with lower levels of education tend to have higher risks of diabetes and associate mortality compared to those with higher educational attainment (Turi & Grigsby-Toussaint, 2017; Cunningham et al., 2018; Dugani et al., 2022). Low educational attainment is closely related to unhealthy lifestyle behaviors (unhealthy diet, smoking, tobacco use, and physical inactivity) and contributes to the development of diabetes and associated mortality (Hill-Briggs et al., 2021). Individuals with low education attainment also face socioeconomic challenges, such as higher poverty and reduced access to healthcare services, which lead to delayed diagnosis and poor management of diabetes and associated complications (Hill-Briggs et al., 2021; Nassereldine et al., 2025). Studies have reported that diabetes patients with lower education attainment are at two-fold higher risk of death compared to those with higher educational attainment (Saydah & Lochner, 2010; Hill-Briggs et al., 2021).

1.2.3.1.9 Unemployment

A recent study conducted by Elek et al. reported that the risk of diabetes complications and associated mortalities were 1.5 times higher among populations with higher unemployment rates compared to those with lower unemployment rates (Elek, Mayer & Varga, 2025). Unemployment leads to financial strains that result in lower access to health insurance coverage, fewer regular visits to primary care physicians, and less participation in regular physical activities (Jeon et al., 2009; Breland et al., 2013; Baron et al., 2014; Flores et al., 2016; Green et al., 2020). Additionally, unemployment is closely linked to other socioeconomic challenges, including low educational attainment, poverty, and food insecurity, which contribute to unhealthy behaviors and increase the risk of diabetes, its complications, and associated mortality (Baron et al., 2014).

1.2.3.2 Non-modifiable risk factors

1.2.3.2.1 Family history

Family history is associated with a range of metabolic abnormalities and is an important risk factor of diabetes (Bener et al., 2014; Moon et al., 2017). Individuals with family history of diabetes are 2-6 times more likely to develop type 2 diabetes compared to those who do not have family history of the disease (Scott et al., 2013). Individuals with a family history of diabetes may inherit a genetic predisposition that may impair blood sugar regulation by affecting insulin production, glucose metabolism, and fat storage (Singh et al., 2024). In addition to genetics, family members often share similar lifestyles, including dietary habits, and physical activity, which influence the risk of developing diabetes and associated complications (Abdulaziz Alrashed et al., 2023). This underscores the importance of adopting healthy behaviors, especially for individuals with a family history of diabetes.

1.2.3.2.2 Age

Aging causes changes in metabolism, decreases physical activity, increases body fat, impairment of pancreatic β cell function, and dysfunction of insulin secretion (Halter, 2011; Huang et al., 2023). In addition, aging disrupts the regulation of the hypothalamic-pituitary-adrenal axis and secrets high levels of cortisol hormone which further contributes to hepatic insulin resistance (Herman et al., 2016; Erceg et al., 2025). Moreover, elderly people often engage in less physical activity and commonly experience coexisting obesity and reduced kidney function, all of which are additional factors promoting impairment of glucose metabolism and diabetes (Qin et al., 2010; Erceg et al., 2025). Therefore, regular health screenings are important, especially with advancing age, to manage diabetes and associated complications.

1.2.3.2.3 Race

Race is associated with the risk of diabetes due to a combination of genetic, socioeconomic, and environmental factors. Certain racial and ethnic groups, such as African Americans, Hispanic, and Native Americans have been shown to have a higher prevalence of type 2 diabetes compared to non-Hispanic whites (Rodríguez & Campbell, 2017; Zhu et al., 2019; Hassan et al., 2023). The elevated risk of diabetes among these minority populations is attributed not only to genetic predisposition but also influenced by disparities in healthcare access, lower socioeconomic status, and cultural dietary patterns (Aguayo-Mazzucato et al., 2019; Golden et al., 2020; Kyrou et al., 2020). In addition, Hispanic and African American populations often face poor diabetes management, poor nutrition and healthcare, poor glycemic control, and insufficient medical follow-ups which lead to higher rates of diabetes and associated complications (United States Census Bureau, 2024b; United States Department of Health, 2024).

1.2.4 Signs and symptoms

The signs and symptoms of diabetes are often ignored due to the gradual and chronic nature of disease progression (Ramachandran, 2014). The common symptoms of diabetes are increased thirst (polydipsia), frequent urination (polyuria), weight loss, and increased appetite (Centers for Disease Control and Prevention, 2024b). Diabetes patients may also experience fatigue, blurred vision, slow-healing wounds, and frequent infections, such as urinary tract or skin infections (Centers for Disease Control and Prevention, 2024b). Some other signs such as numbness or tingling in the hands and feet (a sign of nerve damage) are also common in type 2 diabetes. In type 1 diabetes, more acute symptoms like nausea, vomiting, and abdominal pain may occur (Centers for Disease Control and Prevention, 2024b).

1.2.5 Diagnosis

Diabetes diagnosis relies mostly on the measurement of circulating glucose in whole blood, plasma, serum, and capillary blood glucose or interstitial fluid (Nathan, 2015; Pippitt, Li & Gurgle, 2016). The disease is typically diagnosed through the fasting plasma glucose test, oral glucose tolerance test, the random blood glucose test, and the Hemoglobin A1c test.

1.2.5.1 Fasting plasma glucose test

The fasting plasma glucose test is a blood test that measures the level of blood glucose after fasting for at least 8 hours (Centers for Disease Control and Prevention, 2024c). A fasting plasma glucose level <100 mg/dL (<5.6 mmol/L) is normal. However, fasting plasma glucose level ranging from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) is considered prediabetes, and a reading of ≥126 mg/dL (7 mmol/L) on two separate tests is classified as diabetes (Centers for Disease Control and Prevention, 2024c).

1.2.5.2 Hemoglobin A1c test

The hemoglobin A1c test is a common blood test for the diagnosis of diabetes mellitus. This test is also known as glycated hemoglobin, glycosylated hemoglobin, hemoglobin A1c or HbA1c test. An A1c test is a measurement of average blood sugar levels over the past 2-3 months. It measures the percentage of blood sugar attached to hemoglobin, the oxygen-carrying protein in red blood cells. The higher the blood sugar levels the more hemoglobin with sugar attached. Therefore, an A1c level of ≥6.5% on two separate tests is considered diabetes, while between 5.7%-6.4% indicates prediabetes and <5.7% is considered normal (Mayo Clinic, 2024).

1.2.5.3 Glucose tolerance test

The glucose tolerance test evaluates how the body responds to sugar and is commonly used to screen prediabetes and type 2 diabetes before symptoms appear. A specific form of this test is also used to diagnose diabetes during pregnancy. An individual has to undergo an overnight fast, after which a baseline fasting blood glucose level is measured (Mayo Clinic, 2024). Following this, a standardized glucose solution is ingested, and blood glucose levels are subsequently measured at regular intervals for two hours to assess the body's glycemic response (Mayo Clinic, 2024). Blood sugar level of <140 mg/dL (7.8 mmol/L) is considered normal. However, a blood sugar level between 140 and 199 mg/dL (7.8 to 11.0 mmol/L) is classified as prediabetes, and >200 mg/dL (11.1 mmol/L) indicates diabetes (Mayo Clinic, 2024).

1.2.6 Treatment

One of the most important ways to manage diabetes is to maintain a healthy lifestyle. However, people with type 1 diabetes need insulin injections for survival. Those with type 2 diabetes need to take insulin and other medicines, such as metformin, sulfonylureas, and sodium-glucose co-transporters type 2 (SGLT-2) inhibitors to manage blood sugar levels (Abbasi, Heath & McGinness, 2024; Bailey, 2024). Diabetes patients often need medications to lower their blood pressure to reduce the risk of cardiovascular complications. Additional medical care may be needed to treat the complications of diabetes, such as foot care to treat ulcers, screening and treatment for kidney disease, and eye exams to screen for retinopathy (Templer, Abdo & Wong, 2024).

1.2.7 Prevention and control

Prevention of diabetes mainly focuses on promoting a healthy lifestyle, such as maintaining a balanced diet, engaging in regular physical activity, reducing obesity, reducing alcohol consumption, and avoiding tobacco use (Lu et al., 2024; Bowen et al., 2025). In addition, managing blood glucose levels through medication, monitoring, lifestyle changes, regular healthcare visits, and routine screening are important for those who are already living with diabetes. Diabetes self-management education empowers individuals to reduce the risk of diabetes-associated complications such as heart disease, kidney disease, and vision loss (Chrvala, Sherr & Lipman, 2016; Chowdhury et al., 2024). Coordination between healthcare providers, communities, and public health systems is important to improving outcomes and enhancing the quality of life for people at risk of or living with diabetes.

1.2.8 Burden of diabetes

1.2.8.1 Diabetes prevalence and incidence

Diabetes presents a significant burden in the United States (US). Over the last two decades, the age-adjusted prevalence of total diabetes (diagnosed and undiagnosed) among older adults has increased from 9.7% in 2000 to 14.3% in 2023 (Baumblatt et al., 2024). Men had a higher prevalence of diagnosed and undiagnosed diabetes compared to women. In addition, in the last ten years, diabetes prevalence increased with increasing age and obesity prevalence but decreased with increasing educational attainment in the US (Baumblatt et al., 2024).

In 2021, an estimated 1.2 million new cases of diabetes were diagnosed among older adults aged ≥18 years (Centers for Disease Control and Prevention, 2024d). The incidence was significantly higher among adults aged ≥45 years old compared to adults aged 18 to 44 years (Centers for Disease Control and Prevention, 2024d). There were racial and socioeconomic disparities of diabetes incidence: non-Hispanic Black adults and Hispanic adults had higher diabetes incidence than non-Hispanic White and Asian adults (Centers for Disease Control and Prevention, 2024d). Additionally, adults with less than a high school education or only a high school diploma had higher incidence rate compared to those with higher education attainment (Centers for Disease Control and Prevention, 2024d).

1.2.8.2 Economic burden

The economic burden of diabetes in the US is substantial and continues to grow as the prevalence of the disease increases. The estimated total cost of diagnosed diabetes in 2022 was estimated at $412.9 billion. This includes $307 billion in direct medical costs and $106.3 billion in indirect costs (loss of productivity, unemployment from chronic disability, and premature mortality) (Parker et al., 2024). The direct medical cost of the condition increased from $227 billion in 2012 to $307 billion in 2022 (Americal Diabetes Association, 2024; Parker et al., 2024). The American Diabetes Association reports that the cost of medical expenses among people with diagnosed diabetes is 2.6 times higher than among those without the condition (Americal Diabetes Association, 2024). A significant portion of these rising costs is due to increased cost of medication. It is estimated that the cost of insulin increased by 24% from 2017 to 2022, and the total spending on insulin increased almost three-fold (from $8 billion to $22.3 billion) over the last ten years (Parker et al., 2024). Healthcare spending due to diabetes also reveals disparities across demographic groups. African Americans with diabetes bear the highest direct medical cost among racial groups (Parker et al., 2024). In addition, adults over 65 years of age spend nearly twice as much per year on diabetes healthcare compared to individuals who are 18-64 years old (Parker et al., 2024).

1.2.8.3 Diabetes-associated mortality

Diabetes is the 8th leading cause of death in the US. A total of 101,209 people died from the disease in 2022 resulting in a mortality risk of 30.4 per 100,000 persons (Centers for Disease Control and Prevention, 2023a, 2025a). The condition is associated with other life-threatening chronic diseases (heart attack, hypertension, stroke, and chronic kidney disease) (Centers for Disease Control and Prevention, 2023b,c). People with diabetes are at higher risk of death compared to those without the condition. There is evidence of disparities in diabetes-related mortality risk (DRMR) across racial and ethnic groups in the US (Spanakis & Golden, 2013; Turi & Grigsby-Toussaint, 2017; Alva et al., 2018; Clements et al., 2020; Mokdad et al., 2022). In the US, American Indian and Alaskan Native populations are most vulnerable to diabetes-related deaths (35.6 deaths per 100,000 individuals) and experience the highest age-adjusted mortality risk, followed by Black (31.9 per 100,000 population), Hispanic (19.7 per 100,000 population), White (17.6 per 100,000 population), and Asian (12.6 per 100,000 population) (Nassereldine et al., 2025). Non-Hispanic Black Americans have 40% higher risk of diabetes-associated death compared to their non-Hispanic White counterparts (Clements et al., 2020). Similarly, older populations (≥65 years old) are at higher risk of diabetes-related death than adults <65 years old (Dugani et al., 2022). Older adults are also more likely to develop chronic conditions (cardiovascular disease, hypertension, kidney disease), which compound diabetes complications and contribute to poorer health outcomes. These disparities highlight the urgent need for public health strategies to reduce the disproportionate burden of diabetes-related deaths among underserved and high-risk communities.

1.2.9 Spatial pattern of diabetes mortality

1.2.9.1 Geographic disparities of diabetes mortality

There is evidence of geographic disparities in diabetes mortality across the US, which is a result of unequal healthcare access, differences in socioeconomic status, and variations in community resources (Dugani et al., 2022; Nassereldine et al., 2025). A total of 644 counties located in 15 southeastern states are designated as the “diabetes belt” because their average diabetes prevalence (11.0%) is higher than the national average (8.5%) (Barker et al., 2011). These 15 states include: Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, Ohio, Pennsylvania, South Carolina, Tennessee, Texas, Virginia, and West Virginia. High rates of obesity, physical inactivity, poverty, and limited access to healthcare facilities are major concerns in these states, contributing to poorer diabetes management and high diabetes mortality (Geiss et al., 2017; Salerno et al., 2024). In contrast, counties in the northeastern and pacific regions consistently reported lower diabetes mortality compared to the southeastern parts of the country (Dugani, Mielke & Vella, 2021). Additionally, diabetes mortality remains a significant cause of concern in the rural counties of US which experience higher DRMR compared to their urban counterparts (O'Brien & Denham, 2008; Brown-Guion et al., 2013; Callaghan et al., 2020). Rural counties often face challenges in healthcare access, insufficient public transportation, long distances to healthcare facilities, and irregular health checkups leading to lower detection rates of potential health problems, including diabetes. These factors combine to increase the risks of diabetes-related deaths in these populations (O'Brien & Denham, 2008; Agency for Healthcare Research and Quality, 2023).

1.2.9.2 County-level spatial analysis

Diabetes and associated mortality remain a significant public health challenge in the US. Although national and state-level data provide broad information about diabetes burden, such investigations often mask the existence of disparities within smaller geographic areas, including county and neighborhood-levels (Mujahid et al., 2023; Khavjou et al., 2025; Nassereldine et al., 2025). Certain counties, especially those in rural areas, have limited access to healthcare facilities, high rates of obesity, physical inactivity, and medically underserved areas, which result in high diabetes mortality (Nassereldine et al., 2025). Therefore, county-level spatial analysis helps to identify and visualize these disparities which is helpful for public health professionals and policymakers addressing the needs of specific communities (Turi & Grigsby-Toussaint, 2017; Brissette et al., 2019; Lu et al., 2023). Several US, European, and Chinese studies have evaluated the social determinants of diabetes and associated mortality in different geographic locations (county and state level) and reported that county-level geographic analysis is important to better understand needs-based health services (Dugani et al., 2022; Peisong et al., 2024; Nassereldine et al., 2025). In addition, county-level analysis also helps to evaluate the impact of public health programs and policies by comparing trends across counties and guide control programs through allocating health resources to communities most at need (Nassereldine et al., 2025). Therefore, the county spatial scale is an excellent choice to use as the unit of analysis in spatial analyses to identify geographic disparities of DRMR and their determinants.

1.2.10 Trends and future aspects of diabetes mortality

1.2.10.1 Trends of diabetes mortality in the United States

Diabetes is a serious public health concern and consistently remains one of the leading causes of death in the US (Centers for Disease Control and Prevention, 2025a). In 2021, diabetes was the underlying cause of death for 103,294 people and was listed as a contributing factor in an additional 399,401 deaths (American Diabetes Association, 2025). However, over the last ten years, there has been a significant decline in DRMR in the US. The age-standardized DRMR decreased by 32% from 28.1 to 19.1 deaths per 100,000 population from 2000 to 2019 (Nassereldine et al., 2025). Similarly, a significant decline was observed in the same time period among the American Indian/Alaskan Native (from 63.6 to 35.6 per 100,00 population), Black (56.0 to 31.9 per 100,000 population), Latino (39.5 to 19.7 per 100,000 population), White (24.6 to 17.6 per 100,000 population) and Asian population (18.1 to 12.6 per 100,000 population)

(Nassereldine et al., 2025). However, the COVID-19 pandemic disrupted the declining trend in diabetes mortality in the US. Diabetes-related mortality risk increased by 17.85% from 87,647 in 2019 to 103,294 in 2021 with a mortality risk of 31.1 per 100,000 population (American Diabetes Association, 2025). However, recent DRMR data from the third quarter of 2024 indicated a decline to 26.4 deaths per 100,000, showing a potential reversal of the pandemic-induced spike (Centers for Disease Control and Prevention, 2025b).

Diabetes-associated mortality varied by geographic regions in the US from 1999 to 2018 and remained highest (130 per 100,000 population in 2018) in the southern parts of the country (Dugani et al., 2022). Specifically, DRMR was significantly higher in southern rural counties (140 to 153.8 per 100,000 population), compared to metro counties (116 to 110 per 100,000 population) (Dugani et al., 2022). In contrast, diabetes-associated deaths remained constant from 122.3 to 119.6 per 100,000 population over a period from 1999 to 2018 in the Western regions of the country (Dugani et al., 2022).

1.2.10.2 Predicting future burden of diabetes

Since diabetes is one of the leading causes of death, predicting future burden of diabetes can help healthcare professionals and policymakers to address the growing burden of the condition (Linden, 2018). Additionally, forecasting helps to understand the temporal trends of DRMR patterns as it provides insights into how the condition evolves over time and its effects on population health (Lin et al., 2018). A recent study conducted by Lin et al. reported that the percentage of diagnosed diabetes would increase from 9.1% (22.3 million) in 2014 to 13.9% (39.7 million) in 2030 and to 17.9% (60.6 million) by 2060 (Lin et al., 2018). The study also reported that the Black population would continue to have higher diabetes prevalence compared to other racial groups in the US (Lin et al., 2018). Another study by Dong et al. reported that worldwide deaths from type 2 diabetes increased from 606,407 in 1999 to 1,472,934 in 2019 (Dong et al., 2024). Additionally, forecasting showed a gradual decrease of DRMR in the next ten years and highlighted the importance of diabetes prevention and control (Dong et al., 2024). Therefore, predicting future diabetes burden and addressing factors such as obesity, socioeconomic disparities, and access to healthcare will be crucial in mitigating future diabetes-related mortality in the US.

CHAPTER 2

Geographic Disparities and Temporal Changes of Diabetes-Related Mortality Risks in Florida: An Ecological Study

Geographic Disparities and Temporal Changes of Diabetes-Related Mortality Risks in Florida: An Ecological Study

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My contributions to this paper included data preparation, analysis, interpretation of results, gathering and reviewing of literature, formulation of discussion topics, as well as drafting and editing the manuscript.

2.1 Abstract

Background: Over the last few decades, diabetes-related mortality risks (DRMR) have increased in Florida. Although there is evidence of geographic disparities in pre-diabetes and diabetes prevalence, little is known about disparities of DRMR in Florida. Understanding these disparities is important for guiding control programs and allocating health resources to communities most at need. Therefore, the objective of this study was to investigate geographic disparities and temporal changes of DRMR in Florida.

Methods: Retrospective mortality data for deaths that occurred from 2010 to 2019 were obtained from the Florida Department of Health. Tenth International Classification of Disease codes E10–E14 were used to identify diabetes-related deaths. County-level mortality risks were computed and presented as number of deaths per 100,000 persons. Spatial Empirical Bayesian (SEB) smoothing was performed to adjust for spatial autocorrelation and the small number problem. High-risk spatial clusters of DRMR were identified using Tango's flexible spatial scan statistics. Geographic distribution and high-risk mortality clusters were displayed using ArcGIS, whereas seasonal patterns were visually represented in Excel.

Results: A total of 54,684 deaths were reported during the study period. There was an increasing temporal trend as well as seasonal patterns in diabetes mortality risks with high risks occurring during the winter. The highest mortality risk (8.1 per 100,000 persons) was recorded during the winter of 2018, while the lowest (6.1 per 100,000 persons) was in the fall of 2010. County-level SEB smoothed mortality risks varied by geographic location, ranging from 12.6 to 81.1 deaths per 100,000 persons. Counties

in the northern and central parts of the state tended to have higher mortality risks, whereas southern counties consistently showed lower mortality risks. Similar to the geographic distribution of DRMR, significant high-risk spatial clusters were also identified in the central and northern parts of Florida.

Conclusion: Geographic disparities of DRMR exist in Florida, with high-risk spatial clusters being observed in rural central and northern areas of the state. There is also evidence of both increasing temporal trends and Winter peaks of DRMR. These findings are helpful for guiding allocation of resources to control the disease, reduce disparities, and improve population health.

2.2 Introduction

Diabetes is a chronic metabolic disease affecting millions of people worldwide and its prevalence has been increasing among the adult population of the United States (US) over the past few decades (Centers for Disease Control and Prevention, 2023d). According to the Centers for Disease Control and Prevention (CDC), a total of 28.7 million Americans have been diagnosed with diabetes and 8.5 million people are living with undiagnosed diabetes (Centers for Disease Control and Prevention, 2023d).

Diabetes is associated with several life-threatening conditions, including chronic kidney disease, cardiovascular disease, stroke, retinopathy, and visual impairment (Centers for Disease Control and Prevention, 2023b,c). As a result, people with diabetes are at a higher risk of death compared to those without the condition. As of 2021, the Diabetes Related Mortality Risk (DRMR) in the US was 31.1 per 100,000 persons, and the disease is reported to be the 8th leading cause of death in the country (Xu et al., 2022). The condition imposes a significant economic burden, as the average medical expenses of patients with diabetes are 2.3 times higher than for those who do not have the disease (Florida Department of Health, 2023a). In 2017, Florida's total diabetes related costs was approximately $25 billion, with $19.3 billion being direct costs and another $5.5 billion being indirect costs (Florida Department of Health, 2023a).

There is evidence of geographic disparities of diabetes in the US. The diabetes belt, which includes fifteen states of the Southeast US (including Florida), has higher diabetes prevalence (≥11.0%) compared to the nation's average (8.5%) (Barker et al., 2011). Every year an estimated 148,613 people are diagnosed with diabetes in Florida (Florida Department of Health, 2023a), and as of 2021, the DRMR was 24.8 per 100,000 persons (Centers for Disease Control and Prevention, 2023e). Moreover, there has been a significant upward trend in DRMR in the US over the last few decades (US Department of Health and Human Services, 2020) and these temporal changes show evidence of regional disparities (US Department of Health and Human Services, 2020) as certain states and communities have experienced higher mortality risks than others. Addressing these geographic disparities of DRMR is important in providing useful information to guide efforts to reduce disparities and improve population health. Therefore, the objective of this study was to identify geographic disparities and temporal changes of DRMR in Florida.

2.3 Methods

2.3.1 Study area

This retrospective study was conducted in the state of Florida, which comprises 67 counties **(Figure 2.1),** some of which lie within the diabetes belt (Barker et al., 2011). Geographically, the state is located between 27° 66' N and 81° 52' W and spans 65,758 square miles, ranking 22nd by area among the 50 states of the US. As of 2020, 21.5 million people live in Florida, of whom 50.8% are female and 49.2% are male (United States Census Bureau, 2024c). The age distribution among the adult population is as follows: 24% are 18-34 years old, 26% are 35-49 years old, 25% are 50-64 years old, and 22% ≥65 years old. Florida has the 2nd highest percentage of elderly population (≥65 years) in the US (Florida Department of Health, 2023b). The overall racial composition of Florida residents is 76.9% White, 17% Black, and 6.1% all other races (United States Census Bureau, 2024c). In addition, there are 71.2% non-Hispanic, and 28.73% Hispanic population in the state. Miami-Dade County, which is located in the Southeastern part of the state, is the most populous with 2.6 million people, whereas Liberty County is the least populated with 7,987 residents (United States Census Bureau, 2024c). Counties of Florida are classified as rural or urban based on population density (Florida

Department of Health, 2023c). Counties with population densities of ≤100 persons per square mile are classified as rural, while those with higher population densities are classified as urban. Based on this classification, there are 30 rural and 37 urban counties in Florida (**Figure 2.1**).

2.3.2 Data source and management

The 2010–2019 individual-level death data were obtained from the Florida Department of Health (Florida Department of Health, 2023d). The cause of death was recorded using the 10th revision of the International Classification of Disease (World Health Organization, 2019). and the codes E10–E14 were used to identify diabetes-related deaths (World Health Organization, 2019). No differentiation was made between Type 1 and Type 2 diabetes. The number of diabetes-related deaths were aggregated at the county level using R statistical software version 4.2.2 (R Core Team, 2023). County-level DRMR were then calculated and expressed as number of deaths per 100,000 persons. Population estimates for 2010 to 2019 were obtained from the American Community Survey and used as the denominators to calculate the county-level DRMR from 2010 to 2019 time periods (United States Census Bureau, 2024c). Cartographic boundary files were downloaded from the United States Census Bureau TIGER Geodatabase (United States Census Bureau, 2023a) and used for the spatial displays at the county level. GeoDa software version 1.14 (Anselin, 2023) was used to compute the county-level Spatial Empirical Bayesian (SEB) smoothed DRMR to adjust for spatial autocorrelation and small number of cases in some counties (Bernardinelli & Montomoli, 1992; Haddow & Odoi, 2009; Deb Nath et al., 2023; Khan et al., 2023).

2.3.3 Detection of spatial clusters

Evidence of spatial autocorrelation of DRMR was assessed using global Moran's I statistic specifying 1st order queen weights and implemented in GeoDa (Anselin, 2023). Tango's

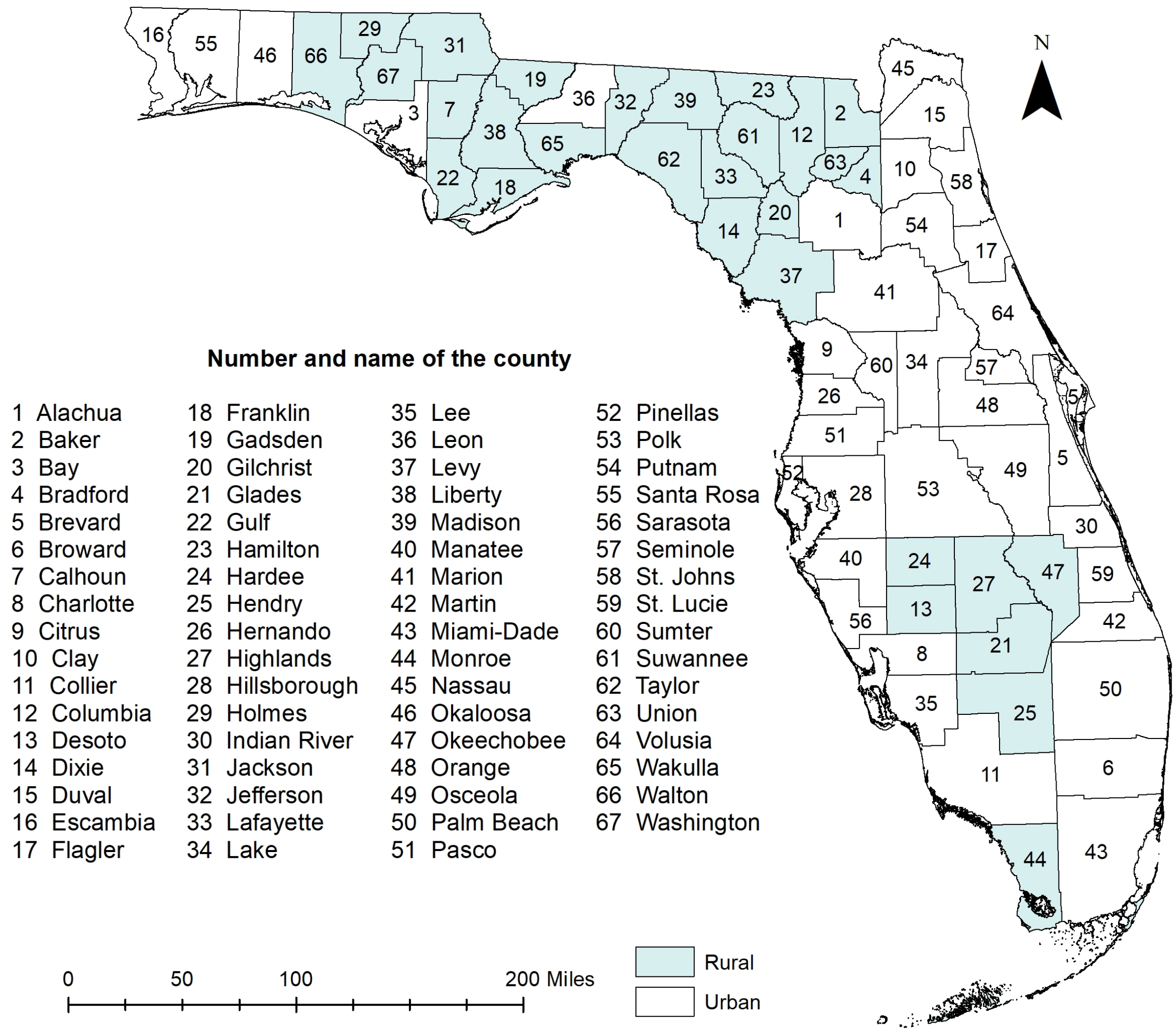

Figure 2.1: Study area showing the geographic distribution of rural and urban counties in Florida, USA.

Flexible Spatial Scan Statistics (FSSS) was used in FleXScan software version 3.1.2 (Tango & Takahashi, 2010) to identify statistically significant irregularly shaped and circular high risk spatial clusters of DRMR (Tango & Takahashi, 2005). The maximum cluster size of 15 counties was specified as spatial scanning window to avoid the identification of excessively large clusters. Poisson probability model with a restricted log likelihood ratio (LLR) was utilized (Tango & Takahashi, 2012). Nine hundred and ninety-nine Monte Carlo replications and a critical p-value of 0.05 were used for significance testing to identify statistically significant high-risk clusters. Potential clusters were then ranked based on their restricted LLR. The cluster with highest restricted LLR value was designated as the primary cluster and the rest were considered secondary clusters. Only high-risk clusters with relative risk of ≥1.20 were reported in this study in order to avoid reporting low risk clusters. To assess if the spatial distribution of the clusters changed between the beginning of the study period and the end, two cluster analyses were performed: one for the first 2 years (2010–2011) and another for the last 2 years (2018–2019) of the study period. The spatial distribution of the clusters was then compared visually.

2.3.4 Identification of temporal changes

The descriptive statistics of DRMR were calculated using R statistical software version 4.2.2 (R Core Team, 2023) implemented in RStudio (R Studio Team, 2020). The number of diabetes associated deaths were aggregated by season (winter: December, January, February; spring: March, April, May; summer: June, July, August; and fall: September, October, November) to identify the temporal changes of DRMR for the period of 2010 to 2019. Seasonal DRMR were computed and expressed as number of deaths per 100,000 persons. The temporal changes in DRMR over the 10-year study period were displayed graphically in Microsoft Excel (Microsoft Corporation, 2023).

2.3.5 Cartographic displays

The cartographic displays were performed using ArcGIS version 10.8.1 (Environmental System Research Institute, 2023). County-level choropleth maps were used to visualize the distribution of both smoothed and unsmoothed DRMR using Jenk's optimization classifications scheme (Jenks, 1967). Choropleth maps, using Jenk's optimization classification scheme, were generated for each of the 10 years of the study period. Identified high-risk spatial clusters of DRMR were also displayed in ArcGIS.

2.4 Results

2.4.1 Geographic distribution of DRMR

A total of 54,684 diabetes-related deaths were reported in Florida during the study period. The spatial patterns of the SEB smoothed maps were more apparent than those of the unsmoothed maps **(Figures 2.2 and 2.3).** The county-level SEB DRMR varied geographically and ranged from 12.6 to 81.1 deaths per 100,000 persons across the state. The lowest mortality risk was observed in Leon County (12.6 deaths per 100,000 persons in 2015), while the highest risk was in Taylor County (81.1 per 100,000 persons in 2018). The northern and central counties of Florida tended to have high mortality risks during 2010–2011 and 2016–2019 time periods **(Figure 2.3).** High DRMRs were observed predominantly in rural counties **(Figure 2.4).** Specifically, the highest mortality risk (58.7 deaths per 100,000 persons) was recorded in northern rural Taylor County, while urban Leon County had the lowest (18.6 deaths per 100,000 persons) mortality risks. The rural counties neighboring Taylor County (i.e. Lafayette, Madison, Suwannee, Hamilton, Columbia, and Highlands counties) had similarly high mortality risks **(Figures 2.1 and 2.4)**. Although a few southern urban counties (including Desoto, Hardee, Highlands, and Glades counties) had high mortality risks, most of the urban counties in the southern parts of the state had low mortality risks **(Figures 2.1 and 2.4).**

2.4.2 Purely spatial clusters of DRMR

There was evidence of global spatial autocorrelation of DRMR (Morans'I = 0.430; $p < 0.001$). Significant high-risk spatial clusters were detected in the central and northern parts of the state **(Figure 2.5).** Six and seven clusters were identified during the 2010–2011 and 2018–2019 time periods, respectively **(Table 2.1).** More counties were involved in the spatial clusters during the 2018–2019 time period (29 counties) than the 2010–2011 time period (28 counties). In 2010–2011, most of the high-risk clusters were identified in the northern parts of the state; however, by 2018–2019, a subtle shift had taken place, as the high-risk clusters moved from the northern parts to the central areas of Florida. Most of the counties involved in the high-risk clusters were located in the rural areas, although some urban counties (Marion, Sumter, Citrus, Hernando, and Pasco) were also part of high-risk clusters.

2.4.3 Temporal changes of DRMR

There was an increasing temporal trend and seasonal patterns in DRMR from 2010 to 2019 **(Figure 2.6).** The risks were consistently high during the winter season and low during the fall season **(Figure 2.6).** The lowest DRMR was recorded during the fall season of 2010 (6.08 deaths per 100,000 persons) while the highest was recorded during the winter of 2018 which had a risk of 8.13 deaths per 100,000 persons.

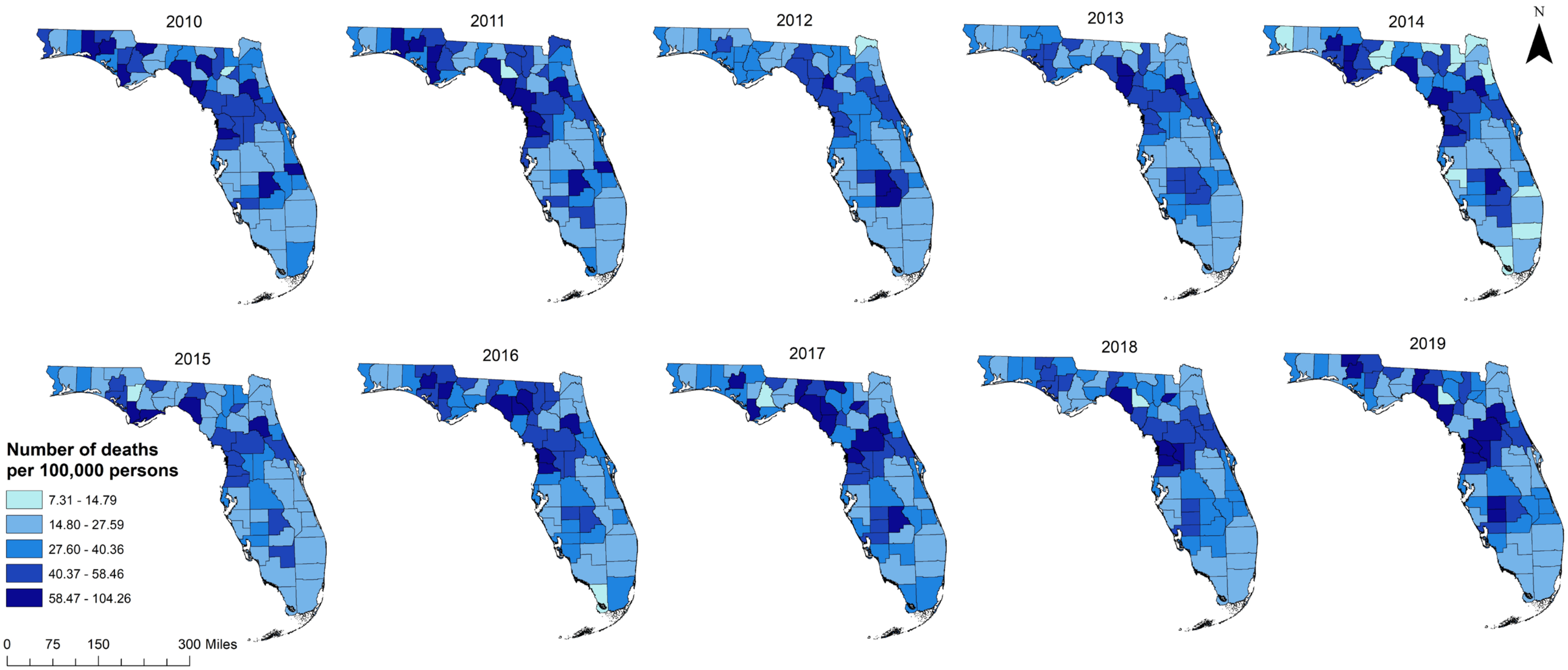

Figure 2.2: Distribution of unsmoothed diabetes-related mortality risks in Florida, 2010 to 2019.

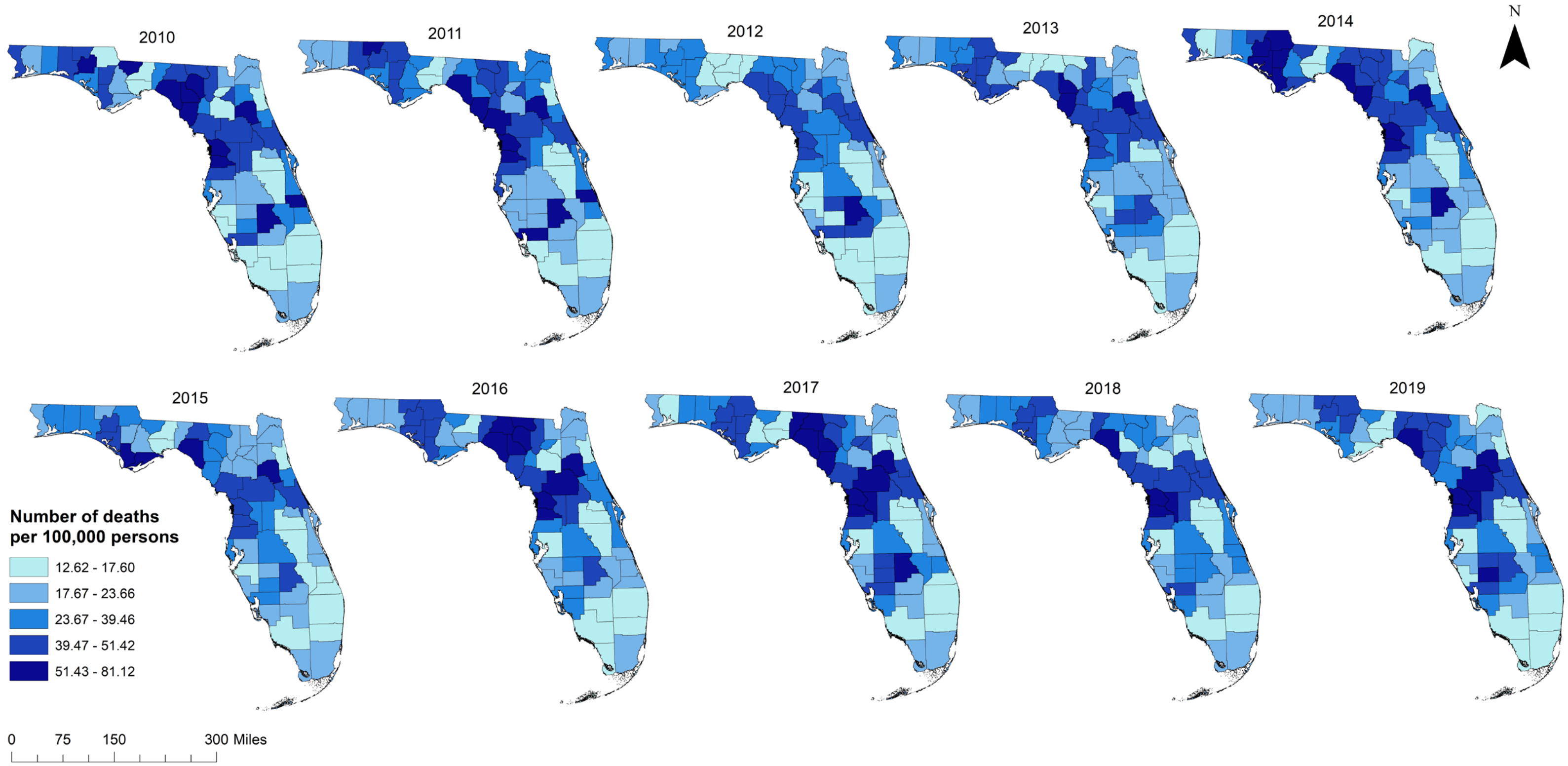

Figure 2.3: Distribution of Spatial Empirical Bayes smoothed diabetes-related mortality risks in Florida, 2010 to 2019.

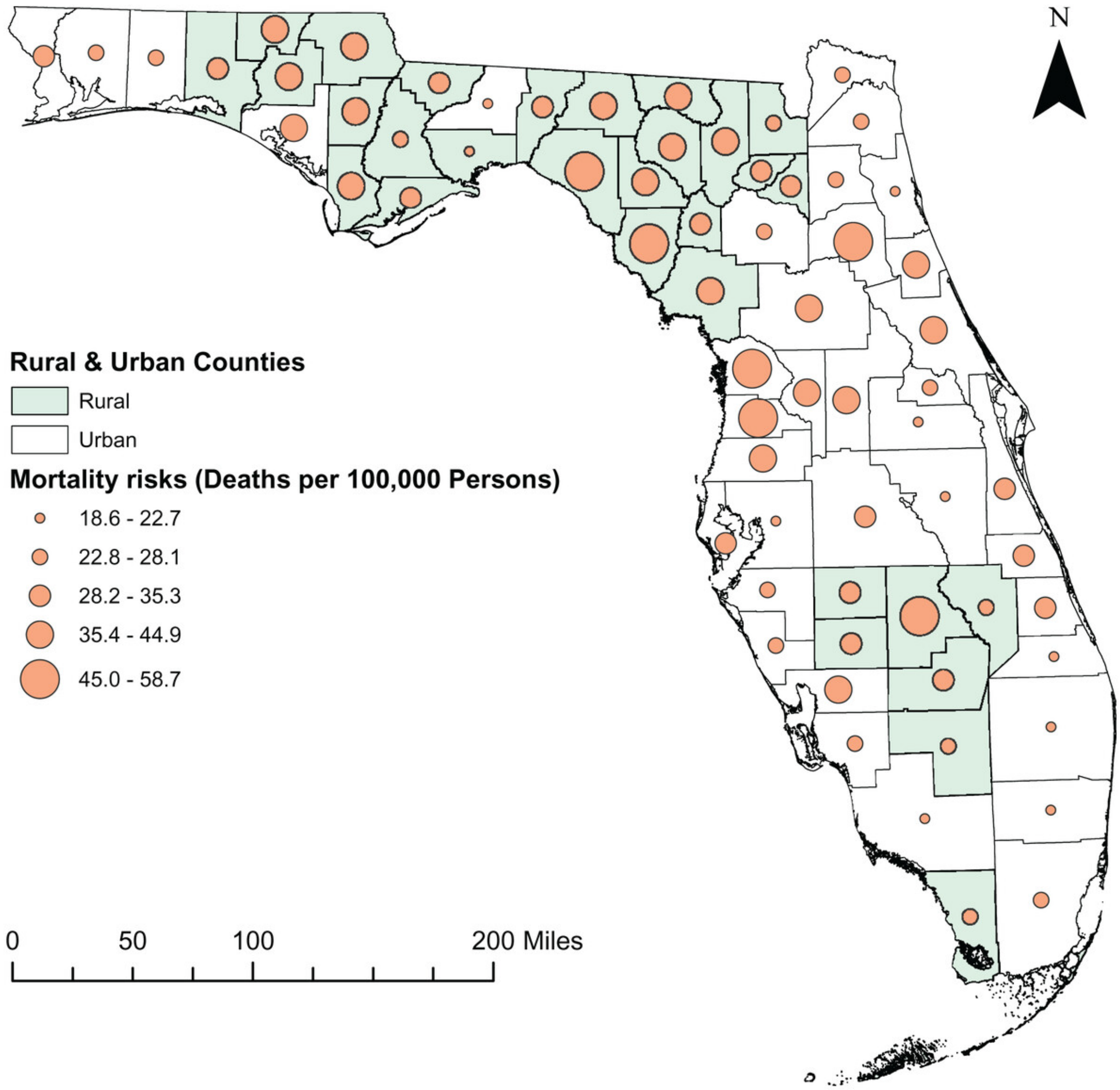

Figure 2.4: Distribution of diabetes-related mortality risks in rural and urban counties of Florida, 2010 to 2019.

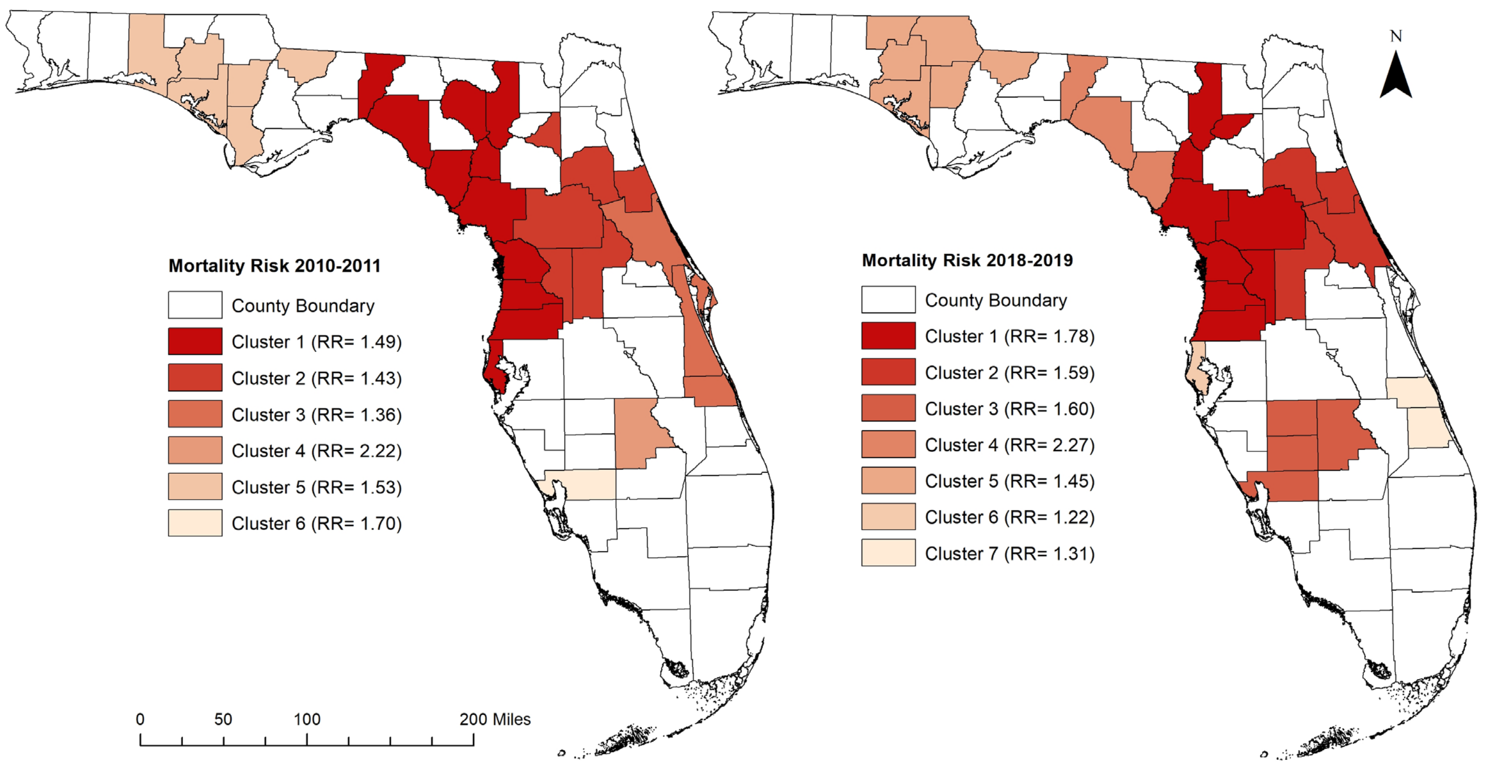

Figure 2.5: High risk spatial clusters of diabetes-related mortality risks in Florida during the time period of 2010-2011 and 2018-2019.

Table 2.1: Purely spatial clusters of high diabetes-related mortality risks identified in Florida from 2010-2011 and 2018-2019.

Period	Cluster	Population	Observed cases	Expected cases	No. of counties	RR*	*p*-value
2010 – 2011	Cluster 1	1,904,985	1,053	1008	10	1.49	0.001
	Cluster 2	926,600	697	486	6	1.43	0.001
	Cluster 3	1,180,052	843	619	3	1.36	0.001
	Cluster 4	987,67	115	51	1	2.22	0.001
	Cluster 5	328,536	263	172	6	1.53	0.001
	Cluster 6	161,115	144	84	1	1.70	0.001
2018 – 2019	Cluster 1	1,180,597	1,535	860	7	1.78	0.001
	Cluster 2	1,077,748	982	617	4	1.59	0.001
	Cluster 3	348,718	320	199	4	1.60	0.001
	Cluster 4	54,010	70	30	3	2.27	0.001
	Cluster 5	318,480	282	194	5	1.45	0.001
	Cluster 6	979,558	687	561	1	1.22	0.001
	Cluster 7	464,381	348	266	2	1.31	0.001

*Relative Risk

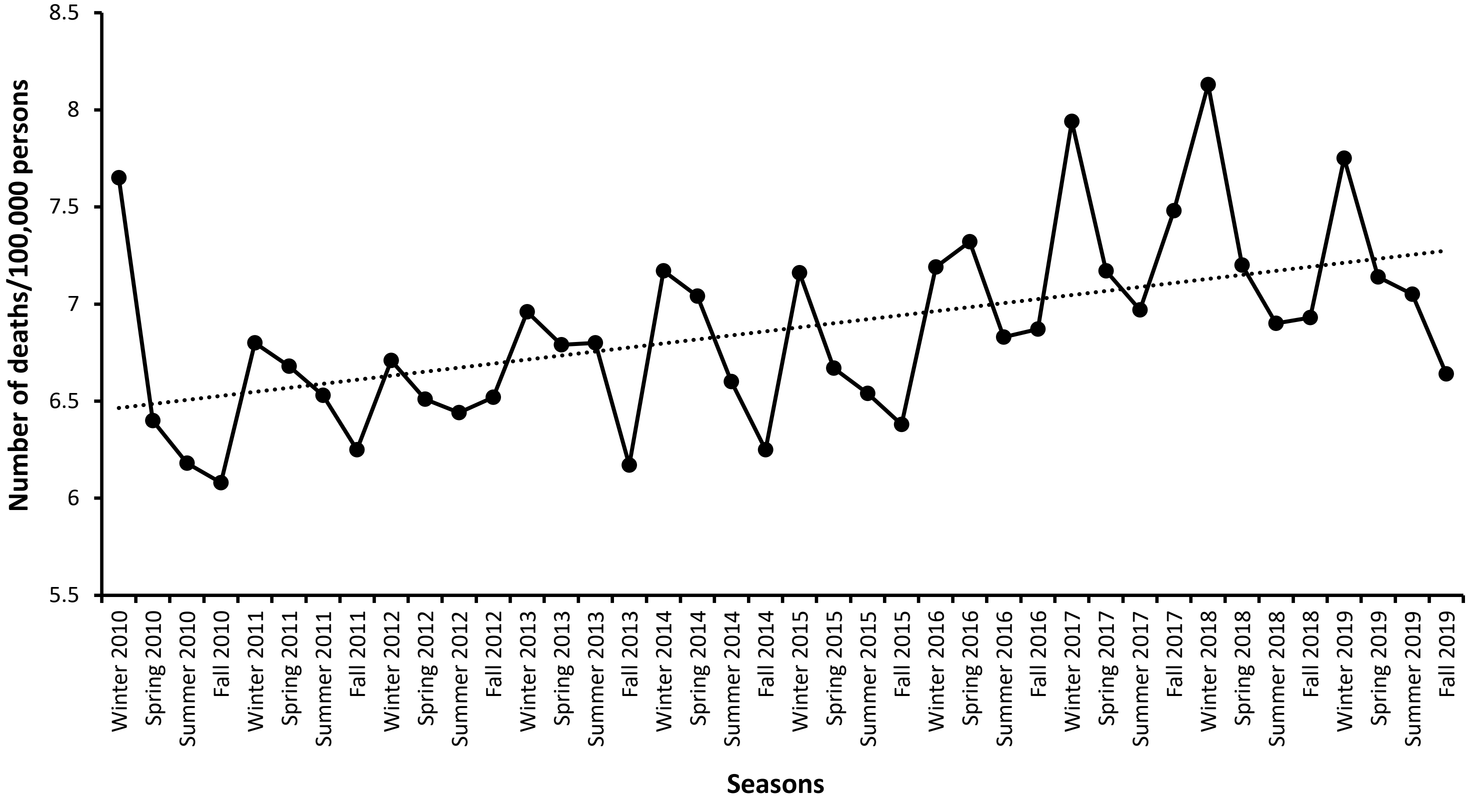

Figure 2.6: Seasonal patterns of diabetes-related mortality risks in Florida, 2010-2019.

2.5 Discussion

This study investigated geographic disparities and temporal patterns of county-level DRMR in Florida. The findings of this study will be useful for guiding evidence-based health planning and resource allocation to reduce disparities and improve diabetes health outcomes by targeting high risk communities with prevention and control programs.

Geographic distribution and clustering of DRMR

There is evidence of geographic disparities of DRMR in Florida, with most of the high-risk counties being located in the rural northern and central parts of the state. Some previous studies also consistently reported that diabetes mortality remains a significant cause of concern in rural America, especially in the Southern rural parts of the US (O'Brien & Denham, 2008; Brown-Guion et al., 2013; Callaghan et al., 2020). These rural areas experienced much higher DRMR compared to their urban counterparts (Callaghan et al., 2020), indicating a significant disparity between rural and urban areas. The lack of healthcare facilities in rural parts of Florida (only 27 hospitals serve rural areas compared to 190 hospitals in urban areas) might be a reason for these disparities (United States Department of Health and Human Services, 2022). Additionally, insufficient public transportation and long distances to healthcare facilities may also hinder the accessibility of healthcare services (O'Brien & Denham, 2008; Agency for Healthcare Research and Quality, 2023). Rural communities face challenges in attending regular health checkups, leading to lower detection rates of potential health problems, including diabetes, and subsequently increase the risks of diabetes-related deaths.

Significant high-risk spatial clusters of DRMR exist in the northern and central parts of the state. The result is consistent with the previous findings, which reported that some counties in the north regions of Florida are located within the diabetes belt and have excess diabetes prevalence and diabetes-related complications (Ford et al., 2005; Barker et al., 2011). Geographic disparities in the Diabetes Self-Management Education (DSME) program, which aims to educate diabetic patients on disease management, might be a reason behind these observed results. Some previous studies reported that the implementation of DSME program remains low in northern counties of Florida despite these regions having high prevalence (Paul et al., 2018; Khan et al., 2021). As a result, residents of the counties of north Florida are less aware of diabetes and diabetes-associated complications, hence increasing the risks of death.

Differences in socioeconomic conditions of the communities might be another reason for the observed cluster patterns. Most of the counties with below median household income are located in the northern and central regions of Florida (Florida Department of Health, 2023e). This disparity in income level may result in limited access to essential health insurance, preventive care, proper nutrition, and physical activity (Loftus et al., 2018), directly or indirectly influencing diabetes and associated complications. Studies report that adults with diabetes living in societies of low-income brackets are at a two-fold higher risk of death compared with their affluent family counterparts (Saydah & Lochner, 2010; Mackenbach, 2012; Dalsgaard et al., 2015). It is also possible that geographic differences in comorbidities play a role in the observed DRMR clustering. Previous research indicated that the northern parts of Florida exhibit significantly higher rates of comorbidities, including hypertension, heart disease, and kidney disease, compared to other regions within the state (Smith et al., 2018; Odoi et al., 2019). Comorbidities in individuals with diabetes can further increase the risk of mortality through their adverse effects on blood pressure, myocardial infarction, cancer risks, kidney function, and blood sugar control. Some previous studies already reported that cardiovascular disease is a strong predictor of diabetes-related mortality, and it was three to four times higher in patients with diabetes than those without diabetes (Khaw et al., 2004; Rawshani et al., 2017; Lu et al., 2021).

Temporal pattern of DRMR

The observed high mortality risks during the Winter months, followed by a decline from Summer to Fall and a subsequent increase in the Winter season throughout the study period, were comparable with reports from other previous studies (Tseng et al., 2005; Zhang et al., 2021). A recent study conducted by Yuanfeng et al. reported that the mean level of fasting blood glucose is significantly higher during winter than summer for many individuals including those with or without diabetes (Zhang et al., 2021), which may contribute to an increased risk of diabetes-related complications and death. Additionally, hemoglobin A1c (A1c) which is an indicator of the past 90 days' average blood glucose level, is also associated with microvascular and macrovascular risk in diabetes patients (Teitelbaum et al., 1993), and fluctuation of A1c level can increase risk of death. Tseng and his team recently reported that A1c level was higher during the winter season and lower in summer with a difference of 0.22 A1c unit (Tseng et al., 2005). A number of factors such as physiological, dietary, BMI, and physical activity changes in the Winter might be possible explanations for the observed seasonal pattern of DRMR. Physical inactivity and sedentary behavior have been reported to increase in winter months (Pivarnik, Reeves & Rafferty, 2003; Cepeda et al., 2018), which also increases high blood glucose as well as diabetes-related deaths.

Strengths and limitations

This study used a rigorous spatial epidemiological approach to investigate the geographic distribution and spatial clusters of DRMR in Florida. Tango's FSSS is a robust method of identifying spatial clusters as it does not involve multiple comparisons and it identifies both circular and irregularly shaped clusters. Moreover, this is the first study that has investigated geographic disparities of diabetes-related mortality risks in Florida. The information gathered is useful for guiding health planning and resource allocation for control and prevention programs. However, this study has some limitations. Tango's FSSS has low power for detecting circular clusters. Additionally, this study used surveillance data which might have some limitations in terms of case attainment and reporting. Finally, this study only investigated geographic disparities of DRMR at the county level; therefore, it was not possible to assess/identify lower-level disparities.

2.6 Conclusions

Geographic disparities in diabetes-related mortality risks exist in Florida, with notable high-risk clusters in the rural central and northern regions of the state. There was also evidence of increasing temporal trend and seasonal patterns of DRMR with the highest mortality risks being observed during the winter season. The study findings are useful for guiding health resource allocation targeting high risk communities so as to reduce health disparities in Florida. Future research will investigate predictors of the identified disparities.

CHAPTER 3

Predictors of County-Level Diabetes-Related Mortality Risks in Florida, USA: A Retrospective Ecological Study

Predictors of County-Level Diabetes-Related Mortality Risks in Florida, USA: A Retrospective Ecological Study

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My contributions to this paper included data preparation, analysis, interpretation of results, gathering and reviewing of literature, formulation of discussion topics, as well as drafting and editing the manuscript.

3.1 Abstract

Background: Diabetes is an increasingly important public health problem due to its socioeconomic impact, high morbidity, and mortality. Although there is evidence of increasing diabetes-related deaths over the last ten years, little is known about the population level predictors of diabetes-related mortality risks (DRMR) in Florida. Identifying these predictors is important for guiding control programs geared at reducing the diabetes burden and improving population health. Therefore, the objective of this study was to identify geographic disparities and predictors of county-level DRMR in Florida.

Methods: The 2019 mortality data for the state of Florida were obtained from the Florida Department of Health. The 10th International Classification of Disease codes E10-E14 were used to identify diabetes-related deaths which were then aggregated to the county-level. County-level DRMR were computed and presented as number of deaths per 100,000 persons. Geographic distribution of DRMR were displayed in choropleth maps and ordinary least squares regression model was used to identify county-level predictors of DRMR.

Results: There was a total 6,078 diabetes-related deaths in Florida during the study time period. County-level DRMR ranged from 9.6 to 75.6 per 100,000 persons. High mortality risks were observed in the northern, central, and southcentral parts of the state. Relatively higher mortality risks were identified in rural counties compared to their urban counterparts. Significantly high county-level DRMR were observed in counties with high percentages of the population that were: 65 years and older ($p < 0.001$), current smokers ($p = 0.032$), and insufficiently physically active ($p = 0.036$). Additionally, percentage of households without vehicles ($p = 0.022$) and percentage of population with diabetes ($p < 0.001$) were significant predictors of DRMR.

Conclusion: Geographic disparities of DRMR exist in Florida, with high risks being observed in northern, central, and southcentral counties of the state. The study identified county-level predictors of DRMR disparities in Florida. The findings are useful in guiding health professionals to better target intervention efforts.

3.2 Introduction

Diabetes affects millions of people worldwide. The number of diabetes patients in the United States (US) has been increasing over the last two decades, and it is projected to double or triple by 2050 (Boyle et al., 2001). As of 2021, 38.4 million people in the US had the disease, of which 29.7 million were diagnosed, while 8.7 million were undiagnosed and unaware of their illness (Centers for Disease Control and Prevention, 2022). The condition is closely associated with other chronic diseases such as heart disease, kidney disease, hypertension, stroke, and cardiovascular disease (Adailton da Silva et al., 2018; Centers for Disease Control and Prevention, 2023c, 2023e; Khan et al., 2018; Zinman et al., 2017). Therefore, the risk of death is higher among people with diabetes compared to those without the condition (Centers for Disease Control and Prevention, 2023b,c). Diabetes is the eighth leading cause of death in the US (Centers for Disease Control and Prevention, 2023f), and a total of 103,294 people died from the disease in 2021 (Centers for Disease Control and Prevention, 2023a). However, recent studies indicate that the impact of diabetes on overall mortality is significantly underestimated (Stokes & Preston, 2017; Xu et al., 2022). In reality, diabetes mortality risk in the US is nearly 12%, implying that it is the third leading cause of death in the nation, after heart disease and malignant neoplasms (Stokes & Preston, 2017; Xu et al., 2022).

Fifteen Southeastern states, including Florida, have higher prevalence (≥11.0%) compared to the nation's average (8.5%) (Danaei et al., 2009; Barker et al., 2011). In 2011, the Centers for Disease Control and Prevention (CDC) declared the 644 counties of those 15 states as the "diabetes belt" (Barker et al., 2011). In Florida, the prevalence of the disease is estimated at 12.5% and has been increasing over the past ten years (Florida Department of Health, 2023a). The economic cost of the disease in Florida was estimated at approximately $25 billion ($19.3

billion direct costs and $5.5 billion indirect costs) in 2017 (Florida Department of Health, 2023a). It is reported that medical expenses for individuals with diabetes in Florida are 2.3 times higher than for those without diabetes (Florida Department of Health, 2023a).

Despite advances in diabetes management and treatment, the mortality risk associated with diabetes remains high in Florida. It is estimated that the age-adjusted diabetes-related mortality risk (DRMR) in the state has increased from 16.9 to 24.2 per 100,000 persons over the last ten years (Florida Department of Health, 2023f). Although some previous studies used rigorous epidemiological/statistical approaches to investigate diabetes prevalence and pre-diabetes (Khan et al., 2021; Lord et al., 2020, 2023; Okwechime et al., 2015), very little is known about DRMR and associated predictors in Florida. Therefore, the objective of this study was to identify county-level predictors of DRMR in Florida. This information will be useful for guiding control efforts and would contribute towards achieving one of the objectives of the Healthy People 2030 of reducing health disparities and enhancing overall population health.

3.3 Methods

3.3.1 Ethics approval

This study was approved by the University of Tennessee Institutional Review Board (IRB number: UTK IRB-23-07809-XM). The review board determined that the study "is eligible for exempt review under 45 CFR 46.101 pursuant to category 4ii: Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects". The data were accessed for research purposes beginning November 7, 2023. The authors did not have access to information that could identify participants during or after data collection. All the methods were carried out according to relevant guidelines and regulations.

3.3.2 Study area

This study was conducted in the state of Florida which is located between 27° 66' N and 81° 52' W and spans 65,758 square miles. County land area ranges from 243.6 square miles (Union county) to 1,998 square miles (Collier county) (United States Census Bureau, 2023b). As of 2022, Florida was one of the most populous states in the US. About 22.2 million people live in the state, 50.8% of whom are female and 49.2% are male (United States Census Bureau, 2024a). Miami-Dade county is the most populous (2.6 million population), whereas Liberty county, located in the northern part of the state **(Figure 3.1),** is the least populated with only 7,987 people (United States Census Bureau, 2024a). The age distribution of the adult population in Florida is 24% 18-34 years old, 26% 35-49 years old, 25% 50-64 years old, and 22% are seniors (≥65 years old) (United States Census Bureau, 2024a). There are 76.8% White, 17% Black, and 6.2% all other races in Florida. Of the 67 counties in the state, 30 are rural and 37 are urban **(Figure 3.1).**

3.3.3 Diabetes-related death data

Individual-level death data covering the time period January 1 to December 31, 2019, were obtained from the Florida Department of Health. The International Classification of Disease (ICD) 10^{th} revision was used to identify the cause of death, and ICD-10 codes E10-E14 were used to identify diabetes-related deaths (World Health Organization, 2019). No distinction was made between type 1 and 2 diabetes. The number of diabetes-related deaths were aggregated at

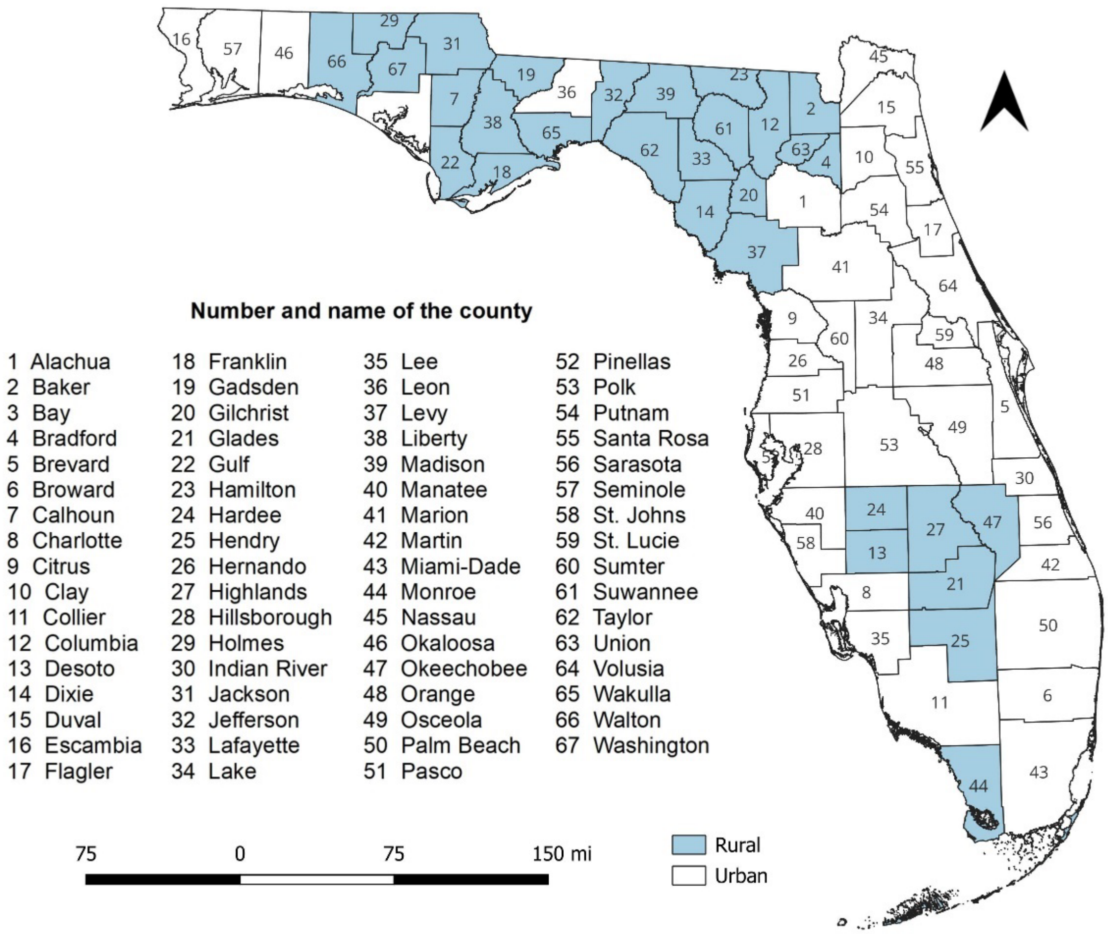

Figure 3.1: Study area showing the geographic distribution of rural and urban counties in Florida, USA.

the county level using R statistical software version 4.2.2 (R Core Team, 2023). Population estimates for 2019 were obtained from the American Community Survey (ACS) (United States Census Bureau, 2024c) and used as denominator to calculate DRMR. County-level DRMRs were then calculated and expressed as number of deaths per 100,000 persons. A conceptual model of the potential predictors of DRMR was constructed **(Figure 3.2).** Data on potential predictors of DRMRs were extracted from several data sources **(Table 3.1)**

3.3.4 Descriptive Statistics

Descriptive analyses were conducted using R statistical software version 4.2.2 (R Core Team, 2023) and implemented in R studio version 1.4.1717 (R Studio Team, 2020). Normal distribution of continuous variables was evaluated using the Shapiro-Wilk test. Since some of the continuous variables were not normally distributed, medians and interquartile ranges were used for summary statistics **(Table 3.2).**

3.3.5 Investigation on county-level predictors of DRMR

A global ordinary least squares regression (OLS) model was used to identify county-level predictors of DRMR in Florida. After selecting potential predictors using the conceptual model, a two-step process was used to fit a multivariable model with the outcome specified as DRMR. The first step in model-building was to assess the univariable associations between each potential predictor and the outcome. A liberal p-value of ≤ 0.20 was used for this assessment. Using p-value ≤ 0.20 allows for assessment of potentially important confounders during the multivariable analysis stage (Dohoo, Martin & Stryhn, 2012). All the variables that showed significant associations (based on a relaxed p-value of ≤ 0.20) in the univariable analyses were subjected to two-way Spearman rank correlation analyses. Spearman rank correlation analysis was appropriate for this assessment because some continuous variables were not normally distributed

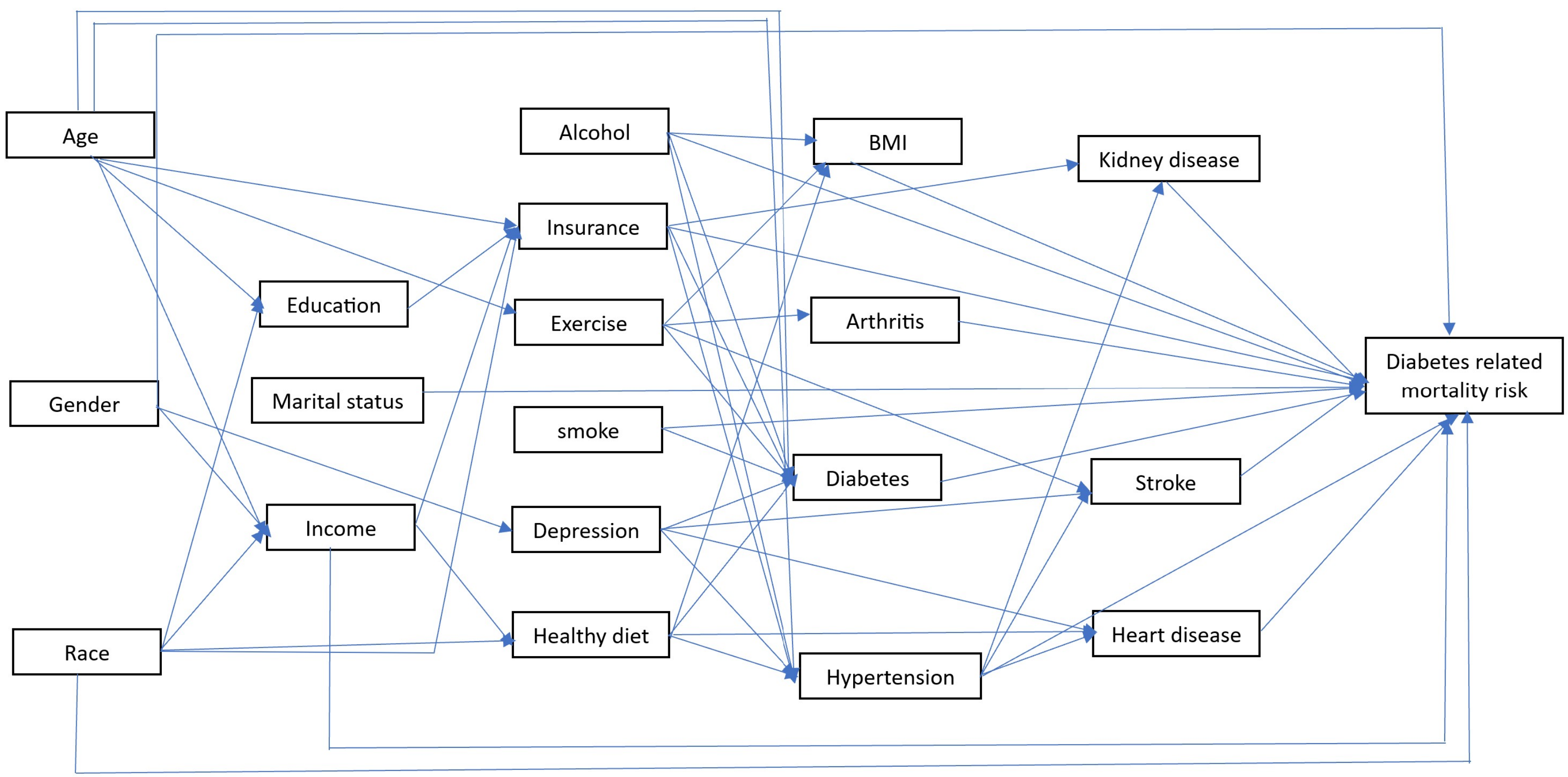

Figure 3.2: Conceptual model showing potential predictors of diabetes-related mortality risks.

Table 3.1: Data source and variables used in the identification of predictors of diabetes-related mortality risks in Florida, 2019.

Source	Data obtained
Florida Behavioral Risk Factors Surveillance System	Percentage of population with diabetes
	Percentage of population attending DSME[1]
	Percentage of population reporting depressed
	Percentage of population that are heavy drinkers
	Percentage of population that have disability
	Percentage of population with hypertension
	Percentage of population with kidney disease
	Percentage of population that get regular checkups
	Percentage of population taking medication for cholesterol
	Percentage of population with heart disease
	Percentage of population that have had stroke
	Percentage of population with arthritis
	Percentage of population with insurance coverage
	Percentage of population not going to a doctor for medical cost
	Percentage of population that have personal doctor
	Percentage of population reporting poor health
	Percentage of population reporting good health
	Percentage of population reporting normal weight
	Percentage of population with obesity
	Percentage of population who are overweight
	Percentage of population that are underweight
	Percentage of population that are current smoker
	Percentage of population that are snuff users
	Average age when diagnosed with diabetes
	Percentage of population that are current e-cigarette users
	Percentage of population with high cholesterol
	Percentage of population taking medication for hypertension
	Percentage of population eating vegetables once a day
	Percentage of population eating fruits once a day
	Percentage of population that are highly physically active
	Percentage of population that are physically active

Table 3.1 Continued

Source	Data obtained
	Percentage of population that are insufficiently physically active
	Percentage of population that are physically inactive
American Community Survey	Percentage of population <20 years old
	Percentage of population 20-44 years old
	Percentage of population 45-64 years old
	Percentage of population ≥65 years old
	Percentage of population with income <25k per year
	Percentage of population with income 25k-50k per year
	Percentage of population with income >50k per year
	Percentage of population that are non-Hispanic White
	Percentage of population that are non-Hispanic Black
	Percentage of population that are non-Hispanic Others
	Percentage of population that are Hispanic
	Percentage of population that have <high school education
	Percentage of population with high school education
	Percentage of population with some college education
	Percentage of population with college education
	Percentage of population that are married
	Percentage of population that are divorced/widow/separated
	Percentage of population that never married/unmarried couple
	Percentage of population that are male
	Percentage of population that are female
	Percentage of households without vehicle
County Health Rankings and Roadmaps	Percentage of rural population
	Average parts per million of CO_2 or Air pollution
	Percentage of population with limited access to healthy food
	Percentage of population having food insecurity
	Percentage of population not having access to exercise
	Percentage of population that are unemployed
United States Census Bureau TIGER Geodatabase	County-level cartographic boundary shapefile

[1]Diabetes Self Management Education

Table 3.2: Summary statistics of potential predictors of county-level diabetes-related mortality risks in Florida, 2019.

Predictor	Mean	SD[1]	Median	Minimum	Maximum	IQR[2]
Percentage of population with diabetes	13.37	3.09	12.9	6.4	20.8	2.3
Percentage of population attending DSME[1]	54.40	10.75	53.10	29.60	76.60	16.05
Percentage of population reporting depressed	17.78	3.26	17.9	10.30	24.70	3.7
Percentage of population that are heavy drinkers	7.22	2.24	7.00	1.30	12.20	2.85
Percentage of population that have disability	34.46	5.38	34.60	21.00	45.90	7.85
Percentage of population with hypertension	38.21	5.07	37.60	25.30	47.00	7.20
Percentage of population with kidney disease	3.76	1.16	3.60	1.70	7.70	1.50
Percentage of population that get regular checkups	76.12	3.88	76.10	63.20	89.10	4.85
Percentage of population taking medication for cholesterol	61.33	5.12	61.40	47.60	70.50	7.60
Percentage of population with heart disease	5.65	1.48	5.70	2.50	9.00	2.00
Percentage of population that have had stroke	4.52	1.29	4.50	1.20	7.00	2.00
Percentage of population with arthritis	28.97	5.31	28.70	17.80	40.20	6.90
Percentage of population with insurance coverage	82.61	4.31	83.20	68.60	90.50	4.60
Percentage of population not going to a doctor for medical cost	16.41	3.01	16.00	9.50	21.90	4.45
Percentage of population that have personal doctor	73.65	5.12	74.40	57.60	86.00	6.80
Percentage of population reporting poor health	22.55	4.86	22.60	8.60	33.10	7.15
Percentage of population reporting good health	77.45	4.86	77.40	66.90	91.40	7.15
Percentage of population reporting normal weight	29.71	5.27	29.60	19.40	43.90	6.20
Percentage of population with obesity	32.46	6.06	32.20	18.20	48.10	7.85
Percentage of population who are overweight	35.68	3.64	36.10	124.60	43.80	3.55
Percentage of population that are underweight	2.14	0.91	2.10	0.30	5.40	1.25
Percentage of population that are current smoker	19.14	5.08	18.50	11.00	32.40	6.65
Percentage of population that are snuff users	4.98	3.27	3.60	1.20	13.50	5.10
Average age when diagnosed with diabetes	48.94	2.49	49.10	42.40	53.50	3.05
Percentage of population that are current e-cigarette users	5.73	1.84	5.70	2.00	13.10	2.15
Percentage of population with high cholesterol	32.32	3.82	31.80	23.60	43.70	4.45
Percentage of population taking medication for hypertension	78.95	4.07	78.83	67.32	89.25	4.95
Percentage of population eating vegetables once a day	82.05	4.75	82.56	66.58	93.33	5.87
Percentage of population eating fruits once a day	60.50	5.77	60.85	49.11	72.77	7.96
Percentage of population that are highly physically active	34.53	5.61	33.78	24.35	54.60	7.00
Percentage of population that are physically active	15.24	3.45	14.86	9.09	27.53	4.41

Table 3.2 Continued

Predictor	Mean	SD[1]	Median	Minimum	Maximum	IQR[2]
Percentage of population that are insufficiently physically active	15.85	3.16	15.69	9.41	26.20	3.57
Percentage of population that are physically inactive	34.35	0.28	33.58	22.67	51.23	10.68
Percentage of population <20 years old	21.68	3.40	21.70	8.30	29.50	4.05
Percentage of population 20-44 years old	29.98	5.19	30.80	13.90	41.50	6.10
Percentage of population 45-64 years old	26.67	2.09	27.00	20.80	31.70	2.10
Percentage of population ≥65 years old	21.64	7.73	20.10	11.60	56.70	8.25
Percentage of population with income <25k per year	33.96	7.14	34.27	20.30	53.39	12.52
Percentage of population with income 25k-50k per year	27.88	4.21	28.35	20.55	40.20	5.28
Percentage of population with income >50k per year	38.15	9.41	37.17	19.39	58.94	16.29
Percentage of population that are non-Hispanic White	69.75	15.02	74.07	13.07	89.53	15.68
Percentage of population that are non-Hispanic Black	13.07	9.50	9.97	1.10	54.42	10.96
Percentage of population that are non-Hispanic Others	3.83	1.65	3.64	0.92	8.59	2.05
Percentage of population that are Hispanic	13.36	12.44	8.97	2.77	69.79	10.40
Percentage of population that have <high school education	15.81	6.23	14.75	5.38	38.37	6.89
Percentage of population with high school education	35.23	7.11	35.00	19.88	54.82	11.78
Percentage of population with some college education	29.89	4.54	30.83	17.57	35.54	7.35
Percentage of population with college education	19.07	8.06	18.44	6.06	35.62	13.31
Percentage of population that are married	50.75	2.67	50.38	38.49	66.98	5.62
Percentage of population that are divorced/widow/separated	24.19	3.28	24.85	16.34	30.61	4.46
Percentage of population that never married/unmarried couple	25.06	5.79	23.88	10.60	45.16	7.26
Percentage of population that are male	51.12	4.46	48.77	46.84	70.09	5.49
Percentage of population that are female	48.88	4.46	51.23	29.91	53.16	5.48
Percentage of rural population	37.50	32.26	23.77	0.02	100.00	58.63
Percentage of households without vehicle	5.72	1.91	5.26	1.89	10.33	2.07
Average parts per million or Air pollution	7.52	0.91	7.70	5.20	9.10	1.30
Percentage of limited access to healthy food	9.33	5.74	9.00	0.00	31.00	6.00
Percentage of food insecurity	14.00	2.22	14.00	10.00	20.00	3.50
Percentage of not having access to exercise	68.94	24.52	77.00	10.00	100.00	35.00

[1]Diabetes Self Management Education

and Spearman correlation analysis does not assume normal distribution (Zar, 2014). When two variables showed a strong correlation ($r>0.7$), only one of them was included in the subsequent multivariable model. The decision on which variable to include in the multivariable model from a pair of highly correlated variables was based on biological and statistical considerations. Backward elimination process was then performed, using a critical p-value of 0.05, to fit the final multivariable model. The backward elimination approach allows for assessment of confounders during the modeling process (Dohoo, Martin & Stryhn, 2012), enhances the accuracy of prediction, and reduces the likelihood of overfitting the data (Draper & Smith, 1998). Confounding variables were then evaluated by comparing changes in regression coefficients after running the model with and without the suspected confounder. If there was ≥20% change in the coefficients of any of the variables in the model, the suspected variable was then identified as a confounder and retained in the model regardless of its statistical significance. Two-way interaction terms of the variables of final multivariable model were evaluated based on biological relevance, and only those with a p-value ≤0.05 were included in the final model. Variance Inflation Factor (VIF) was used to assess multicollinearity in the final model. If the VIF value of a variable was ≥10, it was considered to have high collinearity with the other variables. Overall goodness-of-fit of the final model was assessed using Adjusted R-squared (R^2) and Akaike Information Criterion (AIC). Residual plots, Jarque-Bera test, and Breusch-Pagan test were used to evaluate the assumptions of normality and homoscedasticity. The residuals were also used to identify outliers, while leverage, Cook's distance, and Difference in Fits (DFITS) were used to identify influential observations. All the analyses were performed using R statistical software version 4.2.2 (R Core Team, 2023). Moran's I, implemented in GeoDa (Anselin, Syabri & Kho, 2006), using 1st order queen contiguity spatial weights, was used to assess for spatial effects or spatial autocorrelation in the residuals.

3.3.6 Cartographic display

Cartographic boundary files were downloaded from the TIGER geodatabase (United States Census Bureau, 2023b) and used to generate maps. QGIS 3.34 (QGIS org, 2024) was used for all cartographic displays. Choropleth maps for the distribution of county-level diabetes-related mortality risks and significant predictors from the final multivariable model were generated using Jenk's optimization classification scheme.

3.4 Results

3.4.1 Geographic disparities in distribution of diabetes-related mortality risks

There was a total of 6,078 diabetes-related deaths reported in Florida in 2019. Of these, 59.3% were male, 40.7% were female, 75.7% were White, 20.4% were Black, and 3.9% were all other races. The percentage of diabetes-related deaths was highest (69.6%) among seniors (≥65 years old). The county-level mortality risks varied across the state, ranging from 9.6 per 100,000 persons in St. Johns County to 75.6 in Desoto County **(Figure 3.3).** Of the 67 counties in the state, 35 had mortality risks equal to or greater than the national average (31.1 per 100,000 persons). Counties with high mortality risks were mainly in the northern (Holmes, Washington, Jefferson, Taylor, Santa rosa, and Dixie), central (Citrus, Hernando, Sumter, Marion, and Putnam), and south-central (Desoto and Hardee) parts of Florida **(Figures 3.1 and 3.3).** Conversely, the southernmost counties (Broward, Collier, and Monroe) had relatively lower mortality risks compared to other parts of the state. It is worth noting that most counties with high mortality risks were mainly in rural areas.

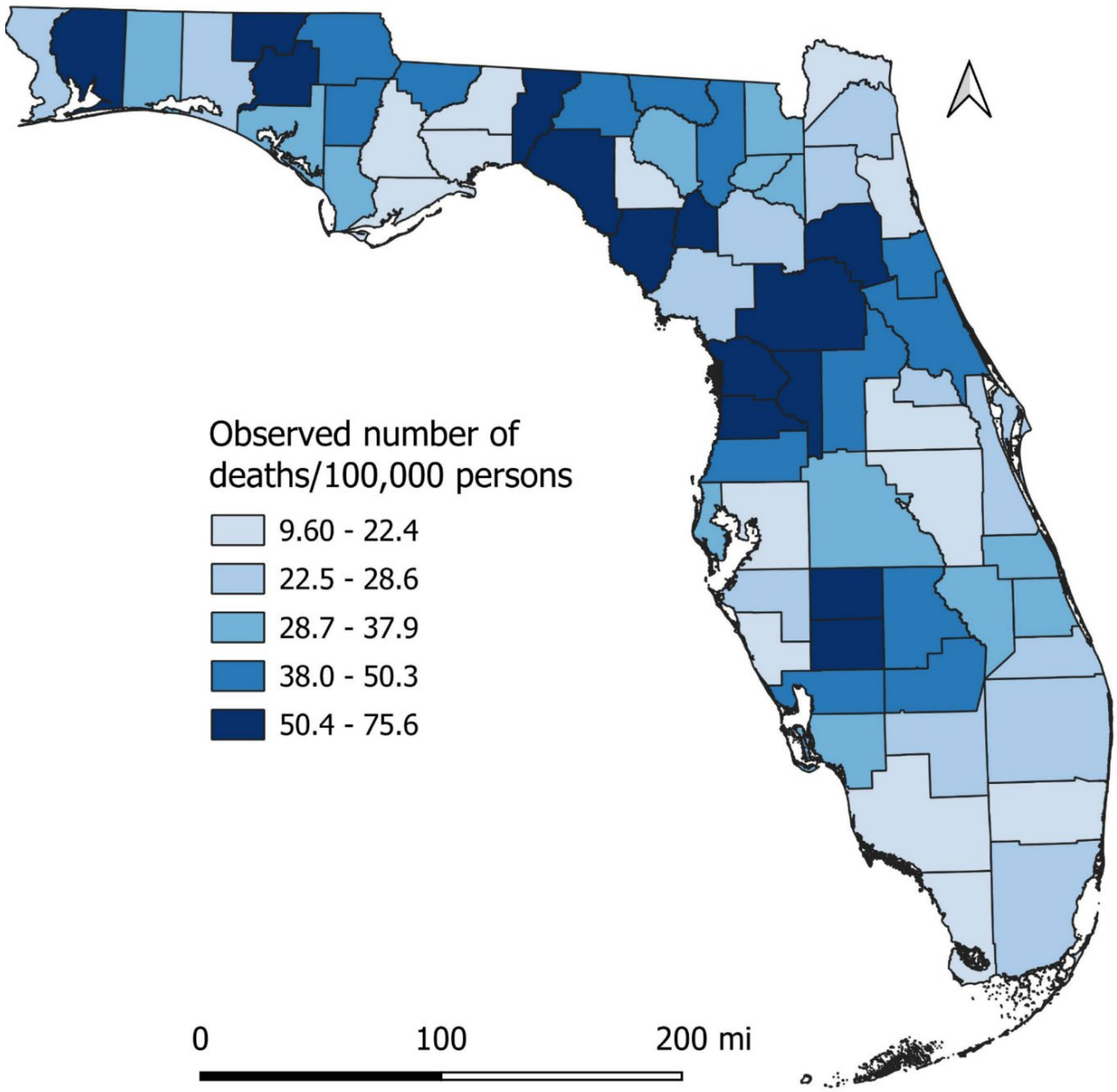

Figure 3.3: Geographic disparities in distribution of diabetes-related mortality risks in Florida, 2019.

3.4.2 Predictors of diabetes-related mortality risks

Results of the univariable associations between county-level DRMR and its potential predictors are shown in **Table 3.3**. Forty-six of the 59 variables assessed had significant univariable associations with DRMR using a relaxed critical p-value of ≤0.20. However, based on the final multivariable model, significant predictors of disparities in county-level DRMRs were percentage of population that had diabetes (p<0.001), were aged 65 or above (p<0.001), were current smokers (p=0.032), were insufficiently physically active (p=0.036), and percentage of households without vehicles (p=0.022) **(Table 3.4).** No significant interactions and confounders were detected. The p-value of Moran's I (p=0.747) indicated that there was no spatial effects or spatial autocorrelation in the residuals and hence the model did not violate the independence assumption. A comparison of the observed DRMR and the model estimates of the DRMR is shown in **Figure 3.4.** The general pattern in distribution of the model estimates is quite similar to that of the observed DRMR indicating that the model is doing well in predicting DRMR in the study area **(Figure 3.4).** The northern, central, and south-central counties had high percentages of population with diabetes **(Figure 3.5)** and insufficiently physically active population, mirroring the spatial patterns of DRMRs **(Figure 3.3).** High percentages of population with diabetes and insufficient physical activity tended to mainly occur in rural counties. The percentage of smokers tended to be high in the northern regions of the state, whereas high percentages of households without vehicles were evident across both northern and southern parts of the state **(Figure 3.5).** Despite lower DRMR in the southernmost counties of the state, these regions had higher percentages of population aged 65 or above compared to other parts of the state **(Figure 3.5).**

Table 3.3: Results of univariable associations between potential predictors and county-level diabetes-related mortality risks in Florida, 2019.

Predictors	Coefficient (95% CI[1])	p-value
Percentage of population with diabetes	2.989 (2.069, 3.908)	<0.001
Percentage of population attending DSME[2]	-0.259 (-0.593, 0.073)	0.124
Percentage of population reporting depressed	0.519 (-0.593, 1.631)	0.354
Percentage of population that are heavy drinkers	-1.595 (-3.173, -0.016)	0.048
Percentage of population that have disability	1.328 (0.736, 1.921)	<0.001
Percentage of population with hypertension	1.329 (0.689, 1.969)	<0.001
Percentage of population with kidney disease	5.272 (2.417, 8.128)	<0.001
Percentage of population that get regular checkups	0.259 (-0.678, 1.196)	0.583
Percentage of population taking medication for cholesterol	0.788 (0.102, 1.474)	0.025
Percentage of population with heart disease	4.602 (2.420, 6.783)	<0.001
Percentage of population that have had stroke	4.926 (2.368, 7.483)	<0.001
Percentage of population with arthritis	1.587 (1.024, 2.149)	<0.001
Percentage of population with insurance coverage	-0.624 (-1.456, 0.209)	0.139
Percentage of population not going to a doctor for medical cost	1.627 (0.483, 2.772)	0.006
Percentage of population that have personal doctor	0.239 (-0.469, 0.949)	0.502
Percentage of population reporting poor health	1.351 (0.679, 2.023)	<0.001
Percentage of population reporting good health	-1.351 (-2.023, -0.679)	<0.001
Percentage of population reporting normal weight	-0.641 (-1.314, 0.033)	0.062
Percentage of population with obesity	0.768 (0.197, 1.339)	0.009
Percentage of population who are overweight	-0.860 (-1.839, 0.119)	0.084
Percentage of population that are underweight	1.073 (-2.921, 5.067)	0.593
Percentage of population that are current smoker	0.674 (-0.024, 1.372)	0.058
Percentage of population that are snuff users	1.110 (0.028, 2.192)	0.045
Average age when diagnosed with diabetes	0.761 (-0.693, 2.214)	0.300
Percentage of population that are current e-cigarette users	-0.362 (-2.346, 1.622)	0.717
Percentage of population with high cholesterol	1.559 (0.687, 2.431)	<0.001
Percentage of population taking medication for hypertension	0.798 (-0.086, 1.664)	0.078
Percentage of population eating vegetables once a day	0.122 (-0.645, 0.889)	0.751
Percentage of population eating fruits once a day	-0.732 (-1.338, -0.126)	0.019
Percentage of population that are highly physically active	-0.118 (-0.767, 0.532)	0.718

Table 3.3 Continued

Predictors	Coefficient (95% CI[1])	p-value
Percentage of population that are physically active	-1.197 (-2.213, -0.181)	0.022
Percentage of population that are insufficiently physically active	-1.031 (-2.157, 0.096)	0.072
Percentage of population that are inactive	0.641 (0.114, 1.168)	0.018
Percentage of population <20 years	-0.818 (-1.872, 0.236)	0.126
Percentage of population 20-44 years old	-0.804 (-1.477, -0.131)	0.020
Percentage of population 45-64 years old	-0.817 (-2.552, 0.917)	0.350
Percentage of population ≥65 years old	0.575 (0.126, 1.025)	0.013
Percentage of population with income <25k per year	0.695 (0.214, 1.176)	0.005
Percentage of population with income 25k-50k per year	1.601 (0.831, 2.372)	<0.001
Percentage of population with income >50k per year	-0.721 (-1.065, -0.377)	<0.001
Percentage of population that are non-Hispanic White	0.164 (-0.076, 0.403)	0.177
Percentage of population that are non-Hispanic Black	0.081 (-0.303, 0.464)	0.676
Percentage of population that are non-Hispanic Others	-2.970 (-5.059, -0.882)	0.006
Percentage of population that are Hispanic	-0.234 (-0.521, 0.054)	0.109
Percentage of population that have <high school education	0.850 (0.303, 1.396)	0.003
Percentage of population with high school education	0.921 (0.461, 1.379)	<0.001
Percentage of population with some college education	-1.059 (-1.818, -0.299)	0.007
Percentage of population with college education	-0.888 (-1.283, -0.493)	<0.001
Percentage of population that are married	0.009 (-0.684, 0.701)	0.981
Percentage of population that are divorced/widow/separated	2.034 (1.042, 3.026)	<0.001
Percentage of population that never married/unmarried couple	-0.659 (-1.268, -0.051)	0.034
Percentage of population that are male	0.375 (-0.438, 1.188)	0.360
Percentage of population that are female	-0.375 (-1.187, 0.438)	0.361
Percentage of rural population	0.131 (0.023, 0.239)	0.018
Percentage of households without vehicle	1.654 (-0.211, 3.519)	0.081
Average parts per million of CO_2 or Air pollution	1.401 (-2.603, 5.404)	0.487
Percentage of population with limited access to healthy food	0.664 (0.050, 1.278)	0.034
Percentage of population having food insecurity	3.441 (2.039, 4.844)	<0.001
Percentage of population of not having access to exercise	-0.209 (-0.348, -0.069)	0.004

[1]Confidence Interval

[2]Diabetes Self Management Education

Table 3.4: Results of multivariable model showing significant predictors of county-level diabetes-related mortality risks in Florida, 2019.

Predictors	Coefficient (95%CI[1])	p-value
Percentage of population ≥65 years old	0.009 (0.004, 0.014)	<0.001
Percentage of population that are current smokers	0.008 (0.001, 0.015)	0.032
Percentage of insufficiently physically active population	0.013 (0.001, 0.026)	0.036
Percentage of households without vehicle	0.021 (0.003, 0.038)	0.022
Percentage of population with diabetes	0.034 (0.022, 0.046)	<0.001

[1]Confidence Interval

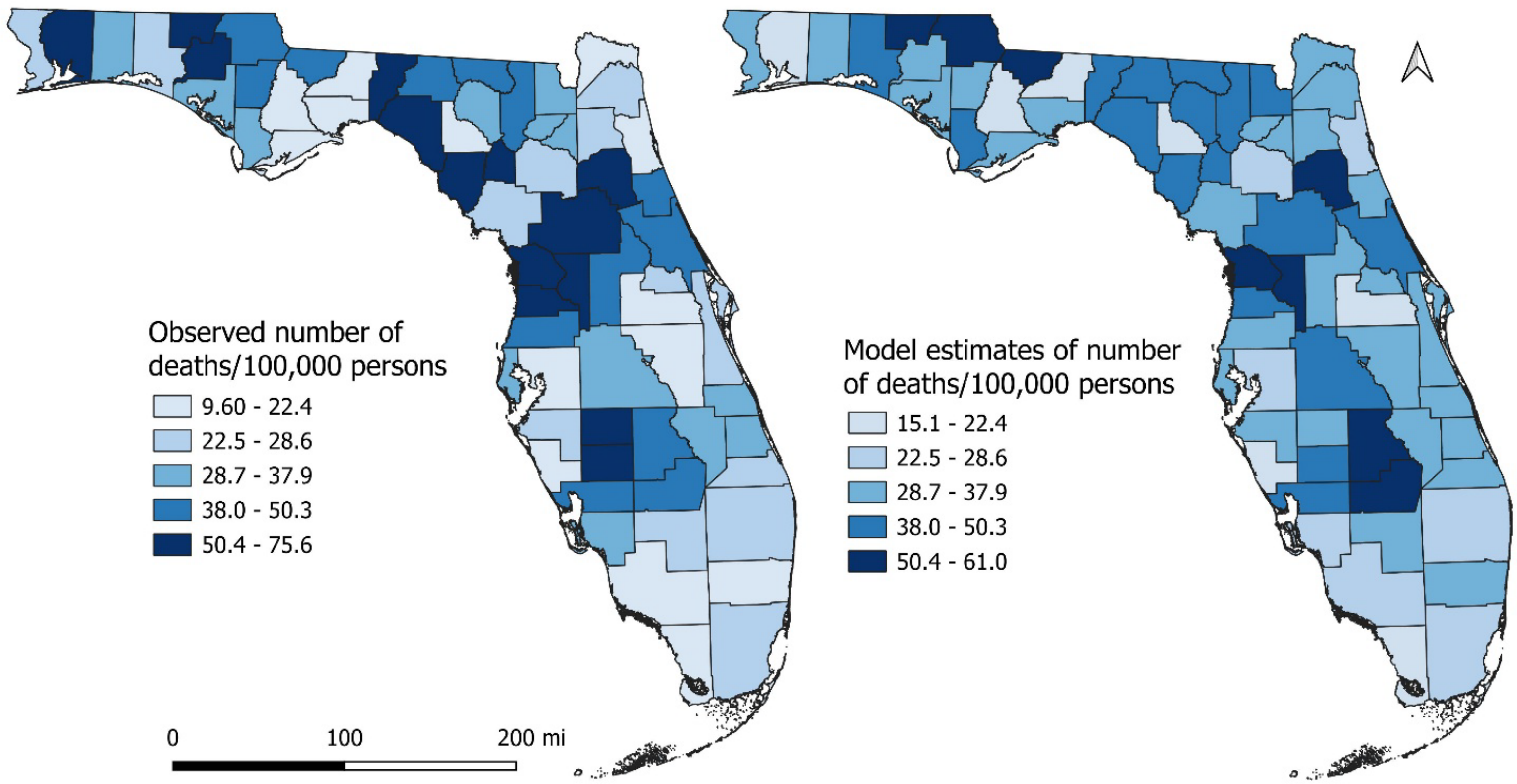

Figure 3.4: Comparison of actual diabetes-related mortality risk with model estimates of the diabetes-related mortality risks.

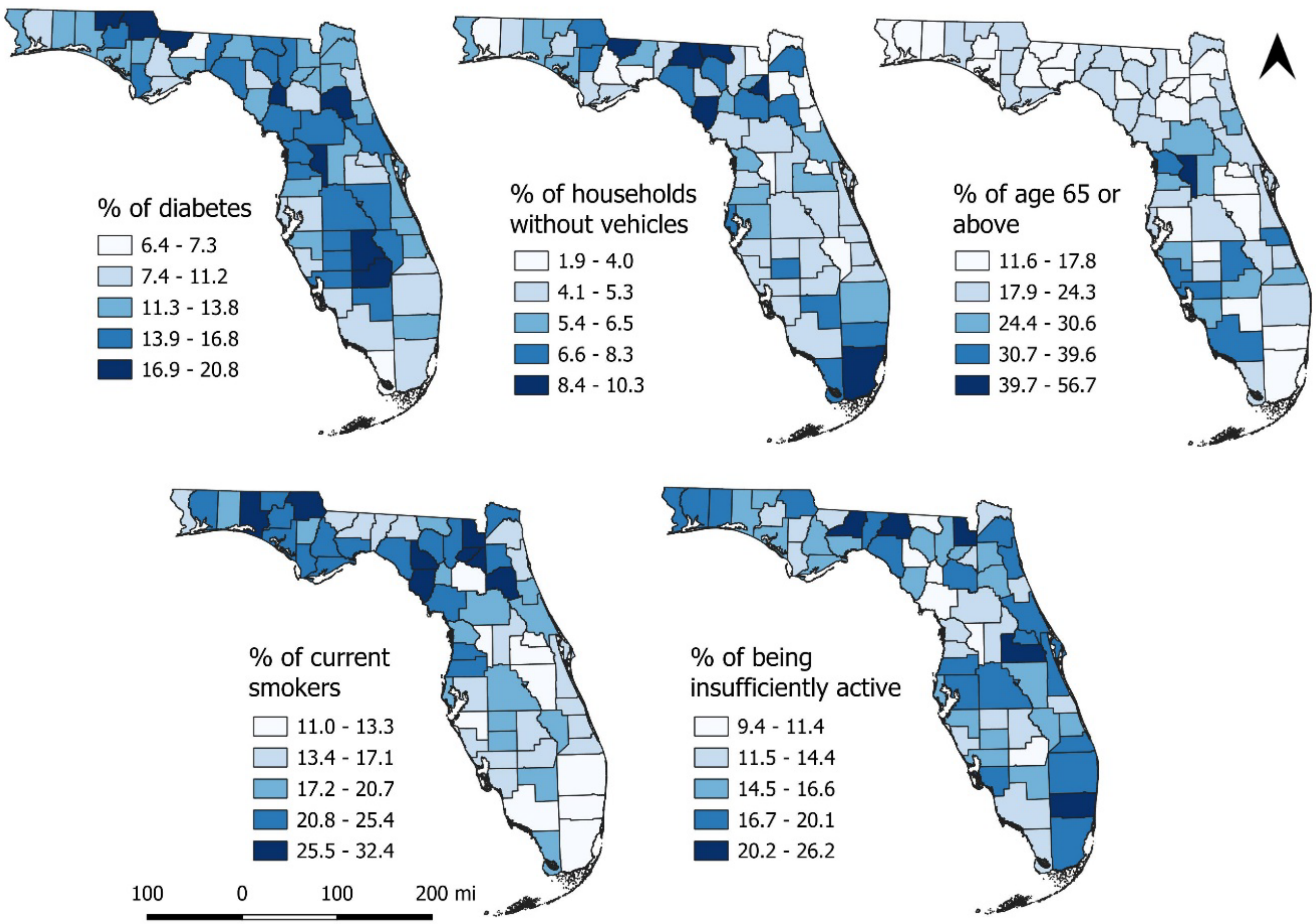

Figure 3.5: Geographic distribution of the predictors of diabetes-related mortality risks in Florida, 2019.

3.5 Discussion

This study investigated geographic disparities of county-level DRMR and its predictors in Florida. The findings are crucial in identifying counties with high mortality risks and predictors of the identified spatial patterns so as to provide information for targeted evidence-based health programs to reduce DRMR in Florida.

The identified significant association between high county-level DRMR and the high percentage of older population (age ≥65 or above) is consistent with findings of a previous study conducted by Dugani et al., who reported that county-level DRMR was significantly higher among the older population (greater than 55 years old) compared to younger adults (Dugani et al., 2022). It is worth noting that Florida has the second-highest percentage of adults aged 65 or above (22%) (United States Census Bureau, 2023c). This demographic trend in Florida is associated with higher rates of diabetes-related comorbidities, resulting in higher DRMR in this older age group. Additionally, data from the Florida Department of Health (FDH) indicated that the mortality risk from diabetes among adults 65 or above (116.7 per 100,000 persons) was approximately 7.5 times higher than the mortality risk among those less than 65 years old (15.5 per 100,000 persons) (Florida Department of Health, 2023g).

The association between county-level percentage of physical inactivity and high DRMR observed in this study has been reported in several previous studies (Hu et al., 2004; Hamilton, Hamilton & Zderic, 2014; Tiang et al., 2023). One study reported that DRMR was 1.65 times higher among counties with high percentages of physically inactive people compared to those counties with lower percentages of physically inactive people (Turi & Grigsby-Toussaint, 2017). This might be due to the fact that the counties with high percentages of physical inactivity are closely linked to higher risk of chronic conditions and shorter life expectancy (University of

Wisconsin Population Health Institute, 2023). There is evidence that a large percentage of the population in counties with high DRMR do not meet the recommended physical activity guidelines compared to those in counties with low DRMR (Florida Department of Health, 2023h). This suggests the need to encourage the population to increase levels of physical activity. Green spaces, including parks, trails, community gardens, and playgrounds, are important components of local built environments that impact physical activity and overall community health (Taylor et al., 2007). Therefore, increasing access to these green spaces and physical fitness areas would potentially help to increase the percentage of population attaining the recommended level of physical activity (Centers for Disease Control and Prevention, 2023g) and potentially reduce the risk of chronic conditions including diabetes.

The observed positive association between the percentage of current smokers and DRMR is consistent with reports by the FDH that counties with percentage of current smokers higher than the national average (11.5%) experienced 1.3 times higher DRMR than those counties where the percentages of current smokers were below the national average (Florida Department of Health, 2023i). This might be due to the fact that most Florida counties with high percentage of current smokers are located in the northern rural regions of the state, where the educational attainment is generally lower, and the population might be unaware of the detrimental effects of smoking and diabetes (United States Census Bureau, 2023d). Smoking and diabetes are double hazards to the health of rural communities and aggravate diabetes complications, thereby increasing the risk of death (Zheng et al., 2020). Although not directly compared with the current study, several previous studies conducted at the individual level reported that smoking was an independent risk factor for diabetes-related mortality because of increased risk of other chronic conditions like cardiovascular disease and coronary heart disease among diabetes patients (Ford

& DeStefano, 1991; Colhoun et al., 2001; Cederholm et al., 2008; Fagard & Nilsson, 2009; Campagna et al., 2019; Abdelhamid et al., 2023). It has also been reported that the risk of diabetes-related death is 1.6 times higher among smokers than non-smokers (Ford & DeStefano, 1991). Therefore, smoking cessation programs are important in reducing the risks of death from these conditions. The World Health Organization reported that smoking cessation not only reduces the risk of developing diabetes but also reduces the risk of diabetes complications and death (World Health Organization, 2023). Hence, continuing educational programs are encouraged for those counties with high percentage of current smokers and diabetes patients.

Reliable transportation plays a fundamental and crucial role in ensuring access to healthcare and medication. Persons with diabetes need reliable transportation to ensure regular clinician visits, access to medications, and adjustments in treatment plans as needed. The current study identified a significant association between high DRMR and high percentage of households without vehicles in Florida. Insufficient public transportation and long drive times to healthcare facilities in counties with a high percentage of households without vehicles might reduce accessibility to healthcare services (United States Department of Health and Human Services, 2022), leading to high DRMRs. A recent study conducted by Lord et al. at the zip code level in Florida also reported that lack of access to vehicles was significantly associated with diabetes-related hospitalization rates (Lord & Odoi, 2024), thereby increasing the risk of complications associated with the disease. Furthermore, another previous study also reported that transportation barriers to healthcare facilities were more likely to be associated with South and Midwest US counties compared to those from other parts of the country (Wolfe, McDonald & Holmes, 2020). As a result, understanding the relationship between county-level high DRMR and percentage of households without vehicles is important for addressing population health in most vulnerable regions of the state.

Strengths and limitations

This is the first study to investigate county-level predictors of diabetes-related mortality risks in Florida using rigorous statistical approaches. The findings of this study are useful for guiding evidence-based interventions by identifying DRMR disparities and its predictors. However, this study has some limitations. The BRFSS survey data are self-reported and so might have reporting bias. The survey does not distinguish between type 1 and type 2 diabetes. These limitations notwithstanding, the findings provide useful information regarding disparities and determinants of DRMR in Florida.

3.6 Conclusions

There is evidence that geographic disparities in DRMR exist and are determined by distribution of percentages of the population aged 65 or older, current smokers, population having insufficient physical activity, population with diabetes, and households without vehicles. These findings are important for guiding targeted health planning and service provision to reduce the disease burden and DRMR in Florida.

CHAPTER 4

Time Series Analysis and Prediction of Diabetes-Related Mortality Risk in Florida

Time Series Analysis and Prediction of Diabetes-Related Mortality Risk in Florida

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This chapter is a manuscript that is under review in PLOSONE journal.

My contributions to this paper included data preparation, analysis, interpretation of results, gathering and reviewing of literature, formulation of discussion topics, as well as drafting and editing the manuscript.

4.1 Abstract

Introduction: Diabetes is the seventh leading cause of death and represents a significant disease burden in Florida. Although there is evidence of geographic disparities of diabetes-related mortality risk (DRMR) in Florida, little is known about the temporal trends, seasonality, and prediction of future burden of DRMR in the state and yet this information is important for health planning and disease control efforts. Therefore, the objectives of this study were to identify temporal trends and predict the occurrence of DRMR in Florida.

Methods: Retrospective monthly mortality data from January 1999 to December 2023 were obtained from the Centers for Disease Control and Prevention WONDER database. The International Classification of Disease codes E10-E14 were used to identify diabetes-related deaths. Monthly DRMRs were computed and presented as number of deaths per 100,000 persons. The DRMR data were then split into a training dataset (January 1999 to June 2021) and a testing dataset (July 2021 to December 2023). Seasonal Autoregressive Integrated Moving Average model with Exogenous variable (SARIMAX) and Neural Network Autoregressive model with Exogenous variable (NNARX) were used for time series analysis of the training and full datasets. The number of Corona Virus Disease 2019 (COVID-19) cases was used as an exogenous variable in both models to adjust for the impact of COVID-19 on DRMR. The forecasted values obtained from the above time series models applied to the training dataset were compared to the actual values from the testing dataset to evaluate their predictive performance. Finally, predictions of DRMR from January 2024 to December 2027 were generated using models applied to the full dataset.

Results: A total of 139,085 diabetes-related deaths were reported during the study period. The Black population consistently had higher mortality risks than the White population throughout

the study period. The DRMR was relatively stable from 1999 to 2008, declined from 2009 to 2015, and then increased from 2016 to 2023. There were seasonal patterns of DRMR in Florida with the highest mortality risks recorded during the winter months. The SARIMAX model performed better than the NNARX model. Additionally, the prediction of SARIMAX model using the full data set suggests a gradual increase in DRMR from January 2024 to December 2027.

Conclusions: The study identified seasonal patterns and forecasted a gradual upward trend of DRMR in Florida. The findings are useful in guiding health planning and future intervention programs to reduce DRMR.

4.2 Introduction

Diabetes is a chronic metabolic disease characterized by fasting plasma glucose levels ≥126 mg/dl or glycated hemoglobin ≥6.5% (American Diabetes Association, 2024a). Over the last 2 decades, the number of people with diabetes in the United States (US) has been increasing and is projected to double by 2050 (Boyle et al., 2001). As of 2021, 38.4 million people in the US had the condition, of whom 29.7 million were diagnosed, while 8.7 million were undiagnosed (Centers for Disease Control and Prevention, 2022). Diabetes is the 8th leading cause of death in the US (Centers for Disease Control and Prevention, 2023f), and a total of 103,294 people died from the disease in 2021 (Centers for Disease Control and Prevention, 2023a). However, findings from recent studies suggest that mortality attributable to the disease is underestimated (Stokes & Preston, 2017; Xu et al., 2022). In fact, diabetes accounts for approximately 12% of all deaths in the US, making it the 3rd leading cause of death (Stokes & Preston, 2017; Xu et al., 2022). The burden is especially high among older people aged ≥60 years, and results in an average of 5 years of life lost (Campbell et al., 2012; Gordon-Dseagu, Shelton & Mindell, 2014).

In Florida, where diabetes is considered an epidemic, approximately 107,700 new cases of the disease are diagnosed each year (American Diabetes Association, 2024b). The mortality risk due to diabetes in the state is estimated at 24.8 per 100,000 persons (Centers for Disease Control and Prevention, 2023e). The burden of the condition is expected to increase in the state because of the aging population since the risk of diabetes mortality increases with age (Dugani et al., 2022). It is reported that the percentage of senior (>65 years) population in Florida has been increasing over the last 10 years and the state currently has the 2nd highest percentage of this population in the US (Florida Department of Health, 2023b). Moreover, the demographic profile of the state is unique due to migrations into the state. Data from the United States Census Bureau indicate that approximately one million people migrated to Florida from other states in 2023 (United States Census Bureau, 2024d). These migrations into the state include a substantial proportion of Black and Hispanic individuals (United States Census Bureau, 2024d), a segment of the population that has higher prevalence and mortality due to diabetes compared to their white counterparts (McBean et al., 2004; Jain et al., 2023). Thus, the burden of diabetes mortality is expected to worsen in Florida because of the growth of the elderly as well as Black and Hispanic populations.

Accurate prediction of diabetes-related mortality is crucial for effective health planning (Ward, Iglesias & Brookes, 2020; Punyapornwithaya et al., 2023). Therefore, time series analysis serves as a useful method for accurately predicting disease events and assessing their impact (Linden, 2018). Additionally, it helps to understand the temporal dynamics of disease patterns because this provides insights into how the condition evolves over time and its effects on population health. Hence, forecasting diabetes-related mortality risk (DRMR) is crucial in Florida in order to make early predictions and guide health planning and service provision. Unfortunately, no such studies have been conducted and yet this information is important for planning. Therefore, the objective of this study was to identify temporal patterns and forecast diabetes-related mortality risk in Florida.

4.3 Methods

4.3.1 Ethics approval

This study was approved by the University of Tennessee Institutional Review Board (IRB number: UTK IRB-23-07809-XM). The review board determined that the study "is eligible for exempt review under 45 CFR 46.101 pursuant to category 4ii: Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects". The authors did not have access to information that could identify participants during or after data collection. The research data were accessed for research purposes on September 30, 2024.

4.3.2 Data source and management

This study was conducted in the state of Florida which has a population of approximately 22.2 million people (United States Census Bureau, 2024a). Individual-level monthly diabetes-related death data covering the time period from January 1999 to December 2023 were downloaded from the Centers for Disease Control and Prevention (CDC) WONDER database (Centers for Disease Control and Prevention, 2024e). This is a comprehensive online public health information system developed by the CDC to provide timely, actionable information to public health professionals (Friede, Reid & Ory, 1993). The mortality data were derived from death certificates filed in the state of Florida. Deaths of non-residents, including non-resident aliens, nationals living abroad, and residents of US territories such as Puerto Rico, Guam, the Virgin Islands, and other territories, as well as fetal deaths, were excluded (Centers for Disease Control and Prevention, 2024e). The International Classification of Disease (ICD) 10th revision was used to identify the cause of death, and ICD-10 codes E10-E14 were used to identify all diabetes-related deaths (World Health Organization, 2019). Additionally, population estimates for each year from 1999 to 2023 were obtained from the American Community Survey and used as denominators to calculate DRMR (United States Census Bureau, 2024c). Finally, monthly DRMRs were calculated and expressed as number of deaths per 100,000 persons.

4.3.3 Time series decomposition and determination of temporal trends and seasonality of DRMR

Monthly DRMR data were converted into a time series object using “ts()” function in R statistical software version 4.2.2 for further analysis (R Core Team, 2023). A time series decomposition approach was then applied to analyze the three main components: trend, seasonality, and residuals (noise). The plots derived from the decomposition helped to identify the patterns in the data, particularly the seasonal effects and long-term trends. Additionally, Ollech and Webel's combined seasonality test (WO-test) was used to assess for the seasonality (Ollech & Webel, 2021). The WO-test was performed using the “seastests” package via the “combined_test” function in R (Ollech, 2022; R Core Team, 2023). This test combines the results of both the Q-statistic test for seasonal autocorrelations (QS) test and the Kruskal-Wallis (KW) test, which are calculated using the residuals from an automatically fitted non-seasonal Auto Regressive Integrated Moving Average model. The WO-test classified the diabetes mortality time series as seasonal if the p-value of the QS test was <0.01 or the p-value for the KW test was <0.002 (Ollech, 2022).

4.3.4 Modeling approach

Two time series models were used to predict future DRMRs: (i) Seasonal Autoregressive Integrated Moving Average with Exogenous variable (SARIMAX) and (ii) Neural Network Autoregressive model with Exogenous variable (NNARX). The full dataset (Jan. 1999-Dec. 2023) was split into a training dataset (Jan. 1999 to Jun. 2021) which comprised 90% of the data, and a testing dataset (Jul. 2021-Dec. 2023) which comprised 10% of the data **(Figure 4.1).**

Forecasts for the test period (Jul. 2021-Dec. 2023) were then generated using the training dataset and subsequently compared to the observed values of the testing dataset to evaluate the forecasting performance of the models. To ensure the accuracy of the forecasts, it was important to use the most recent data for predictions (Punyapornwithaya et al., 2023). Therefore, the full dataset (Jan 1999-Dec 2023) was used in the time series models to generate forecasts for the next four years (Jan. 2024-Dec. 2027) **(Figure 4.1).** The analysis involved two steps. First, the most effective forecasting model was identified by comparing the performance of the two time series models with the validation dataset (testing data). Second, the best-performing time series model, determined in the 1st step, was applied to the full dataset to forecast DRMR for the time period Jan. 2024-Dec. 2027.

4.3.4.1 SARIMAX model

The SARIMAX model is an extension of the Seasonal Autoregressive Integrated Moving Average (SARIMA) model that not only accounts for seasonal effects but also incorporates exogenous variables to enhance forecasting accuracy. This model introduces three new hyperparameters to define the autoregression, differencing, and moving average components specific to the seasonal aspect of the series along with an additional parameter to indicate the seasonal period. The SARIMA component within the SARIMAX model is represented as SARIMA (p, d, q) (P, D, Q), where p, d, and q correspond to the order of autoregression, the degree of differencing, and the order of moving average, respectively. Similarly, P, D, and Q represent the seasonal orders of autoregression, seasonal differencing, and seasonal moving average, respectively. Thus, the SARIMAX model is expressed mathematically as,

$$\phi_p(B)\phi_p(B^s)\nabla^d\nabla_s^D y_t = \beta_k x'_{k,t} + \theta_q(B)\Theta_Q(B^s)\varepsilon_t \ldots\ldots (1)$$

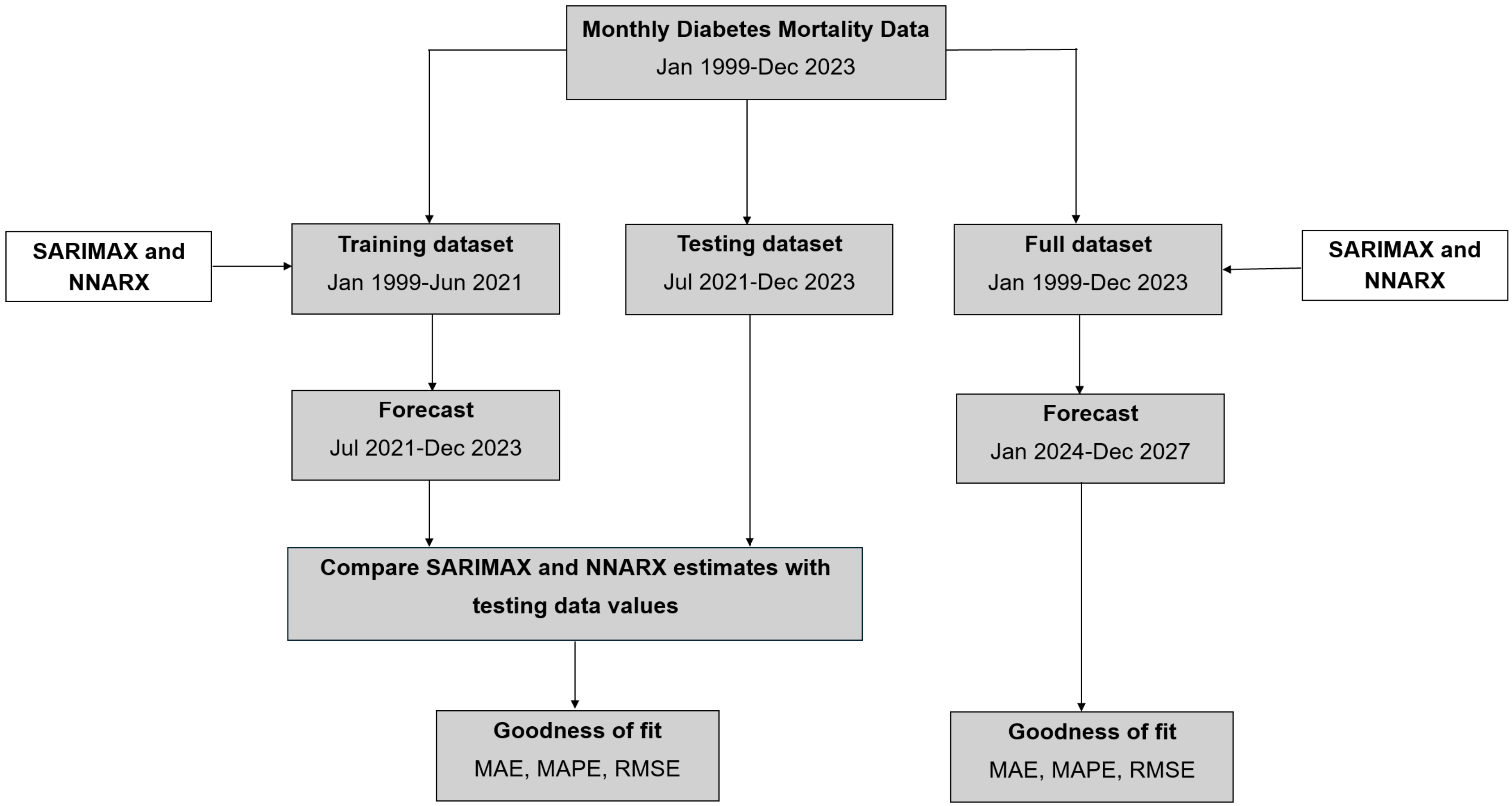

Figure 4.1: Time series modeling and forecasting approach of diabetes-related mortality risks in Florida from 1999 to 2027.

Where,

$\phi_p(B)$ is the regular autoregressive (AR) polynomial of order p

$\phi_p(B^s)$ is the seasonal AR polynomial of order P

∇^d non-seasonal differencing operator

∇_s^D seasonal differencing operator

y_t is the forecast variable which is future diabetes-related mortality risk

β_k is the coefficient value of the k^{th} exogenous input variable

$x'_{k,t}$ is the vector including the k^{th} exogenous input variable at time, t

$\theta_q(B)$ is the regular moving average (MA) polynomial of order, q

$\Theta_Q(B^s)$ is the seasonal MA polynomial of order, Q

B is the backshift operator, which operates on the observation y_t by shifting it one point in time (i.e. $B^k(y_t) = y_{t-k}$). The term ε_t follows a white noise process and s defines the seasonal period. The number of Corona Virus Disease-19 (COVID-19) cases in the state was used as an exogenous variable in this SARIMAX model to adjust for the impact of COVID-19 on DRMR.

4.3.4.2 NNARX model

Neural Network (NN) model replicates the functioning of the human brain's neural network as follows: (a) information is processed within elements called neurons (nodes); (b) information is transferred between these neurons through their connections; (c) each connection has a specific weight, which acts as a multiplier for the information passed between neurons; (d) each neuron typically applies a non-linear transfer function to calculate its output (Banihabib, Bandari & Peralta, 2019). Therefore, the NN model can be visualized as a network of interconnected neurons or nodes that capture complex, non-linear relationships and functional forms. Similarly, the NNARX is a specialized type of NN model that integrates information from exogenous variables into its framework. The NN (p, k) term of NNARX model is defined to indicate that there are (p) lagged inputs and (k) nodes in the hidden layer. With seasonal data, the NN model can be written as,

$$NN(p, P, K)m \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Where p is the number of non-seasonal lagged inputs for the linear autoregressive process (AR), P indicates the seasonal lags for the AR process, k denotes the number of neurons in the hidden layer, and m represents the seasonal period. The NNARX is a hybrid model that includes the function of NN, autoregressive components, and exogenous variables. The model can be expressed mathematically as follows (Ardalani-Farsa & Zolfaghari, 2010),

$$y_t = \mathrm{F}(y_{t-1}, y_{t-2}, y_{t-3}, \ldots \ldots \ldots u_t, u_{t-1}, u_{t-2}, u_{t-3}, \ldots \ldots) + \epsilon_t \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots (3)$$

Where,

F is the function of the neural network NN

y is the variable of interest (i.e. future DRMR)

u is the exogenous variable (i.e. number of COVID-19 cases)

ϵ is the error term

4.3.4.3 Evaluation of model performance

The full dataset was used to develop final time series models and predict future DRMRs for the next four years following the most recent observation in the dataset (Hyndman, 2018). Several evaluation error metrics, including mean absolute error (MAE), mean absolute percent error (MAPE), mean absolute scaled error (MASE), and root mean squared error (RMSE) were then used to assess the predictive performance of models developed using both the full dataset and the training dataset (Hyndman, 2018).

Data preparation, including organization, decomposition, and segmentation of the time series, was conducted using the R statistical software. The "forecast" package (Hyndman, 2018) provided essential functions for developing the time series models and evaluating their predictive performance. The auto.arima() function was used for the SARIMAX model, while the nnetar() function was employed for the NNARX model. Detailed descriptions of these functions are available in the respective package manuals (Hyndman et al., 2020). Additionally, for graphical visualization, the "ggplots" package was used to create detailed and interactive representations of the data and forecasts.

4.4 Results

4.4.1 Descriptive statistics

A total of 139,085 diabetes-related deaths, comprising 65.1% males and 43.9% females, were reported during the study period (1999-2023). The annual DRMR ranged from 26.2 (in 2011) to 36.9 (in 2021) per 100,000 persons **(Figure 4.2).** The DRMR was relatively stable from 1999 to 2008 and then slightly declined from 2009 to 2015, followed by an increase from 2016 to 2023 **(Figure 4.2).** During the COVID-19 pandemic (2020-2023), the mortality risk increased steadily from 28.7 in 2019 to 34.9 in 2020 and remained high for the remainder of the study period. Similar patterns of high DRMR during the pandemic were observed among both the Black and White populations. However, the Black population consistently had higher mortality risks than their White counterparts throughout the study period **(Figure 4.3).**

The decomposition of monthly diabetes mortality time series data into its trend, seasonality, and remainder (residuals or error) components is shown in **Figure 4.4.** The trend appears to be relatively stable or slightly increasing over the years, with some minor fluctuations. The fluctuations were regular and repeated at fixed intervals, suggesting a predictable pattern of high and low DRMR. There was seasonal pattern as evidenced by the results of both the Q-statistic test for seasonal autocorrelations ($p<0.001$) and Kruskal-Wallis tests ($p<0.001$). However, the residuals showed no clear pattern (appeared random and evenly spread around zero), suggesting that the residuals had only random noise and captured most of the systemic variation in the data.

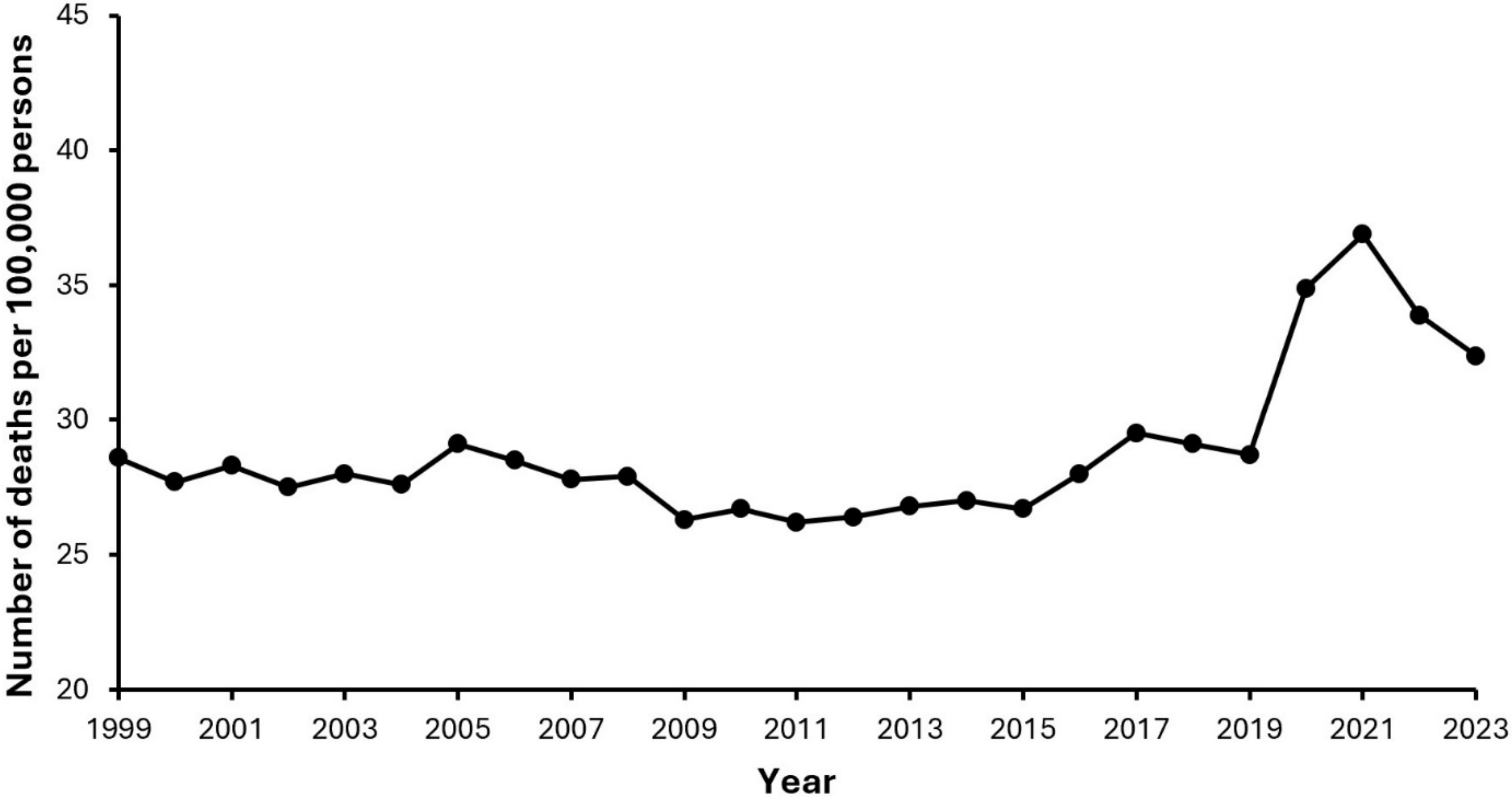

Figure 4.2: Annual diabetes-related mortality risk in Florida, 1999-2023.

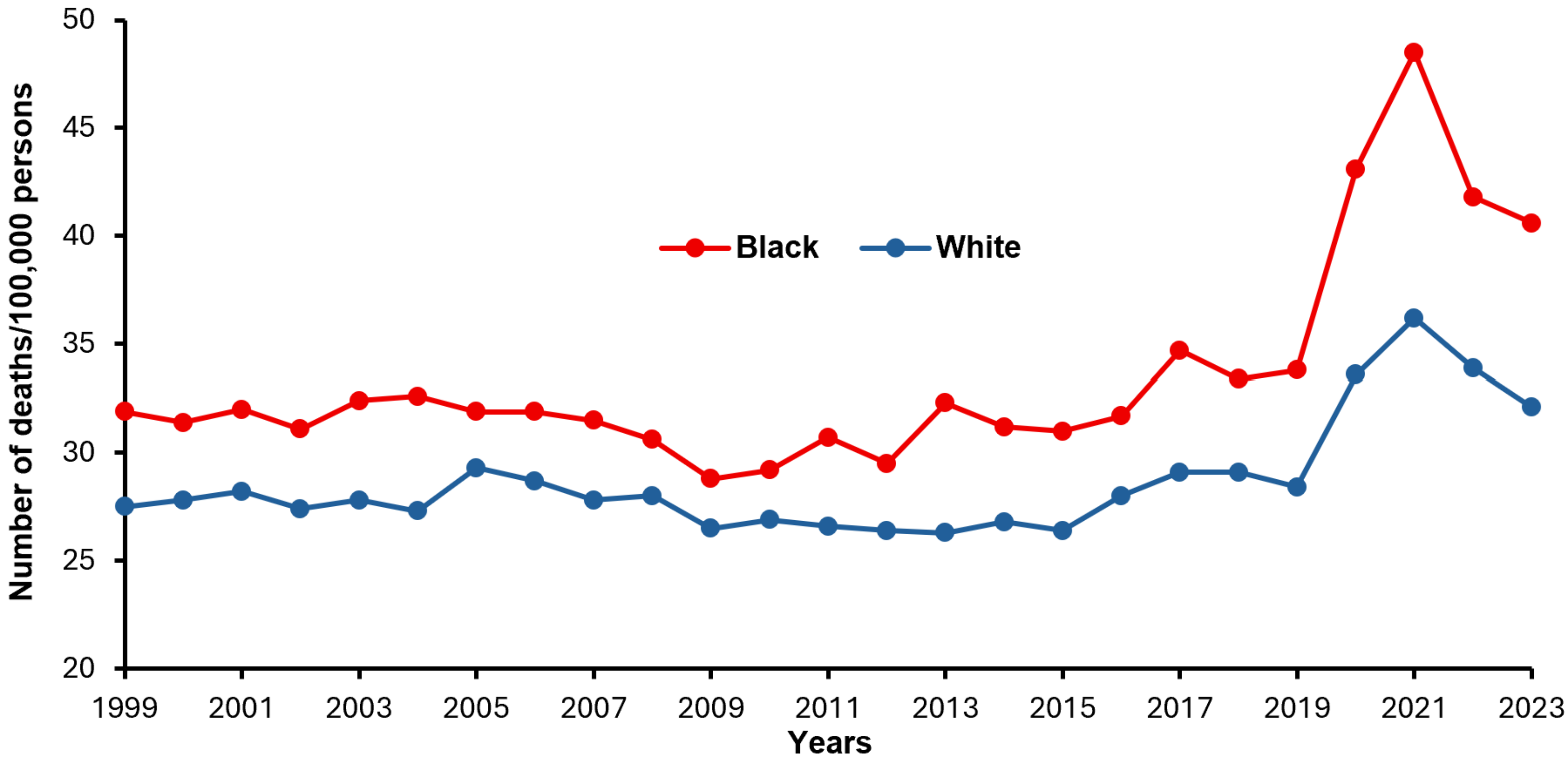

Figure 4.3: Annual diabetes-related mortality risks in Florida among Black and White populations, 1999 to 2023.

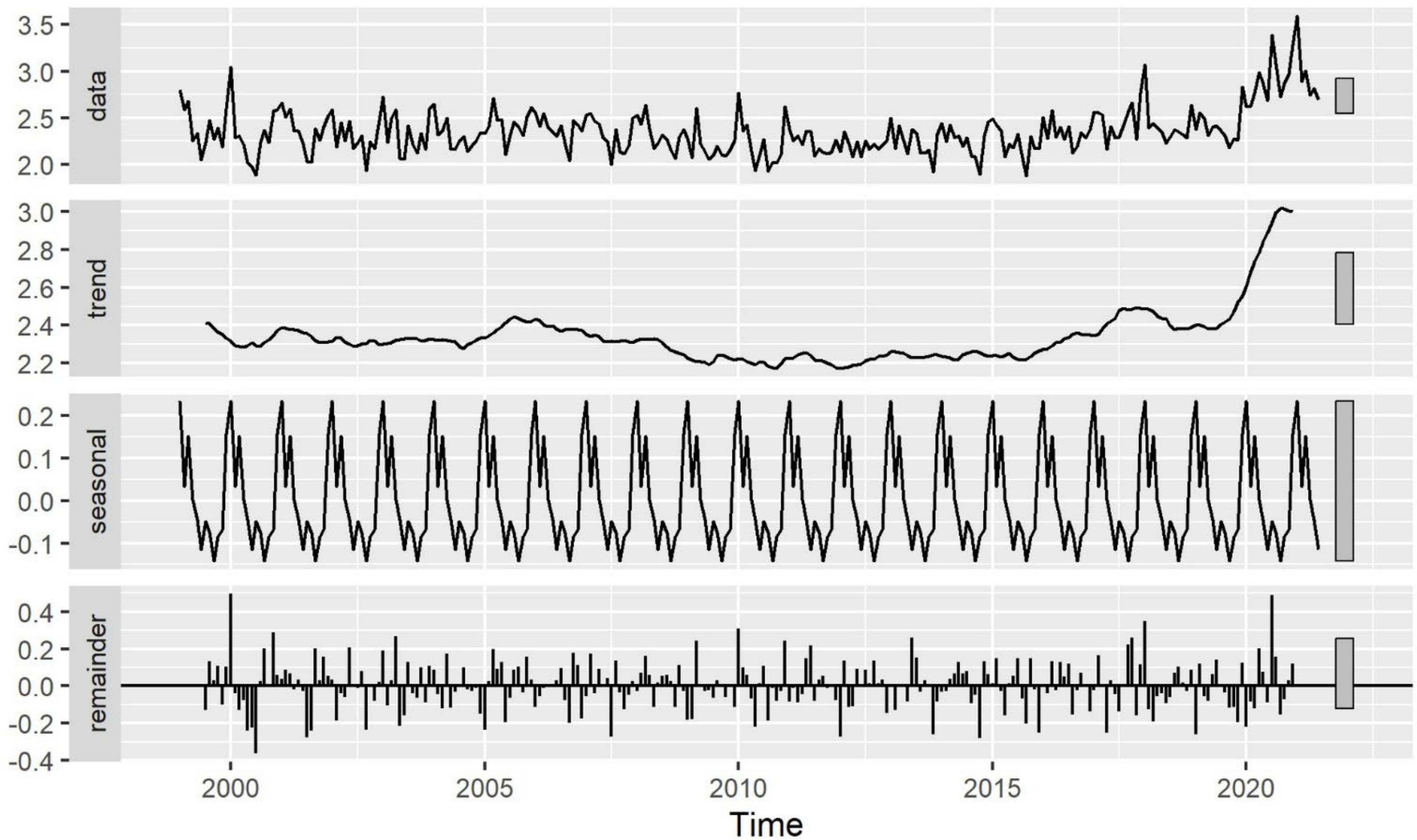

Figure 4.4: Decomposition of monthly diabetes-related mortality risks time series data into trend, seasonality, and remainder (residuals).

4.4.2 Model selection and prediction performance

Since the SARIMAX(1,1,2)(1,1,1) [12] model had the lowest Akaike Information Criterion (AIC), it was selected to fit the SARIMAX model for the training data (Jan 1999-Jun 2021). The results of the comparison of forecasted DRMR values (July 2021-Dec 2023) with observed DRMR values during the same time period are shown in **Figure 4.5.** The figure shows the DRMR obtained from the predictions of SARIMAX (1,1,2)(1,1,1) [12] model is quite close to the observed data series values and therefore the model fits the data well **(Figure 4.5).** The residuals of the forecasted SARIMAX (1,1,2)(1,1,1) [12] model were normally distributed as evidenced by the bell-shaped curve in the histogram **(Figure 4.6A).** Additionally, the majority of the ACF values fall within the confidence interval bounds **(Figure 4.6B)**, suggesting that the residuals are uncorrelated. This is further confirmed by the results of Ljung-Box test ($p=0.105$).

An NNARX(12,1,7) [12] neural network model was selected as the best fit for the training data spanning January 1999 to June 2021. A comparison of the forecasted DRMR (Jul 2021-Dec 2023) and observed DRMR for the same time period is shown in **Figure 4.7.** The residuals of the forecasted NNARX(12,1,7) model [12] are normally distributed as evidenced by the bell-shaped distribution in the histogram **(Figure 4.8A).** Additionally, most ACF of the residuals lie within the confidence interval bounds **(Figure 4.8B)** indicating that the residuals are uncorrelated. However, the forecasted DRMR values do not closely match the observed values in this time series model **(Figure 4.7).**

The error metrics for the SARIMAX and NNARX time series models applied to the training and testing datasets are shown in **Table 4.1.** The low errors of the NNARX model indicate that it performs exceptionally well on both the training and testing data. However, it shows signs of overfitting, as evidenced by its strong performance on the training data but suboptimal results on the testing data. In contrast, the SARIMAX model demonstrates consistent performance across both datasets. Almost all the error metrices for the training dataset from the SARIMAX model, except for RSME, are slightly higher than those for the testing dataset. This suggests that the SARIMAX model performs reasonably well on both the training and testing data, making it a better model than the NNARX model.

4.4.3 Forecasting of DRMRs based on SARIMAX model

The forecasted DRMR for the time period January 2024-December 2027, based on the SARIMAX model applied to the full dataset, is shown in **Figure 4.9.** The average monthly DRMR in Florida was estimated at 2.73 (95% Confidence Interval (CI): 2.32-3.14) per 100,000 persons. The forecasts reveal a strong seasonal pattern, characterized by consistent peaks in January and dips in June throughout the forecasted period. The mortality risk is higher during the winter months (December-March) compared to other months of the year. Specifically, the average DRMR in winter is 2.87 (95% CI: 2.46–3.28) per 100,000 persons, which is higher than the average for all other seasons (2.66 per 100,000 population). The forecasts also indicate a gradual upward trend over the years with values increasing slightly each year. For instance, the January forecasts increase from 2.98 in 2024 to 3.00 in 2027, and the June forecasts increase from 2.58 in 2024 to 2.61 in 2027. The forecasts are consistent across years with similar patterns repeating annually indicating the model is stable and reliable.

4.5 Discussion

This study identified temporal patterns and forecasted diabetes-related mortality risk in Florida. Study findings revealed that DRMR is higher among non-Hispanic Black people compared to non-Hispanic Whites. This is consistent with findings from some previous studies

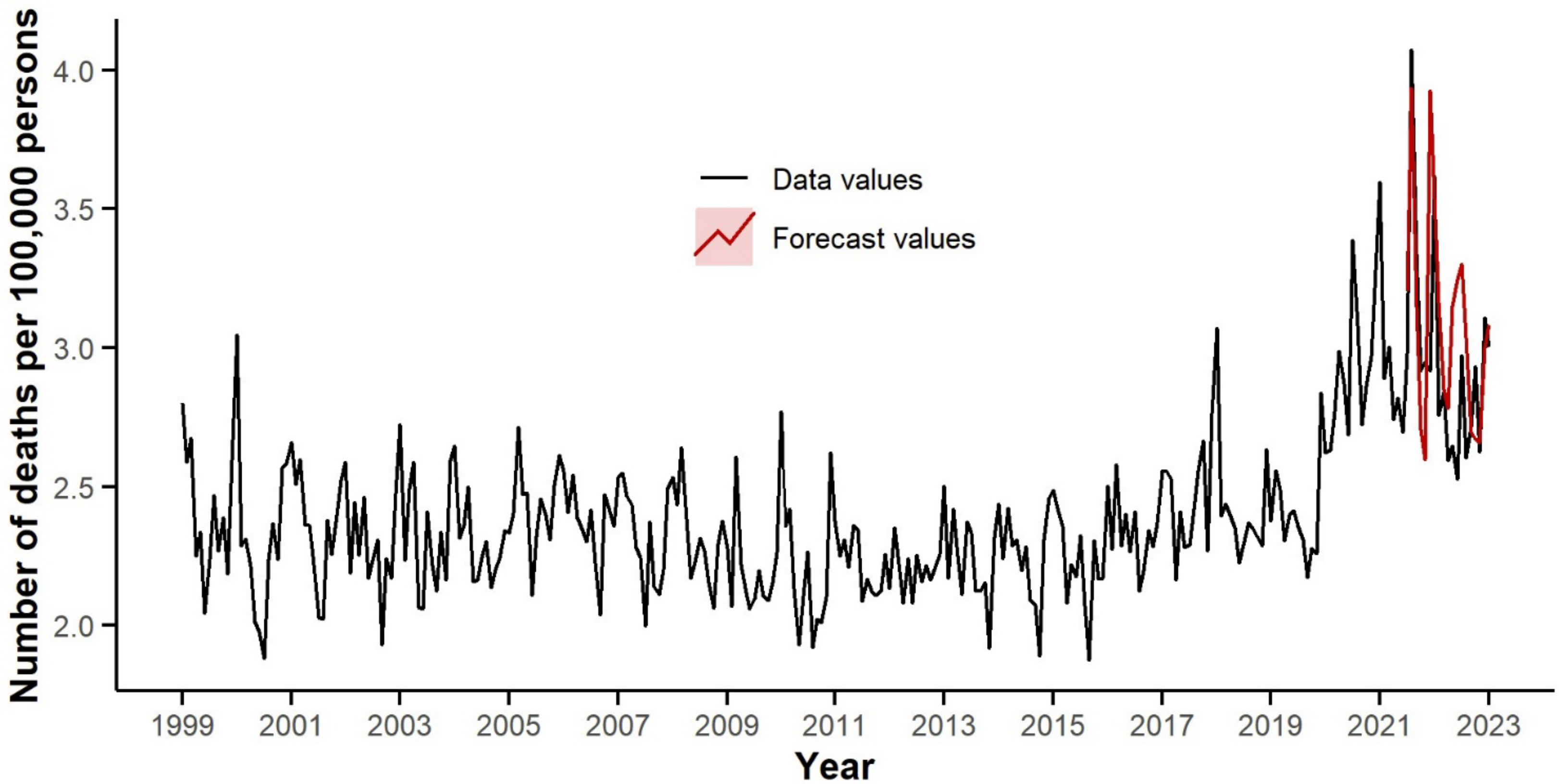

Figure 4.5: The SARIMAX model comparing the forecasted diabetes-related mortality risks (red color) with observed diabetes-related mortality risks (black color) in Florida, July 2021-December 2023.

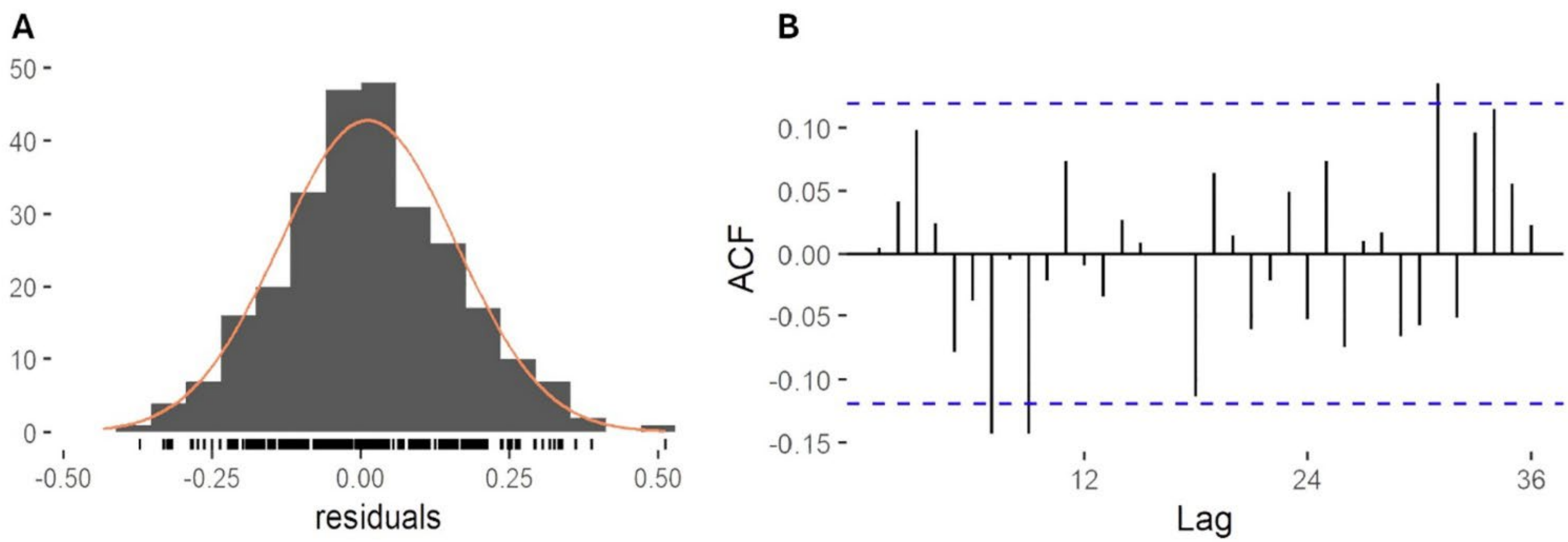

Figure 4.6: Residuals for forecasted SARIMAX (1,1,2)(1,1,1) [12] model of diabetes-related mortality risks using training data.

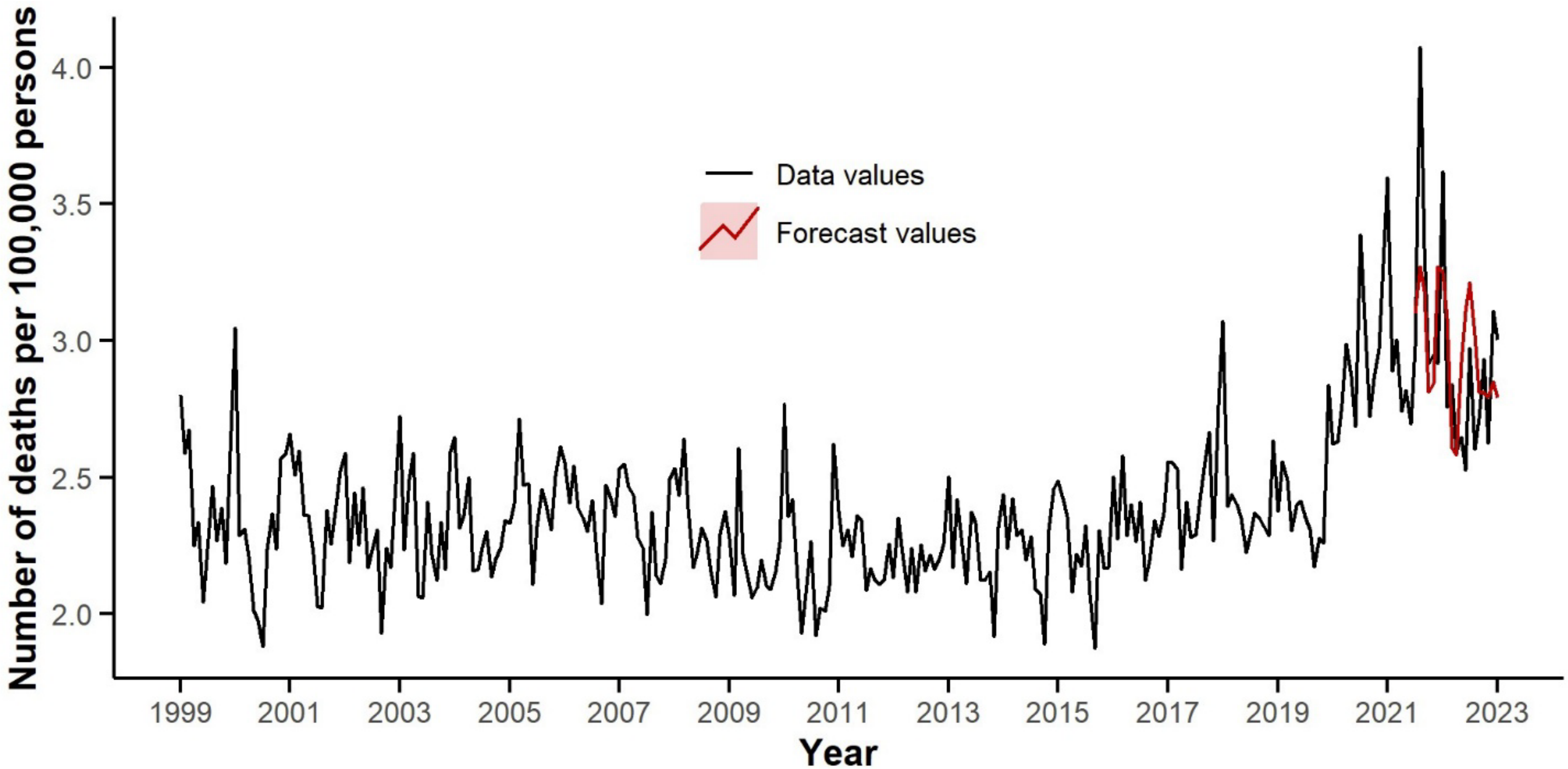

Figure 4.7: The NNARX model comparing the forecasted diabetes-related mortality risks (red color) with observed DRMR (black color) in Florida, July 2021-December 2023.

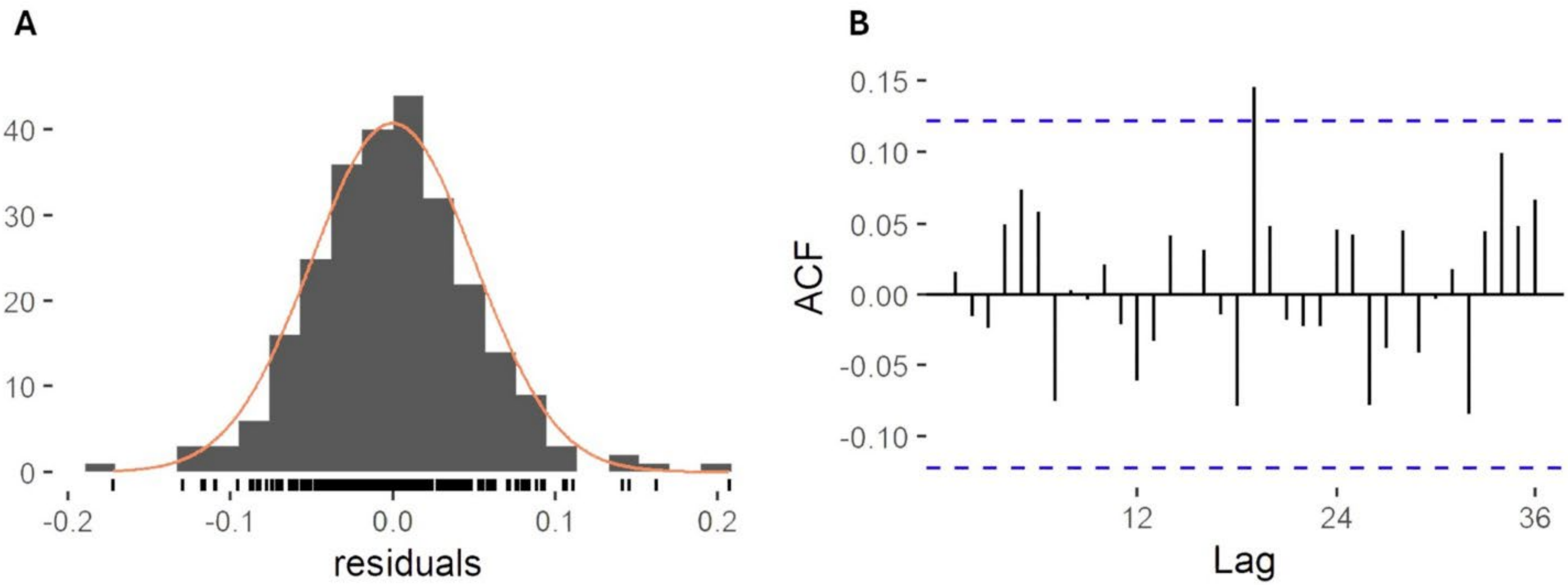

Figure 4.8: Residuals for forecasted NNARX (12,1,7) [12] model of diabetes-related mortality risks (DRMR) using training data.

Table 4.1: Error metrics of training and testing datasets of SARIMAX and NNARX models.

Model	Training data				Testing data			
	RMSE*	MASE†	MAE‡	MAPE§	RMSE*	MASE†	MAE‡	MAPE§
SARIMAX	0.15	0.65	0.13	4.86	0.23	0.49	0.13	4.73
NNARX	0.04	0.21	0.03	1.61	0.05	0.17	0.04	1.64

*Root Mean Square Error
†Mean Absolute Scaled Error
‡Mean Absolute Error
§Mean Absolute Percent Error

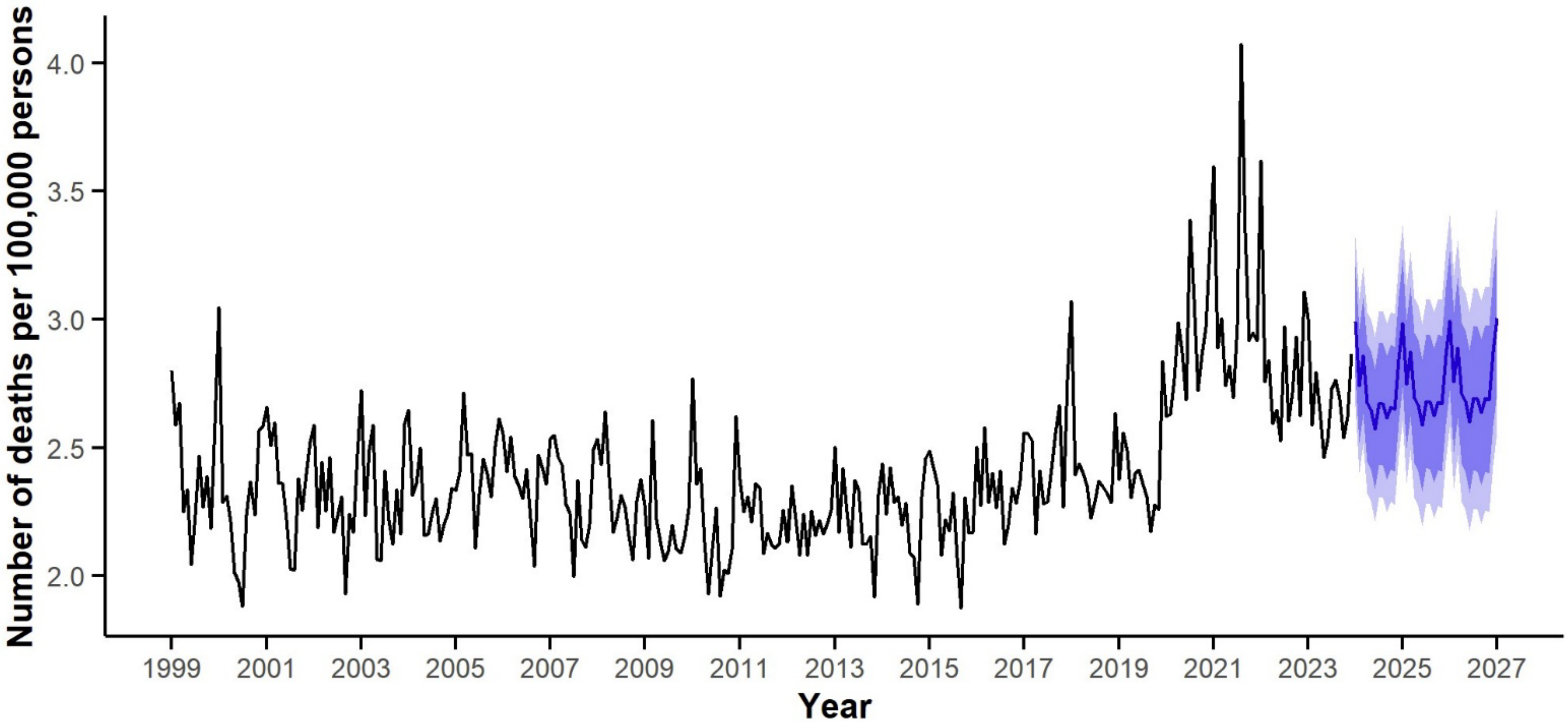

Figure 4.9: Forecast of monthly diabetes-related mortality risks in Florida using SARIMAX model, January 2024-December 2027.

which reported that diabetes is a significant cause of concern among Black individuals who are twice as likely to die from diabetes compared to their White counterparts (Rosenstock et al., 2014; Buscemi et al., 2021; Jain et al., 2023; Deb Nath & Odoi, 2024; Nath & Odoi, 2025). This might be due to the fact that health literacy is significantly lower among Black compared to White populations (Agarwal, Simmonds & Myers, 2022). In addition, data from the United States Census Bureau showed that around 19% of Black people in Florida live below the poverty line and are unable to afford health insurance coverage (United States Census Bureau, 2024e). Lack of health insurance restricts their access to services for managing diabetes. Therefore, increasing health literacy and diabetes self-management education programs among the Black population are encouraged to reduce the disparities in DRMR in the state.

The observed temporal trend of DRMR is comparable to findings reported by the Centers for Disease Control and Prevention in the US (Centers for Disease Control and Prevention, 2025c). Since diabetes is a risk factor for cardiovascular disease, the decline of DRMR from 2009 to 2015 might be due to lower cardiovascular disease risk reported in the state during that time period (Florida Department of Health, 2024). Similarly, a recent study conducted by Rodriguez et al. reported that diabetes-related mortality declined from 2003 to 2016 in the US, with a decreasing risk of cardiovascular diseases among individuals dying from diabetes (Rodriguez et al., 2019). The significant increase in DRMR after 2019 might be attributed to the impact of COVID-19 infection during the pandemic. Severe Acute Respiratory Syndrome Coronavirus-2 can induce human pancreatic beta cell apoptosis, leading to reduced insulin levels and secretion, thereby increasing the risk of diabetes, it's complications, and associated mortality (Wu et al., 2021; Deng et al., 2024). Additionally, during the pandemic, most of the residents avoided or delayed routine medical care due to fear of contracting COVID-19 during medical care visits resulting in missed appointments (Czeisler et al., 2020; Shukla et al., 2022). The healthcare systems were also overwhelmed during the pandemic which delayed diagnoses and resulted in interruptions in diabetes management (Czeisler et al., 2020; Shukla et al., 2022). Lockdowns and movement restrictions also led to reduced physical activity, which ultimately worsened blood sugar control and contributed to high mortality risks (Elliott et al., 2022; Macedonia et al., 2024).

The current study identified seasonal patterns in DRMR, with pronounced spikes occurring from December to March, consistent with findings from some previous studies (Tseng et al., 2005; Zhang et al., 2021). A combination of environmental, behavioral, and physiological factors during the winter months might be possible explanations for the observed seasonal patterns. It has been reported that the mean value of fasting plasma glucose is significantly higher during the colder months than the warmer months, which might contribute to a higher risk of diabetes-related complications and death (Zhang et al., 2021). Additionally, cold weather can cause blood vessel constriction, raise blood pressure, and increase the workload on the heart (Ikäheimo, 2018). Therefore, for individuals with diabetes, who are already at higher risk of cardiovascular diseases, this added stress can lead to complications such as heart attacks or strokes resulting in high diabetes-related deaths. Moreover, physical inactivity and sedentary behavior tend to increase during the winter months, which can lead to high blood glucose levels and contribute to high diabetes mortality (Cepeda et al., 2018). Addressing these factors through targeted public health interventions, such as encouraging healthy holiday habits, and improving access to care during winter months, could help reduce seasonal spikes in diabetes mortality.
The SARIMAX model forecasted seasonal patterns and a gradual upward trend in DRMR. The increasing number of older adults, high prevalence of obesity, limited Medicaid expansion, and

unhealthy diets may be key factors driving the predicted upward trend in the DRMR in Florida (Filipp et al., 2018; Owusu et al., 2023). The better performance of the SARIMAX model over the NNARX model may be attributed to proficiency of the SARIMAX model in managing strong seasonal patterns (Ebhuoma, Gebreslasie & Magubane, 2018; Mao et al., 2018). Additionally, the SARIMAX model uses differencing, which enhances the accuracy of error metrics and ensures reliable performance (Alharbi & Csala, 2022). On the other hand, the NNARX model did not effectively model the complex seasonal patterns and showed evidence of overfitting. Its failure to effectively model seasonality impacted its forecasting accuracy (Hyndman, 2018).

Strengths and limitations

This study used a rigorous time series statistical approach, SARIMAX model, to investigate temporal trends and seasonal patterns. This model is highly effective for handling seasonal data, as it explicitly incorporates seasonal components and provides interpretable results (Alharbi & Csala, 2022). This study also integrated COVID-19 data into the SARIMAX model so as to ensure a more accurate fit during the pandemic period. However, this study is not without limitations. Deaths occurring outside of healthcare settings (e.g., at home or in rural areas) may not have been captured.

4.6 Conclusions

There is evidence of seasonal patterns and a gradual upward trend of DRMR in Florida. The Black population consistently had higher mortality risks compared to the White population. The findings of this study will be helpful in guiding health planning, and future intervention programs to reduce DRMR in the state. Such investigations should be integrated into regular health programs to provide up-to-date information for healthcare professionals, disease control efforts, and health policy development.

CHAPTER 5

Summary, Conclusions, and Recommendations

This study investigated geographic disparities, county-level socioeconomic and demographic predictors, temporal patterns, and forecasted future diabetes-related mortality risks (DRMR) in Florida. Understanding these disparities is important for improving health outcomes especially in areas where substantial increases in the prevalence of diabetes and its associated mortality have been observed over the past two decades (Khan et al., 2021; American Diabetes Association, 2023). The overall goal of this work was to generate empirical evidence to guide health planning, service provision, and health policies aimed at reducing the burden of DRMR, eliminating disparities, and improving population health in Florida.

The county-level DRMR varied geographically across the state with counties located in the north and central parts of the state consistently having high DRMR. Similarly, significant high-risk spatial clusters of DRMR were detected in the central and northern parts of the state. Not surprisingly, most of the counties that were included in the high-risk clusters were located in rural areas. An increasing temporal trend and distinct seasonal patterns of DRMR were observed with the highest DRMR being observed during the winter season and lowest in the fall season. Socioeconomic and demographic factors as well as health behaviors were significant predictors of DRMR in Florida. Diabetes-related deaths were higher in counties with high percentages of seniors (≥65 years old) compared to those with younger adults (<65 years old). The older populations often face challenges with multiple chronic conditions, such as heart disease, hypertension, and kidney disease which increase the risk of developing diabetes-associated complications and deaths (Boersma, Black & Ward, 2020). This finding highlights the importance of managing comorbidities especially among elderly diabetes patients. Additionally, more than half of the counties had mortality risks equal to or greater than the national average. These high mortality risk counties were mainly in the rural northern, central, and south-central parts of the state. Similarly, significantly high percentages of populations with diabetes and those that were insufficiently physically active tended to live in the northern, central, and south-central counties of Florida. Programs to encourage physical activity in these populations are recommended. This highlights the importance of green spaces, such as parks, trails, community gardens, and playgrounds that support no-charge physical activities (Taylor et al., 2007).

Counties with high percentages of smokers and households without vehicles tended to have high DRMR and were mainly located in the northern and southern parts of the state. Most of these counties were rural and had generally low educational attainment (United States Census Bureau, 2023d). Smoking cessation programs as well as continuing educational programs are encouraged especially for those counties with high percentage of current smokers. Moreover, lack of public transportation and long drive times to healthcare facilities in rural counties with a high percentage of households without vehicles reduce accessibility to healthcare services potentially resulting in high DRMRs (United States Department of Health and Human Services, 2022). Improved public transportation at subsidized rates would be beneficial to help people get to health care providers.

The DRMR has been increasing over the last ten years in Florida. During the Corona Virus Disease-2019 pandemic, DRMR increased steadily and remained high to the end of the study period. Movement restrictions during the pandemic resulted in reduced physical activities and canceled/delayed routine medical care, which ultimately resulted in lapses in diabetes management increasing the likelihood of diabetes complications and potential deaths (Czeisler et al., 2020; Shukla et al., 2022; Macedonia et al., 2024). The observed higher DRMR among the Black population might be due to lower health literacy compared to their White counterparts (Agarwal, Simmonds & Myers, 2022; United States Census Bureau, 2024e). Poverty rates also tend to be high among the Black population which leads to inability to afford health insurance coverage, resulting in limited access to health services including those needed for managing diabetes and associated complications (Agarwal, Simmonds & Myers, 2022; United States Census Bureau, 2024e). Addressing socioeconomic disparities and increasing health literacy as well as diabetes self-management education programs among the Black population is encouraged to reduce diabetes mortality in Florida.

There was evidence of seasonal patterns of DRMR with spikes occurring in the Winter months (December to March). It has been reported that fasting plasma glucose levels are significantly higher during winter months. This results in higher risks of diabetes-related complications and death during the colder months of the year (Zhang et al., 2021). Moreover, rates of physical inactivity and sedentary behavior tend to increase during the festive winter season, a period when people consume more unhealthy diet and alcohol, which ultimately increases blood glucose levels leading to diabetes complications and deaths (Cepeda et al., 2018). Addressing these factors through targeted public health interventions, such as encouraging healthy holiday habits, and improving access to diabetes management programs during all seasons but especially the winter months, could help reduce seasonal spikes in diabetes mortality. The time series model forecasted a gradual upward trend over the years with values increasing slightly each year. The increasing number of older adults, high obesity rates, limited Medicaid expansion, and increased consumption of unhealthy diets might be responsible for the forecasted upward trend of DRMR in Florida (Filipp et al., 2018; Owusu et al., 2023).

The key strength of this study was the use of rigorous spatial epidemiological approach to investigate the geographic distribution and spatial clusters of DRMR in Florida. Tango's FSSS is a robust method as it does not involve multiple comparisons and identifies both circular and irregularly shaped spatial clusters. This study also used a rigorous time series model (SARIMAX) which is appropriate for modeling seasonal data and provided more efficient interpretable results (Alharbi & Csala, 2022). Additionally, this is the first study to investigate geographic disparities, county-level socioeconomic and demographic predictors, and conduct time series analysis of DRMR in Florida using rigorous statistical approaches. However, this study has some limitations. Although type 1 and type 2 diabetes have different etiologies, this study did not distinguish between them. Moreover, this study investigated geographic disparities of DRMR at the county level; therefore, future research should focus on exploring disparities at lower-level, such as the ZIP code level, to identify lower-level disease patterns. Finally, deaths occurring outside of healthcare settings (e.g., at home or in rural areas) may not have been captured in this study.

In conclusion, geographic disparities of DRMR exist in Florida, with notable high-risk clusters in the rural central and northern regions of the state. Counties with high percentages of the population aged 65 or older, current smokers, population having insufficient physical activity, population with diabetes, and households without vehicles tended to have high DRMR. The Black population consistently had higher mortality risks compared to the White population. In addition, there is evidence of seasonal patterns and a gradual upward trend of DRMR in Florida. The study findings are useful for guiding health resource allocation and evidence-based policies targeting high-risk communities so as to reduce health disparities in Florida. These kinds of investigations should be integrated into regular health programs to provide up-to-date information for health planning, disease control efforts, and health policy development.

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