UNIVERSITY OF CAPE COAST

MARKOV CHAIN MODEL OF NEUROPATHY PROGRESSION OF TYPE 2 DIABETES: A CASE STUDY IN BONO EAST REGION

GLADYS BAYELDENG

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BY

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Thesis submitted to the Department of Statistics of the School of Physical Sciences, College of Agriculture and Natural Sciences, University of Cape Coast, in partial fulfilment of the requirements for the award of Master of Philosophy degree in Statistics

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DECLARATION

Candidate's Declaration

I hereby declare that this thesis is the result of my own original research and that no part of it has been presented for another degree in this University or elsewhere.

Candidate's Signature ……………………… Date ………………….

Name: Gladys Bayeldeng

Supervisor's Declaration

I hereby declare that the preparation and presentation of the thesis were supervised in accordance with the guidelines on supervision of thesis laid down by the University of Cape Coast.

Supervisor's Signature ……………………… Date ………………….

Name: Dr. Irene Kafui Vorsah Amponsah

ABSTRACT

Type 2 diabetes mellitus (T2DM) is a chronic non-communicable disease that causes damage to the kidneys, heart, nerves, and blood vessels. In recent times, there has been a surge in T2DM cases, and it has been associated with overweight, obesity, lack of adequate physical activity, gender, urbanisation, and the educational level of people. The study modelled the neuropathy progression of T2DM in patients using the Markov Chain model. The fasting blood sugar (FBS) levels of patients and neuropathy conditions developed during the time of this study were classified into eight states: State 1 (low FBS level), State 2 (normal FBS level), State 3 (moderate FBS level), State 4 (high FBS level), State 5 (numbness), State 6 (ulcers), State 7 (amputation), and State 8 (death). The study found that females were more exposed to the disease than their male counterparts, and 96% of the patients were hypertensive. Most patients fall within the age bracket of 40-60 years. Patients in the long term have a high risk of their conditions deteriorating rather than improving. Patients who have low FBS levels have a 50% chance of dying within the year, and patients in the ulcer state have two options: they either remain in the same condition or progress to the next state, which is the amputation state. Patients in the low FBS state have a mean sojourn time of 14 years, while patients in the normal and moderate states have a mean sojourn time of 27 years each. Patients in high and numbness states have mean sojourn times of 26 and 23, respectively. However, patients in an ulcer state have a mean sojourn time of two years before they enter the absorbed states. The study therefore recommends intense public education on the factors associated with diabetes, the risk of progression of T2DM, and prevention measures.

KEY WORDS

Absorbed States

Hyperglycaemia

Hypoglycaemia

Neuropathy

Retinopathy

Transient States

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DEDICATION

To my auntie, Veronica Bayeldeng and my children.

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LIST OF ABBREVIATIONS

A1C	Glycated Haemoglobin
BMI	Body Mass Index
CKD	Chronic Kidney Disease
DM	Diabetes Mellitus
eGFR	Estimated Glomerular Filtration Rate
FBG	Fasting Blood Glucose
FBS	Fasting Blood Sugar
H0	Null Hypothesis
H1	Alternative Hypothesis
HTA	Health Technology Assessment
IFG	Impaired Fasting Glucose
KATH	Komfo Anokye Teaching Hospital
NCD	Non-Communicable Diseases
NLP	Natural Language Processing
OGTT	Oral Glucose Tolerance Test
SSA	Sub-Saharan Africa
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organisation

CHAPTER ONE

INTRODUCTION

Diabetes is one of the non-communicable diseases that dates back to the seventeenth century. Recently, there has been a surge in diabetes cases, making it one of the top ten diseases that cause death in the world. This has triggered a lot of studies into the root cause of the disease and the factors that are associated with it. Most of these studies conducted on diabetes focused on the risk factors of diabetes, the prevalence rate, the complications developed, and the hospitalisation trend of patients affected by the disease. Diabetes is a lifestyle disease and is mostly caused by unhealthy eating habits such as eating junk foods, and consuming too much alcohol, coupled with a lack of regular exercise, which is mostly associated with urban residents.

This study assessed the progression stages of people living with Type 2 diabetes mellitus (T2DM), which constitutes 96% of all diabetes cases (Dalton et al., 2023) in a non-urban setting, and also explored the risks of progression in each stage of the disease using a statistical model, the Markov Chain. This model studied how the disease progresses in the various states identified based on fasting blood sugar (FBS) levels of patients, and neuropathy conditions developed. The model also established how long diabetes patients stayed in each state of the progression stages before they developed complications and made future predictions concerning the health state of patients.

Background to the Study

Diabetes mellitus (DM) is a chronic metabolic disorder that is characterised by high levels of sugar in the blood, which can cause serious damage to the kidneys, heart, blood vessels, eyes, and nerves. During digestion, carbohydrates are broken down into simple sugars or glucose, which is the main source of energy for the body's cells. The pancreas produces insulin, which is responsible for maintaining the amount of sugar that the body needs. T2DM occurs when the body cells resist the effects of insulin produced, thereby causing blood sugar levels to rise, a condition known as hyperglycaemia. In recent times, there has been a surge in type 2 diabetes mellitus cases globally, and in Africa, it is one of the major causes of death, and Ghana is not an exception (WHO, 2023)

Diabetes was first documented by the Egyptians and was characterised by weight gain and polyuria. The word mellitus was coined by the English anatomist and physician, Thomas Willis, to describe the sweet taste of the urine in diabetic patients.(Karamanou, Protogerou, Tsoucalas, & Androutsos , 2016).

There are about seven types of diabetes classified by the World Health Organisation (WHO) in Geneva, 2019, but the three major types of diabetes are:

- Type 1 diabetes: This occurs due to the inability of the pancreas to produce insulin,
- Type 2 diabetes: this is when the body cells resist the action of insulin that is being produced, and over time, the production of insulin progressively decreases; and

- Gestational diabetes: It occurs during pregnancy and can cause some complications during pregnancy and at birth, thereby increasing the risk of Type 2 diabetes in the mother and obesity in the child

Type 2 Diabetes Diagnosis and Tests

Various forms of blood tests are used to detect T2DM in people. The glycated haemoglobin (A1C) test measures the average percentage of one's blood glucose level within a period of two to three months. Fast plasma glucose is another test known as the fasting blood sugar (FBS) test, which measures your blood sugar level when you have not eaten for about eight hours. Aside these two tests, the oral glucose tolerance test (OGTT) can also be used to see how the body responds to sugar or glucose by first taking the blood glucose level of a person and after the person has taken a drink that contains sugar for two hours, the test is repeated and the results are compared.

Stages of Type 2 Diabetes

There are four stages of T2DM; the insulin resistance stage, the prediabetes stage, the diabetes stage, and diabetes with complications. The Insulin resistance stage is when one's body cannot respond properly to the insulin produced by the pancreas, and blood sugar begins to rise gradually. In the prediabetes stage, the blood glucose level is higher than the normal blood glucose level (3.9 - 5.7mmol/L) but not very high. The blood glucose levels for prediabetes range from 5.8 - 6.9mmol/L. This stage can easily be reversed if one adopts a healthy lifestyle by eating a good fibre-rich diet and exercising. Stage 3 is where one is declared to have diabetes. In this stage, blood glucose level has gone very high and is above 7mmol/L, and symptoms such as increased thirst, frequent urination, blurred vision, numbness, and slow healing wounds. The last stage is diabetes with complications that include atherosclerosis, diabetic retinopathy, and diabetic nephropathy.

According to Roglic (2023), there are about 422 million people worldwide living with diabetes, with the majority of these people in the lower and middle-income countries. About 1.5 million people die every year of diabetes.

The Institute for Health Metrics and Evaluation (2023) has also estimated global diabetes cases to increase from 529 million to 1.3 billion by 2050, with a global prevalence rate of 6.1%. This makes diabetes one of the top ten leading causes of death and disabilities. T2DM is ranked as one of the most rapidly increasing non-communicable diseases (NCDs) in the world today. Over 371 million people worldwide were diagnosed with diabetes in 2011, with an expected 7.7% increase by 2030 (Doherty *et al.*, 2014). This increase is especially pronounced in urban Sub-Saharan Africa (SSA), where soaring diabetes rates are expected to double within the same timeframe.

In Africa, the prevalence rate of T2DM cases has increased to 4.9%, and the majority of these patients are aged below 60 years (Motala, 2014). Ghana is not an exception, as T2DM affects at least 6% of the adult population, and this is associated with age and obesity. About 23% of these adults are overweight, and this has been attributed to advanced age, female gender, urban environment, high income, and tertiary education (Danquah *et al.*, 2012).

Statement of the Problem

T2DM is a significant health problem with increasing prevalence worldwide. In urban Ghana, 23% of adults aged 40-60 years are overweight, and this has been attributed to advanced age, female gender, urban environment, high income, and tertiary education (Danquah *et al*., 2012). There are multiple risk factors associated with diabetic patients, some of these include the development of micro-vascular and macro-vascular complications, life-threatening complications, and financial burden to the patient in treating the disease (Wu *et al*., 2014). The burden of diabetes was assessed in the Ghanaian population to provide comprehensive information for policymakers to make a decision concerning this non-communicable disease (Kazibwe *et al*., 2024).

The rise in the burden of this chronic disease has initiated measures to assess the risk of diabetes in the existing population, but few measures and models are available to assess the possibility of developing diabetes in the future. The reviews in related literature have identified a methodological gap that this study aims to address. Projecting future prevalence helps estimate the burden of diabetes and develop preventive measures. While the Markov Chain model offers a powerful framework for understanding and stimulating disease progression and has been used to model other diseases in the country, this has not been effectively explored in analysing diabetes data. Danquah *et al.* (2012) and others used qualitative, systematic review methods, and regression models in their research. Hence, this study aims to develop a Markov Chain Model that accurately depicts the multi-stage progression of T2DM to neuropathy stages.

Objective of the Study

The study aims to develop a Markov Chain Model of the progression of type 2 diabetes mellitus in patients to neuropathy stages. Specifically, this study seeks to:

1. To determine some factors associated with T2DM
2. To establish a transition probability matrix of T2DM cases
3. To make future projections on the state of health of patients within three and five years.
4. To determine the average time patients, stay with the disease before their limbs are amputated or they die of the disease.

Significance of the Study

This study will be beneficial to diabetes patients (especially those under this study) since they will be able to assess their risk in each stage of their condition based on the probabilities calculated and ensure a healthy lifestyle to prevent getting to complication stages, which could easily lead to death. The study will also be beneficial to healthcare providers who will have a better understanding of the progression stages of T2DM and make informed clinical decisions.

Delimitations

The study looks at the progression of T2DM cases to neuropathy stages within a year and does not include other microvascular complications such as retinopathy and nephropathy complications.

Limitations

Some patients' information was not up to date; hence, they were not included in the study because they did not meet the criterion for selection. Also, patients whose diabetes status could not be established were also taken out to ensure completeness and adequacy of data for the study.

Organization of the Study

The study consists of five chapters. Chapter one provides information on the introduction, background of the study, statement of the problem, objective of the study, significance of the study, and limitations and delimitations. Chapter two reviews related literature; it provides information on similar research that other researchers have done on diabetes and T2DM. Chapter three elaborates on the methodology employed in this study to achieve its objective. Chapter four deals with the results and discussions of the study, and lastly, Chapter five provides the summary, conclusions, and recommendations of the study.

Chapter Summary

This chapter explains what diabetes is and the three major types of diabetes. It also gives a brief history of the diagnosis and testing of diabetes, the stages of diabetes, and the prevalence of diabetes globally and in Ghana. The chapter also gives the motivation for this study and how the study is organised.

CHAPTER TWO

LITERATURE REVIEW

Introduction

Diabetes is a chronic disease that is characterised by a metabolic disorder, mostly due to obesity and physical inactivity. The progression of type 2 diabetes to neuropathy stages is a complex process influenced by various factors, including glycaemic control, duration of diabetes, and individual characteristics. This chapter reviews related works that have been done so far on T2DM, the risk factors associated with the disease, the prevalence of the disease, and measures provided to curb the spread of this disease. The chapter also examines some models that have been used to model the disease progression.

Risk Factors of Type 2 Diabetes

The primary risk factors associated with T2DM are being overweight, obese, and not physically active. According to Wu *et al*. (2014) lifestyle and the role of genes are contributing factors to T2DM. Their study reveals that the prevalence of T2DM in both developed and developing countries is increasing exponentially, with high rates of diabetes-related morbidity and mortality. They proposed that therapeutic strategies should be developed for the treatment of T2DM. Though their study identified some contributing risk factors to T2DM, they could not specifically state if the risk factors identified are the exact factors that cause type 2 diabetes, hence, they proposed that further research should be done to find the right mechanism contributing to T2DM and its related complications.

In a similar study conducted on the risk factors associated with T2DM in Europe, Kyrou *et al.* (2020) identified sociodemographic and several lifestyle factors such as age, family history, low socioeconomic status, ethnicity, obesity, and metabolic syndrome associated with the disease. The study was a review of literature on the risk factors of T2DM in European countries. The results also identify socioeconomic status as one of the major risk factors exposing people to prediabetes and T2DM. This study has some shortfalls in terms of coverage since it could not capture all related articles in Europe on the risk factors of T2DM.

In addition, Kyrou *et al*. (2020) tried to identify vulnerable groups of T2DM patients based on social demographics and lifestyle factors. They use the narrative review method to conduct a comprehensive search on the risk factors associated with T2DM in adult cohort studies in Europe that were published in January 2000. The study identified age, ethnicity, family history, low socioeconomic status, metabolic syndrome, obesity, and unhealthy lifestyle behaviours as risk factors relating to T2DM. In addition, low socioeconomic status was a major factor that significantly increased the risk of prediabetes and diabetes. The study emphasised a holistic approach to preventing type 2 diabetes since Europe is a multinational and multicultural region. The study, however, did not mention the criteria used in selecting the articles for their review.

Hussein *et al*. (2022) also used the systematic review method of related literature (qualitative and quantitative) to identify some risk factors associated with T2DM. These factors range from environmental factors, medical factors, cardiovascular diseases such as high blood pressure, hereditary factors, demographic factors, lifestyle, and psychosocial factors such as stress, and the mental status of an individual. These factors associated with diabetes vary from patient to patient. The study also showed a strong correlation between body mass index (BMI) and haemoglobin levels. The two most influential factors identified in the study for developing T2DM are triglycerides and haemoglobin. One limitation of the study was the sample size. Though the study was a review of systematic literature, 24 articles were reviewed, which is relatively small. The study also mentioned qualitative methods used, but did not specify how they were used.

In addition, Xia *et al*. (2021) conducted an observational cross-sectional study in eight communities in Nanchong, China, using multinomial logistic regression models to identify similar risk factors such as obesity, overweight, advanced age, abdominal obesity, comorbidities, smoking, and family history of diabetes. The study involves 53,288 participants aged 45 years and above. The results indicated that the Chinese method of cooking vegetables was associated with an increased risk of T2DM. The study generalised its findings even though only eight communities were used in Nanchong, which is located in the northeast of Sichuan province. This is not a true representation of the Chinese population since it is confined to only one province in China.

Another study conducted in the US by Yang *et al*. (2022) examined the combined associated modifiable risk factors of T2DM in women who had a history of gestational diabetes mellitus. The study was a prospective cohort study that involved 4,275 women. The results revealed a high correlation between gestational diabetes and T2DM. The five modifying factors identified in the research included: not being overweight, eating a healthy diet, regularly exercising, moderately drinking alcohol, and avoiding smoking, all of which have an inverse relationship with T2DM (Yang *et al*., 2022). Though the study puts forth commendable findings, the long period of study of cases (28 years) may have caused some changes in the dynamics of the risk factors, thus reducing the quality of their research.

Prevalence of Diabetes

The prevalence of diabetes, especially type 2 diabetes, has been increasing steadily worldwide, with a standard age prevalence of 6.1%. North Africa and the Middle East Regions recorded the highest age-standardised rates of 9.3% (Collaborators, 2023). Also, Qatar is number one in the world in terms of age-specific prevalence of diabetes at 76.1% (Collaborators). Body Mass Index was also identified as one of the main contributing factors to type 2 diabetes prevalence. In Ghana, the prevalence of diabetes in adults who are 50 years and above is 3.95% (Gatimu *et al*., 2016). Gatimu *et al* study of prevalence and determinants of diabetes among older adults in Ghana was a cross-sectional study, and the data spanned 2007-2008 and involved 5,565 respondents from another study titled *Aging and Adult Health (SAGE) Wave 1*. The study used bivariate and hierarchical multivariate logistic regression models to study the association between the determinants and diabetes. The results showed that the prevalence rate of diabetes was higher in females than in males. In addition, physical inactivity and obesity increase the odds of diabetes in women, while old age and level of education increase the odds of diabetes in men. The study recommended preventive programs targeting the youth and females to minimize the risk of diabetes. One limitation of the study was that the prevalence of diabetes could have been higher at the time of the research since current data was not used for their analysis, but relied on data from 2007 to 2008.

Asamoah-Boateng *et al*. (2019) also estimated the prevalence and risk factors of diabetes among adults in Ghana using a systematic review and meta-analysis method. The study reviewed 17 published articles on the prevalence of diabetes in known journals such as Medline (PubMed), Embase, CINAHL, Web of Science, Scopus, African journals, and Grey Literature. Their analysis revealed that the prevalence of diabetes among adults in Ghana is 6.46% based on the inverse-variance random-effects model used. The work also showed that the prevalence of diabetes varies from region to region, with some regions recording higher prevalence rates than others. The Ashanti, Central, and Greater Accra regions recorded the highest prevalence rates compared to the other 13 regions. The study had some shortfalls since it could not account for the variations in the prevalence at the regional levels and the factors influencing the high prevalence of the disease in the Ashanti, Central, and Greater Accra regions.

Najafipour *et al*. (2021) used univariate and multivariate logistic regression models to determine likely predictors of diabetes and prediabetes. The study, titled *The Prevale*nce and Incidence Rate *of Diabetes, Prediabetes, Uncontrolled Diabetes, and Their Predictors in the Adult Population in South-eastern Iran* was a household survey that involved 9,959 participants from

2014 to 2018. The results indicated that the prevalence rate of prediabetes was 12% and 10.2% for diabetes. Also, the prevalence rates for educated and illiterate were 10.6% and 15.1%, respectively. The prevalence rate was high (48.8%) in patients who were not able to control their blood glucose level, HbA1c was above 7%, and the illiterate population was the worst affected. The prevalence rate was, however, lower in persons between 15-34 years and among people who smoked. The study, however, did not explain the factors accounting for this. This is not different from similar studies conducted in Ghana on T2DM. The incidence rate of diabetes had a direct association with a person's body mass index and an inverse association with the physical activity of a person. The study concluded that 22.2% of the population was affected by prediabetes and diabetes.

Also, the prevalence of undiagnosed T2DM was quite significant among the adult population. This was revealed in a cross-sectional study in the Tamale metropolis in the northern region of Ghana, consisting of 300 adult participants aged between 18 to 50 years for four months (January to May 2018). The results further revealed that the prevalence rate of undiagnosed diabetes was 4.7%, which is higher than the national prevalence rate of diabetes in the country. The mean age was 34 ± 10.6 years, which is an indication that young adults are at risk of Type 2 diabetes mellitus. Further, the average fasting blood glucose (FBG) is 4.76 ± 0.87 mmol/L among the rural participants as compared to 5.02 ± 1.35 mmol/L among the urban participants. The results also indicated that the urban areas have a high IFG (22.0%) as compared to the rural areas (10.8%) of the metropolis. This suggests that people in urban areas are 12 times more likely to develop T2DM as compared to those in rural areas of the metropolis. Some risk factors, such as overweight, obesity, lack of physical activity, and unhealthy dietary practices, were more common among urban residents than rural residents. However, the non-modifying factors, such as family history of diabetes and age, were the same for both rural and urban areas. The study recommended a healthy lifestyle, such as regular exercise and healthy dietary practices, to reduce the risk of T2DM. Though the study achieved its objectives, it failed to investigate the reasons why urban residents were obese and physically inactive as compared to rural residents. The study did not indicate why urban residents were engaged in unhealthy dietary practices (Shani *et al*., 2022).

Complications of Type 2 Diabetes

According to Paraskevi *et al.* (2020), current cardiology review complications of Type 2 diabetes can be grouped into acute and chronic complications. The acute complications include diabetic ketoacidosis or diabetic coma, (a dangerous complication in which the patient has signs of dehydration, Kussmaul breath, gradually reduction in consciousness eventually leading to coma), hypoglycaemia (a condition in which the blood sugar level is low and may be a result of an incorrect dose of insulin), and hyperglycaemia (a condition where blood sugar levels are so high). Chronic complications are the long-term manifestations of the disease, which affect the functioning of the organs. These include Macroangiopathy, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, and diabetic foot (development of wounds and ulcers below the knee).

Afaya *et al*. (2020) in their cross-sectional study, evaluated the awareness of diabetes complications among 320 T2DM patients in northern Ghana using bivariate and multivariate logistic regression analysis. The study reveals that the majority of the patients (54.1%) had little knowledge of the complications of diabetes, while 45.9% were fully aware of the complications of diabetes. The majority of the patients who had little idea of the complications of the disease were females who did not have formal education, older patients, and rural dwellers. The study concluded that more than half of the studied population did not have a fair knowledge of the complications of diabetes, hence, they recommended a multisectoral approach to educate the general public, especially diabetes patients who visit health facilities, to be aware of the dangers of diabetes complications and adhere to their medications and ensure a healthy lifestyle to prevent developing complications. Afaya *et al*.'s study lacks generalisability since it was conducted in one location; hence, there is a need for further investigation to be conducted in other regions to truly ascertain the knowledge of diabetes complications among diabetic patients in the country.

In another study, Liu *et al*. (2010) explored the prevalence of chronic complications of T2DM in outpatients among Chinese urban dwellers. The study adopted a cross-sectional hospital-based study design in four cities in China: Shanghai, Chengdu, Beijing, and Guangzhou. The study population involved 1,524 T2DM patients (outpatients) from March to July 2007. The results showed that 792 of the study participants had chronic complications, which represent 52.0%, 509 had macrovascular complications (33.4%), and 529 (34.7%) had microvascular complications. The study also showed a variation in chronic complication prevalence between cities and a significant increase with age and the length of time patients had the condition. The study concluded that T2DM outpatients are at high risk of developing chronic complications. The study recommended proper glycaemic and blood sugar control to reduce the risk of complications. Though the study took into consideration factors such as demographics and HbA1c, it did not explore other factors such as the lifestyle of patients, physical activities, family history, and socioeconomic status, which are potential risk factors for developing complications and the progression of these complications.

Furthermore, a cross-sectional study conducted by Berhe *et al*. (2023) revealed a significant prevalence of diabetes complications in the Tigray area of northern Ethiopia. The study aimed to assess the level of chronic diabetes complications among patients with T2DM and their associated factors in general hospitals. The study involved 1,158 T2DM patients who were randomly selected from 10 general hospitals. The study employed both questionnaire and interview methods to obtain data. A multivariate logistic regression model was used to identify factors associated with chronic complications among T2DM patients. The results showed that 54% of patients had chronic complications, 27% were hypertensive, and 19.1% had renal disease and eye problems. Patients who were 60 years and above, together with those who had been diagnosed with diabetes for five years or more, were at risk of chronic diabetes complications. Chronic diabetes complications were found in more than 50% of T2DM patients, and the associated factors were the age of the patient, occupation, diabetes treatment plan, anti-dyslipidaemia medicine, anti-platelet, duration of diabetes, high systolic and diastolic blood pressure, and pill burden. The study recommended that stakeholders put pragmatic measures in place to support diabetes patients who were at risk of developing diabetes complications. Against the backdrop that the motivation for the study was to find out the degree of diabetes chronic complications in general hospitals, it would have been expedient if the study had compared its findings to studies conducted in the tertiary hospitals to find the areas of convergence and divergence. This is because general hospitals are considered lower health care centres and most studies on diabetes complications are conducted in tertiary hospitals, which are often well equipped and more favourable to the middle-income class, who are more susceptible to diabetes complications.

According to Ekoru *et al*. (2019) Hypertension, hyperlipidaemia, and obesity are the most common complications/comorbidities in T2DM patients, with hypertension constituting 71% of these cases. This was revealed in their study on T2DM complications and comorbidity in Sub-Saharan Africans, where 2,784 participants with diabetes were assessed in tertiary healthcare centres, and 3,209 persons without diabetes in Ghana, Kenya, and Nigeria. The complications and comorbidities associated with Type 2 diabetes that were assessed include cardiometabolic, neurological, ocular, and renal failure. Other complications/comorbidities such as cataracts, impaired renal function, erectile dysfunction among men, and diabetic retinopathy were also associated with T2DM patients. One commendable recommendation made by the study was the need to equip health facilities to handle diabetes complications and comorbidity issues, since the burden was substantial in Sub-Saharan Africa. The study was a cross-sectional study, and therefore, could not monitor the progression of complications in diabetes patients. Hence, further investigations (longitudinal study) need to be conducted on the development of complications in diabetes patients. Also, Sub-Saharan Africa is a big region, and more countries should be involved to enable the generalisation of the findings.

Lastly, Annani-Akollor *et al*. (2019) also assessed the predominant complications among T2DM patients in Kumasi, Ghana. The study was a retrospective cross-sectional study that involved 1,600 T2DM patients from the Komfo Anokye Teaching Hospital (KATH) from 2012 to 2016. The results showed that the prevalence of macrovascular and microvascular complications among T2DM patients was 31.8% and 35.3%, respectively. Neuropathy complications accounted for 20.8% of complications, and sexual dysfunction was significant in males than in females. Patients who have been diagnosed with T2DM for at least five years are at risk of developing complications. The study also revealed that patients who are employed have a lower risk of developing T2DM complications, but the study did not indicate the type of employment that accounted for this (formal and informal). The study also did not establish whether it was a peculiar kind of work that reduced T2DM complications in patients.

Economic Burden of Diabetes

The burden of T2DM in Ghana was assessed by Gad *et al*. (2023) in their study on *the Epidemiological and Economic Burden of Type 2 Diabetes*. The study employed the Arksey and O'Malley scope review framework to review 36 published journal articles, such as Embase, Scopus, and Web of

Science. The results revealed a 2.8%-3.95% prevalence rate of T2DM nationwide, with higher prevalence rates at the regional levels. The Western region had the highest prevalence rate of T2DM cases (39.80%), followed by the Ashanti region with a prevalence of 25.20% and the Central region with a prevalence of 24.60%. The prevalence rates were also higher in women than in men, and urban areas than in rural areas. Concerning the economic implications of diabetes, the study showcased that the annual financial burden of treating type 2 diabetes is about 530.35 Ghana Cedis. The study recommended using Health Technology Assessment (HTA) to assist in managing and preventing T2DM in the country. Though the survey identified high prevalence rates of T2DM cases in some regions, the survey could not ascertain the factors causing the high prevalence in the three regions. The study was also silent on the prevalence rates of the other regions.

Furthermore, Amon *et al*. (2017) Conducted a similar survey in the Eastern region of Ghana on the economic burden of T2DM complications among 258 diabetic patients. The results showed that the estimated total cost of managing a complicated type 2 diabetes case is US$9,980.62, which constitutes both direct and indirect costs. Direct cost, which includes: cost of medication, consultation, laboratory test, transportation, etc, accounted for 94%, and indirect cost constitutes 6%. Indirect cost consists of the time spent seeking medical care and productivity loss. Patients on treatment for five or more years incurred a significant cost, which was higher than those below 5 years. This study cannot be used to generalise the burden of type 2 diabetes in the country since it was done in only one hospital in the eastern region.

Modelling Diabetes Cases

Mathematical and statistical models have been widely used to model real-life situations in many fields and make predictions about these situations. In the health sector, both mathematical and statistical models are used to determine the behaviours and associations of some factors to certain diseases, monitor the progression of some diseases, and make projections for the future. For instance, Anthony *et al*. (2021) employed the Poisson regression model to model trends of hospitalisation of diabetes mellitus patients in Ghana. In the study, they collected secondary data from the Ghana Health Service across the country, from both public and private hospitals, on hospitalisation of diabetes mellitus patients from 2012 to 2017. The data was stratified into sociodemographic and health factors, and the Poisson regression model was used to determine the association between the sociodemographic and health factors and hospitalisation. The results suggested that the hospitalisation rate was higher among diabetes patients aged 75-79 and among females than among males. Hospitalisation at the regional level was higher in the Eastern region compared to other regions in the country. The study also predicted that, by 2022, about 11,202 diabetes patients would be hospitalised, and by 2027 and 2032, hospitalisation is expected to increase to 12,414 and 13,651 patients, respectively. Although the study indicated that data was collected across the country, data from Kole Bu Teaching Hospital and Komfo Anokye Teaching Hospitals were not included which I think will have some degree of influence on the results as these hospitals are major centres for treating and hospitalising diabetes patients who have developed macro vascular complications such as kidney diseases, coronary heart diseases, peripheral artery diseases to mention but a few. Moreover, some district hospitals are not well-resourced to handle some of these complications, and patients are almost always referred to teaching hospitals.

A related survey conducted by Gatimu *et al*. (2016) aimed at determining the prevalence of diabetes, also used the bivariate and hierarchical multivariate logistic regression models to model the determinants of diabetes among adults aged 50 years and above. The study was a cross-sectional survey that relied on data collected from 5,565 respondents from another research titled, *Study of Aging and Adult Health (SAGE) Wave 1.* The results showed a 3.95% prevalence of diabetes among adults aged 50 years and above, with females having a higher prevalence rate than males. The results also revealed that low physical activity and obesity were associated with women, which increased their risk of developing diabetes. Furthermore, factors such as old age and educational status increased the risk of diabetes in men than in women. The study concluded that the prevalence of diabetes was underestimated as a result of low self-reporting and undiagnosed diabetes among the general public. The study, therefore, recommended diabetes prevention programs (healthy lifestyle, physical activity, etc.) that target the youth, especially the female gender, to minimise the burden of developing diabetes in the future.

Markov Chain

Markov Chain is a stochastic process and has been widely used in modelling in different fields such as finance, accounting, marketing, production, education, health service, weather forecast, engineering, natural language processing, computer science and artificial intelligence, operation research, social science, games, music, among other sectors.

Finance and Economics

Amadi *et al*. (2022) used the Markov Chain, a stochastic process, to study finite-state stock price formation. The data obtained was used to develop a 5-step transition matrix that involves independent stocks. The study used the expected mean rate of return on each stock to determine which stocks had the highest mean return rate and the best price surge in the future. This would guide investors on the behaviour of stocks when they decide to invest in the stock market.

In a related survey conducted in India on the stock market, (Lakshmi & Manoj, 2020) used the Markov Process to predict the market performance of stocks. The study compared five major stocks in the oil and gas sector over three years. The study was able to determine which stocks in the oil and gas sectors had a high increase in value based on the probabilities calculated, and those that had higher chances of being stable. The study, however, could not determine the factors influencing the increase in value of some stocks and the stability of others.

A similar research conducted by Kallah-Dagadu *et al*. (2022) also used the Markov chain approach to select the best financial stocks listed on the Ghana Stock Exchange using the steady-state probabilities and average recurrent times. The data for the study spanned from January 2017 to December 2020 of weekly stock prices from the Ghana Stock Exchange. A transition matrix was established using three different states. The steady-state probabilities and the mean recurrent times covered a period of three to thirty-five weeks. The best-performing stocks based on the mean recurrent times and steady-state distribution were GCB, Chartered Bank, Cal Bank, and Ecobank.

Weather Forecasts

The Markov Chain model was also used in weather forecasts to determine the weather patterns and rainfall. Tettey *et al*. (2017) employed the Markov Chain approach in their survey to analyse the rainfall patterns in the South-Eastern coast of Ghana, which consisted of five geographical locations (Akatsi, Akuse, Keta, Accra, and Cape Coast). The survey considered data on daily rainfall spanning 1980 – 2010 from these geographical locations to establish transition matrices for each of the towns using the conditional probability of a rainy day or sunny day based on the condition that the previous day, there was rain or there was no rain in the month. The results showed that the probability of rain was, on average, low in Keta, Akuse, Cape Coast, and Akatsi. However, the rainy season in Accra was observed from May to June and from September to October. The southeastern coast of Ghana, particularly from east to west, tends to have an increased probability of rainfall.

Natural Language Processing

Markov Chain model was also used by Almutiri and Nadeem (2022) in natural language processing (NLP). The study reviewed Markov model applications used in natural language processing (NLP): natural language generation, named-entity recognition, and parts of speech tagging. The study focused mainly on researches that apply the Markov chain models to process

NLP and their advantages and disadvantages. The results revealed that the majority of NLP studies used supervised models and Markov models to reduce the dependency on annotation tasks. It further revealed that other studies applied unsupervised solutions to reduce the dependency on lexicon datasets. The study, however, did not point out the merits and demerits of Markov models for processing NLP.

Organisational Management

In social science and humanities, Markov Models have been used to model the allocation of personnel in an organisation. Cao (2022). In his analysis *of the Optimal Allocation of Core Human Resources in Family Enterprises*, used the Markov Model to predict the human resource base of a family business in the next three years. The results showed that there would be low demand for personnel in the future as the business matured. The results also showed variation in competency needs as low-level employees required higher competency but faced less output pressure, while senior employees prioritised performance over raw skill. The study, however, did not consider the development of employees' talent in the future, which is crucial to the growth of human resources. The company needs to retain some employees due to their experience and expertise to facilitate the high productivity growth of the company in the future. Also, succession plan is one of the challenges family businesses are faced with, but this was not factored into the study.

Health

Markov models have been widely used in the health sector to model disease progression and make future predictions on the disease's dynamics. For instance, Senthilvel *et al*. (2012) used the Markov chain to model diabetic retinopathy in T2DM patients. The study was a retrospective study of Type 2 diabetes patients from May to June 2012, involving 200 T2DM patients in Puducherry. Patients were classified into various stages of their condition (retinopathy). The study used MS Excel for data entry and SPSS 16.0 for the analysis. The results showed that out of the 200 patients, 126, representing 63%, were males and 74, that is 37%, were females, with a mean age of 58.80 ± 10.53 years. The results also showed a higher probability (0.82) of patients moving from grade I to Grade II in the first-year transition matrix than in the other grades. Also, patients were likely to move from a lower grade to a higher grade in the five-year transition matrix. The study recommended a comparative study that involved T2DM patients who were undergoing treatment and those who were not on treatment (control group) to study the progression of the disease. One of the study's limitations was its lack of generalizability since it was conducted at a single hospital in India.

Further studies on diabetic retinopathy by Srikanth (2015) also used the Markov Chain model to model the natural progression of diabetic retinopathy in T2DM patients to blind states. The study was an observational study involving 153 T2DM patients from 2010 to 2013. Data on patients' state of condition were recorded each year, and transition matrices were established to model the transitions between years. Chi-square was used to test the robustness of the Markov model and the actual results at the end of the third year, and the results showed that there was no statistically significant difference between the results of the Markov model and the actual results obtained. The results from the Markov model showed that patients who entered the mild NPDR state would stay there for 5 years before transitioning to the moderate NPDR state. In the moderate NPDR state, patients are expected to stay there for about one year before transitioning to a severe NPDR state. The last transition, which is PDR, had a stay time of eight years before a patient entered the absorbed state (blindness). A patient who had mild NPDR was expected to go through the process, spending a total period of 15.29 years before going blind. The study concluded that patients stayed longer in a mild NPDR state than in any other state. Though the study was comprehensive in its analysis, it considers only unidirectional transitions, which means that patients' conditions continue to worsen without improvement. This could not be the case for all patients in this study since these patients were undergoing treatment for their conditions at the hospital; hence, there is a need for another study that will consider the progression and regression of patients' retinopathy conditions.

Lubis *et al*. (2019) also adopted the Markov Chain approach in their survey to detect blood sugar levels in diabetic patients in Indonesia. Data for the study was obtained from a UCI Machine Learning study conducted by Michael Klan, MD, PhD, and Washington University. The study involved 100 diabetic patients. Age, height, weight, and activity of patients were the parameters used to determine the sugar levels of the patients. The model involved a 3-state transition matrix, which predicted the blood sugar levels of patients and predicted the future blood sugar levels of patients by multiplying the transition matrix by the number of years of interest. The study used data from another study, which, in my opinion, is a weakness since Indonesia is ranked fourth with respect to diabetes prevalence in the world (WHO, 2023). Current data could have been obtained by the researcher for the study to add to existing literature and proposed strategies for reducing the prevalence of the disease in the country.

In addition, Grover *et al*. (2019) also employed the Markov Chain approach, a stochastic model to model the progression of chronic kidney disease (CKD) based on the estimated glomerular filtration rate (eGFR) to different stages. The study was a retrospective study involving 117 patients suffering from CKD from March 2006 to October 2016. The progression of the disease was put into five states, and a probability transition matrix was established to determine the movement between states. The effect of prognostic factors on transition rates was examined using the Cox proportional hazard model. The results showed that prognostic factors, such as hypertension, haemoglobin, urea, serum creatinine, and age, were significant in CKD progression. The results also showed a high mean sojourn time in states 1, 2, and 3, which shows a slow progression of the disease. However, the mean sojourn time for state 4 showed a fast deterioration of CKD to renal failure. Though the study covered a long period of study (10 years), which is good for a longitudinal study, the sample size is small and can affect the true nature of the results. Moreover, the study cannot be generalised since data was collected at one location (Delhi and its surrounding area). Further research needs to be conducted in different cities in India to ascertain the general state of CKD progression in the country.

Goel *et al*. (2019) utilised the multistate Markov model approach to predict the natural progression of T2DM based on the haemoglobin A1c. The study involved 246 T2DM patients whose HbA1c was monitored yearly for four years. These patients were classified into three different states based on their HbA1c levels ($4 \leq$ HbA1C ≤ 5.6, $5.7 \leq$ HbA1C ≤ 6.4, and HbA1C $\geq$ 6.5%). The results revealed that the mean age of patients was 26.12 at the point of diagnosis, and the mean confidence interval was between 10-49 years. The results also showed that patients in the normal state were 16.4 times more likely to transition to the diabetic state, and those in a pre-diabetes state were eight times more likely to transition to the diabetic state. The research further revealed that patients who were in the diabetic state had a 79% chance to continue to stay in that state, while those in normal and pre-diabetic states had 4% and 17% chances, respectively, to continue to stay in their current states. The projected time spent in a normal state, pre-diabetes state, and diabetic states was four months, five months, and 39 months, respectively. This indicates that when patients transitioned into the diabetic state, their chances of regression to either the normal or pre-diabetic state were low. The study failed to establish the progression of patients who were in the diabetic state. Is it the last state of their progression? What happens to type 2 diabetic patients who develop hyperglycaemia, which causes severe damage to their nerves? I think further research need to be conducted to fully explore the various stages of the progression of type 2 diabetes, and not limited to the three states of HbA1c.

Howard and Adams (2022) also used the multi-state Markov chain approach to analyse secondary prevention of stroke in Northern Ghana. They obtained secondary data on stroke patients who were undergoing rehabilitation at the medical unit of the Tamale Teaching Hospital to develop an illness-to-death model. Patients' transition rates were observed at distinct periods (every two months) during rehabilitation for two years. The results showed that patients who had a mild stroke would remain in that same state for 10 months before recovery, and they had a zero chance of moving to a severe state if they followed the treatment procedure. Patients who were in the old and older age groups have the same chances of moving to a less severe state and from a mild state to a more severe state. The results also revealed a faster recovery rate of patients from the high state than the low state. The study concluded that patients in a mild state need to adhere to treatment plans to ensure a speedy recovery. The study, however, did not establish factors causing the faster recovery of patients in a high state than in a low state. It was expected that since patients' conditions were not so severe, they should have a faster recovery than those who had severe stroke conditions.

Chapter Summary

The chapter reviewed related works on T2DM cases globally and also, in the country, while concentrating on the risk factors associated with the disease, the prevalence of the disease in the country, complications developed by patients during the progression of the disease, and the economic burden on T2DM patients and the country at large. The chapter also reviewed some mathematical and statistical models that other researchers have used to model the progression of T2DM, including logistic regression models, bivariate and multivariate logistic regression, and Markov chains.

CHAPTER THREE

RESEARCH METHODS

Introduction

This chapter discusses the methodology used for data collection and analysis. Markov Chain, a stochastic model, is used to model the progression of T2DM to neuropathy stages. The model establishes a transition probability matrix, which is used to make projections into the future about the health state of T2DM patients and find the average time patients spend in transient states.

Study Design

This is a retrospective study on T2DM patients who visited the diabetic clinic at the Holy Family Hospital in the Bono East region of Ghana to seek medical care. The hospital is a referral centre and patients from the surrounding districts (Wenchi, Nkoranza, Kintampo, etc.) visit the facility for medical care. Data were obtained on fasting blood sugar (FBS) levels and neuropathy conditions of T2DM patients who visited the diabetic clinic from October 2022 to October 2024. Their fast blood sugar levels and neuropathy conditions were put into groups called states.

Study Area

The study was conducted in the Techiman Municipal and its environs, the capital town of the Bono East region of Ghana. The municipality lies between longitudes 10 49° east and 20 30° west and latitude 80 00° north and 35 70° south. It has a population of about 243,335 people, of which females represent 51.2 %. The municipality occupies a total land size of 669.7 kilometres with a population density of 381 persons per square kilometre (Population and Housing Census, 2021).

Markov Chain

A Markov Chain is a stochastic model that describes the sequence of random variables in a system in which the state at one time epoch depends only on the previous time epoch. (Ching & Michael, 2006). Suppose there are a finite number of states labelled 1, 2, 3 …, s. The discrete-time stochastic process is a Markov chain at time $t = 1,2,3 ...$, if the probability distribution of the state at time $t + 1$ depends on the state at time t (i_t) and does not depend on the states the chain passed through on the way to i_t at time t. The probability, P_{ij} is given as:

$$P(X_{t+1=}j|X_{t=}i) = P_{ij} \tag{1}$$

This property of the Markov chain, where the probability of an event depends only on the last event attained, regardless of all the previous events, is known as the memoryless property of the Markov chain. The transition probability P_{ij} can be represented in a matrix form as:

$$P = \begin{array}{c c} & \begin{array}{cccc} S_1 & S_2 & \cdots & S_z \end{array} \\ \begin{array}{c} S_1 \\ S_2 \\ \vdots \\ S_Z \end{array} & \begin{bmatrix} P_{11} & P_{12} & \cdots & P_{1z} \\ P_{21} & P_{22} & \cdots & P_{2z} \\ \vdots & \vdots & \cdots & \vdots \\ P_{z1} & P_{z2} & \cdots & P_{zz} \end{bmatrix} \end{array} \tag{2}$$

Each entry in the matrix is a non-negative real number that represents a probability, for example, P_{12} = P (X_{t+1} = 2/X_t = 1) is the probability of moving from state 1 to state 2 in one step (one year). If the process is in state i at time 't,' then at the next time stamp, '$t + 1$', it will either stay at i or move to another state. These states are explained through one-step transition probabilities.

Conditions under the transition probability, P_{ij}

1. $P_{ij} \geq 0$ for all i and j

2. $\Sigma_j^n P_{ij} = 1$

Where i= 1, 2, … s

Definition of terms

1. **Accessibility of states**: a state j is said to be accessible from the state i, if a patient can move from i to j denoted as $i \rightarrow$ j, if ${P_{ij}}^n$ >0, then it is assumed that every state is accessible from itself.
2. **Communicate**: states i and j are said to communicate if they are accessible from each other, this is denoted as: $i \leftrightarrow$ j.
3. **Irreducible:** A Markov chain is irreducible if it has one communication class, that is, all states communicate with each other.
4. **Transient State**: This is a state where, when one leaves, the probability of returning is less than one.
5. **Absorbed State**: An absorbed state is a state where, when a patient enters, s/he has zero probability of leaving.

6. **Recurrent State**: A state is said to be recurrent if the probability of returning to that state after you have left that particular state is one.

Classification of Health Status of Patients into States

The health status of patients was grouped into eight classes according to their fasting blood sugar (FBS) levels, the neuropathy conditions developed (numbness, ulcers, and amputation of limbs), and death. Table 1 shows the states of T2DM cases where S1, S2, …, S8 represent states.

Table 1: States of Patient

States	Health status	FBS Level/Condition
S1	Low FBS	3.9mm/L
S2	Normal FBS	3.9 - 5.7mm/L
S3	Moderate FBS	5.8 - 6.9mm/L
S4	High DBS	7.0mm/L
S5	Numbness	hyperglycaemia
S6	Ulcers	wounds
S7	Amputation	loss of limbs/legs
S8	Death	no life

Source: (Researcher's construct, 2025)

State 1 consists of T2DM patients whose fasting blood sugar levels (FBS) are below the normal FBS level of 3.9mmol/L, a condition called hypoglycaemia. State 2 involves patients whose FBS levels are stable and fall within the normal FBS levels of 3.9 – 5.7mmol/L. Patients whose FBS levels are within 5.8 – 6.9mmol/L are classified as moderate or prediabetic. State 4 consists of T2DM patients whose FBS levels are high and equal to or greater than 7mmol/L. In state 5, patients' FBS levels are very high, a condition known as hyperglycaemia, which results in nerve damage, causing poor blood circulation. This causes numbness in the hands or legs. If this condition is not properly managed, patients may develop wounds, which could eventually lead to ulcers, and this state is classified as state 6. State 7 is the state where a patient's hand(s) or leg(s) have been amputated as a result of ulcers that do not heal and spread to other parts of the body. The last state is State 8, which is death. This study is not a sickness-to-death model, but a patient in any of the states can die without necessarily passing through all the various states; hence, death was included. States 1 to 6 are classified as transient states, while states 7 and 8 are classified as absorbed states.

Transient and Absorbing States

A Markov chain is an absorbing chain if it is impossible to leave a state once you enter it (i.e., $P_{ii} = 1$). In an absorbing Markov chain, there is at least one absorbing state, and it is possible to enter an absorbing state from any of the transient states (not necessarily in one step).

A transient state is a state where, when a patient leaves, the probability of the patient returning to the same state is less than one. Let us consider that there are (s-m) transient states $(t_{1,}\ t_{2,} \dots t_{s-m})$ and m absorbing states $(a_1, a_2, \dots a_m)$, then we have a transition probability matrix as shown below:

$$P = \begin{array}{c} \\ t_1 \\ t_2 \\ \vdots \\ t_{s-m} \\ a_1 \\ a_2 \\ \vdots \\ a_m \end{array} \begin{array}{c} \begin{array}{cccccccc} t_1 & t_2 & \cdots & t_{s-m} & a_1 & a_2 & \cdots & a_m \end{array} \\ \begin{bmatrix} q_{11} & q_{12} & \cdots & q_{1(1-m)} & r_{11} & r_{12} & \cdots & r_m \\ q_{21} & q_{22} & \cdots & q_{2(s-m)} & r_{21} & r_{22} & \cdots & r_{2m} \\ \vdots & \vdots & \cdots & \vdots & \vdots & \vdots & \cdots & \vdots \\ q_{(s-m)1} & q_{(s-m)2} & \cdots & q_{(s-m)(s-m)} & r_{m1} & r_{m2} & \cdots & r_{mm} \\ 0 & 0 & \cdots & 0 & 1 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & 0 & 1 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & 0 & 0 & 0 & 1 \end{bmatrix} \end{array} \tag{3}$$

Equation 3 can be represented in the canonical form as:

$$P = \left[\begin{array}{c|c} Q & R \\ \hline O & I \end{array}\right] \tag{4}$$

where Q is a *(s-m) by (s-m)* matrix (a matrix that shows a transition from a transient state to another transient state), R is a (s-m) by m matrix (a matrix that shows a transition from a transient state to an absorbed state), O is an m by (s-m) zero matrix, and I is an m-by-m identity matrix. Thus, Q describes the probability of transitioning from a transient state to another transient state, while R describes the probability of transitioning from a transient state to an absorbing state.

From equation 3, the partitioned matrix gives the following matrices:

$$Q = \begin{bmatrix} q_{11} & q_{12} & \cdots & q_{1(1-m)} \\ q_{21} & q_{22} & \cdots & q_{2(2-m)} \\ \vdots & \vdots & \cdots & \vdots \\ q_{(s-m)1} & q_{(s-m)2} & \cdots & q_{(s-m)(s-m)} \end{bmatrix} \tag{5}$$

$$R = \begin{bmatrix} r_{11} & r_{12} & \cdots & r_{1m} \\ r_{21} & r_{22} & \cdots & r_{2m} \\ \vdots & \vdots & \cdots & \vdots \\ r_{m1} & r_{m2} & \cdots & r_{mm} \end{bmatrix} \qquad (6)$$

$$O = \begin{bmatrix} 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & \cdots & 0 \end{bmatrix} \qquad (7)$$

$$I = \begin{bmatrix} 1 & 0 & \cdots & 0 \\ 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & \cdots & 1 \end{bmatrix} \qquad (8)$$

Waiting Time and Total Time Spent in Transient States before Absorption

Let W be the waiting time in transient states before entering the absorbing state:

$$W = (I - Q)^{-1} \qquad (9)$$

And

W_t be the total periods spent in the transient state before getting absorbed:

$$W_t = (I - Q)^{-1} \; (1_{s-m}) \qquad (10)$$

$w$here

$$1_{s-m} = (1, 1, \dots\ , 1)' \tag{11}$$

Absorption Probability

Let AP be the expected absorption probability in absorbed states, then

$$\text{AP}= WR \tag{12}$$

Equation 12 gives the absorption probability in each state of the absorbed states.

Multinomial Logistic regression

Multinomial logistic regression, also known as polytomous logistic regression, is used to test whether the factors associated with T2DM influence the transition of patients between states. Multinomial logistic regression is an extension of binary logistic regression in which the response variable has more than two possible outcomes, which are not ordered. The predictor variables are either categorical or continuous. Multinomial logistic regression uses maximum likelihood estimation like binary logistic regression. Multinomial logistic regression does not take into consideration the normality, linearity, and homoscedasticity of the data, but rather it considers the independence of the predictor variables (Kwak & Clayton-Matthews, 2002). For instance, if there are j possible outcomes, then there will be j-1 comparisons, and the model is written comparing a particular category to the reference category as π_j

$$In\left(\frac{\pi_j}{\pi_j}\right) = \alpha_j + \beta_j\ x \tag{13}$$

In statistical modelling, the natural log of the ratio between two proportions corresponds to the logit used in standard logistic regression. This logit is sometimes called the generalised logit. Specifically, in a multinomial logistic regression model, this logit is represented as $In\left(\frac{\pi_j}{\pi_j}\right)$, where π_j represents the probability of the j^{th} category.

In generalised linear models, the generalised logit serves as the link function, and the model assumes a multinomial distribution for the outcomes. Unlike standard logistic regression, where comparisons are made between one outcome and the reference category, the multinomial logistic model estimates and compares all categories simultaneously. The j subscript on α_j is the intercept, while the β_j is the slope. The odds ratios are also computed for each category as

$$OR = e^{\beta_j} \tag{14}$$

The odds ratios (OR) indicate an increase or decrease in j multiplicatively to x. The predicted probabilities are computed using the model parameters for a particular value. The standard logistic regression model with k predictor variables $(x_1, x_2, \ldots, x_k)$ for a binary response, the model for the log odds is given as:

$$\pi(x) = \frac{\exp\,(\alpha+\beta_1 x_1+\cdots+\beta_k x_k)}{1+\exp\,(\alpha+\beta_1 x_1+\cdots+\beta_k x_{k})} \tag{15}$$

If there are n independent observations with p-predictor variables and k response categories, the multinomial regression model is given as:

$$\pi_j = \frac{\exp\,(\alpha_{0i}+\beta 1_j x_{1i}+\beta_{2j} x_{2i}+\cdots+\beta_{pj} x_{pi})}{1+\exp\,(\alpha_{0i}+\beta 1_j x_{1i}+\beta_{2j} x_{2i}+\cdots+\beta_{pj} x_{pi})} \tag{16}$$

Where $j = 1,2, \ldots, k-1 \; and \; i = 1,2 \ldots n$

Assumption of multinomial logistic regression

- The observations should be independent
- The outcomes of variables in each category are mutually exclusive and exhaustive.
- There should be a linear relationship between the continuous variables and the logit transformation.
- The independent variables should not be correlated with each other.
- There should not be highly influential points or outliers.

Hypothesis Testing

Hypothesis testing is used to ascertain whether the factors (age, sex, and hypertension) associated with T2DM significantly influence patients' transition from one state to another.

Null Hypothesis (H0): There is no significant relationship between the transition categories and the predictor variables (age, sex, and hypertension).

Alternative Hypothesis (H1): At least one of the predictor variables (age, sex, and hypertension) has a statistically significant effect on the transitioning of patients from one state to another.

Goodness of Fit Test

The Goodness of Fit test was used to measure how well the model fit the data. The Pearson Chi-square statistic, X^2 was used to test the fit of the model.

$$X^2 = \frac{\sum_{k=0}^{g} \sum_{j=0}^{c-1} \left(O_{kj} - E_{kj}\right)^2}{E_{kj}} \tag{17}$$

Where O_{kj} is the observed frequency and E_{kj} is the expected frequency with degrees of freedom $(g-2) \times (c-2)$ (Fagerland *et al*., 2008)

Table 2: Observed O_{kj} and Estimated E_{kj} Frequencies Sorted and Summed into g Groups

	Y=0		Y=1		$\cdots$	Y=c-1	
Group	Obs.	Est.	Obs.	Est.	$\cdots$	Obs.	Est.
1	O_{10}	E_{10}	O_{11}	E_{11}	$\cdots$	$O_{1,c-1}$	$E_{1,c-1}$
2	O_{20}	E_{20}	O_{21}	E_{21}	$\cdots$	$O_{2,c-1}$	$E_{2,c-1}$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\vdots$
g	O_{g0}	E_{g0}	O_{g1}	E_{g1}	$\cdots$	$O_{g,c-1}$	$E_{g,c-1}$

Source: (Fagerland *et al*., 2008)

Hypothesis Test

H_0: The model M_0 fits

H_1: The model does not fit

A significant p-value indicates that the model does not fit the data set, while a non-significant value suggests the model fits the data set.

Chapter Summary

This chapter outlines the steps for applying the Markov Chain model to analyse data on T2DM patients. It outlines the various steps to be used to establish the transition matrix from the data obtained, how the data will be partitioned into the canonical form, and the steps involved in calculating the mean sojourn time for each state in the transient states. It also showed the steps in calculating the absorption probability, and the use of the multinomial logistic regression to test whether the factors associated with T2DM influence transition between states.

CHAPTER FOUR

RESULTS AND DISCUSSION

Introduction

This chapter utilizes basic statistics to describe the association between certain variables related to T2DM, as obtained from the data using the Minitab Software application version 19. Further analysis was conducted using SPSS and MATLAB R2007b application software to examine the risk of progression in patient health from one state of their condition to the next. The average time patients lived with the disease was determined, and projections were made about the future health state of patients. The results obtained are discussed and compared with similar research work that has been done.

Data were collected on all T2DM patients who visited the diabetic clinic for medical care in October 2022. Patients were classified into states based on their FBS levels and the presence of neuropathy complications. State 1 includes patients with low FBS levels (less than 3.9 mmol/L), while State 2 comprises patients with normal FBS levels, ranging from 3.9 - 5.7 mmol/L. State 3 consists of patients with moderate FBS levels (prediabetes), within 5.8 - 6.9 mmol/L. State 4 includes patients with high FBS levels (greater than or equal to 7 mmol/L). State 5 involves patients experiencing numbness in the feet and hands. State 6 consists of patients with ulcers. State 7 includes patients who have undergone limb amputation. Lastly, State 8 comprises T2DM patients who died during the study period. The health status of these same patients was assessed in October 2023, and the results were compared with those from October 2022. A transition matrix was developed to show patient movements from one state to the next within the year. Patients whose medical records did not cover the full 12 months were excluded. By the end of the period, data from 131 T2DM patients who were on medication and visited the hospital regularly for reviews were used for analysis.

The preliminary analyses revealed that out of the 131 patients, 111 were females, representing 84.7%, and 20 were males, representing 15.3%. This is shown in Figure 1.

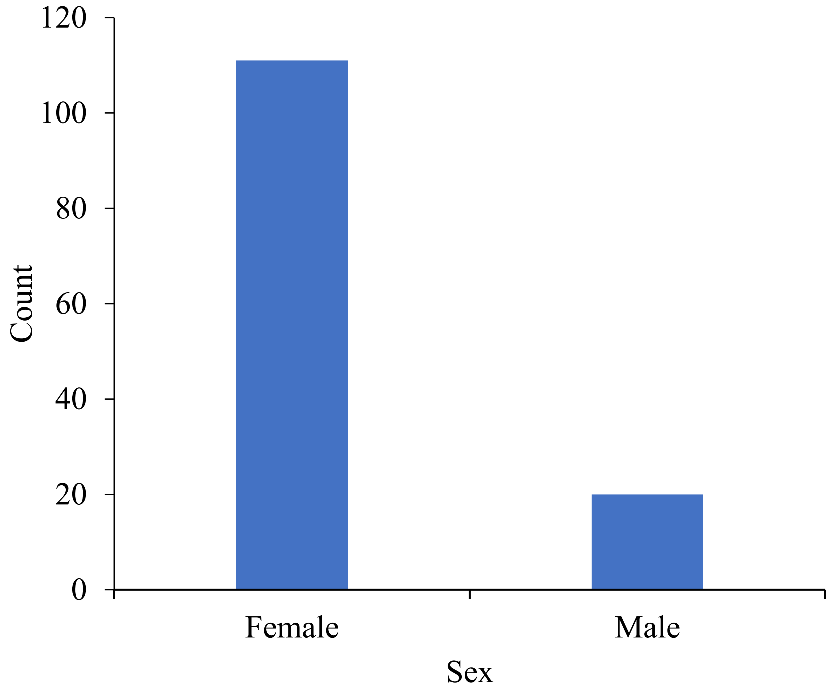

Figure 1: Sex distribution of T2DM patients (Researcher's construct, 2025)

Out of the 131 participants, 127 of them had hypertension, which represents 97%, and the remaining 3% were non-hypertensive. This is shown in Figure 2.

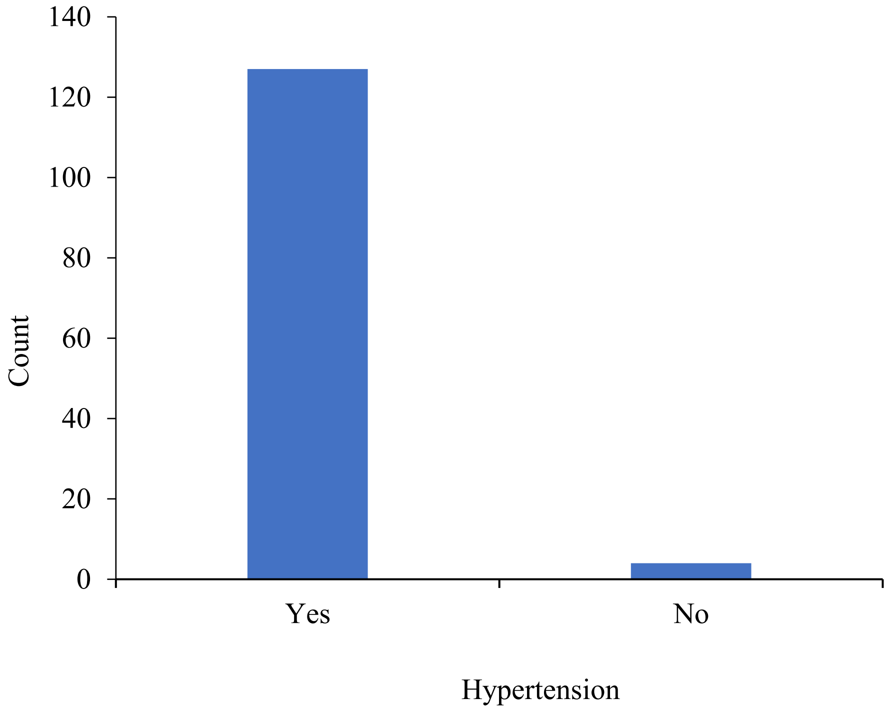

Figure 2: Hypertension status of T2DM Patients

(Researcher's Construct, 2025)

Figure 3 shows the age distribution of T2DM patients with a mean age of 61.5 years. The majority of the participants fall within the age bracket of 50-59 years, followed by the age groups of 60-69 years and 70-79 years.

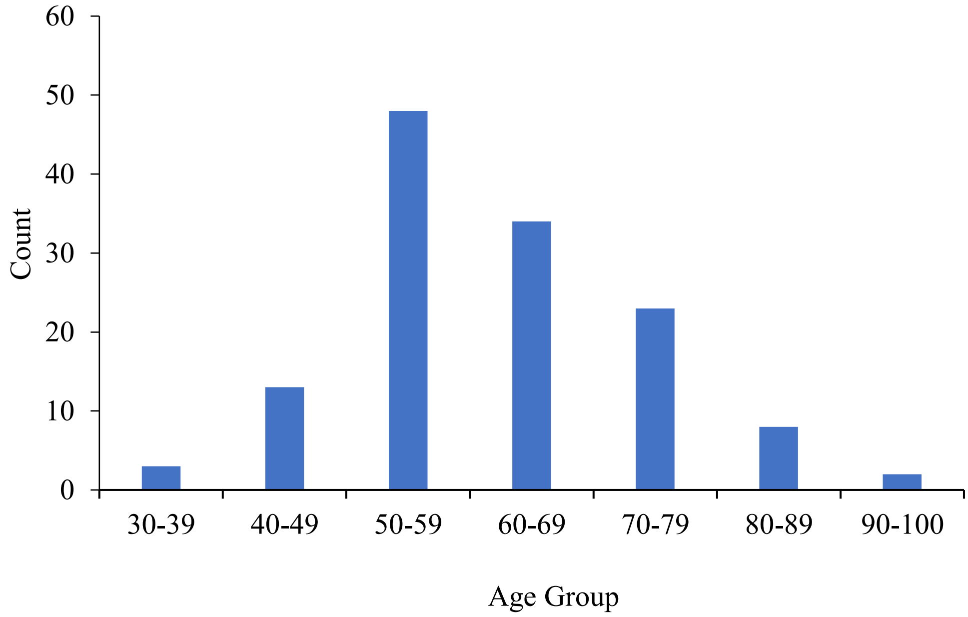

Figure 3: T2DM patients by age group (Researcher's construct, 2025)

The counts for the transition of patients from one state of their condition to another state within the twelve months are shown in Table 3.

Table 3: Frequency Count of Transition T2DM Patients from 2022-2023

Transition	Count	Percent
1,2	1	0.76
1,4	1	0.76
1,8	2	1.53
2,1	1	0.76
2,2	16	12.21
2,3	5	3.82
2,4	6	4.58
2,5	3	2.29
3,2	4	3.05
3,4	14	10.69
3,5	1	0.76

4,1	2	1.53
4,2	9	6.87
4,3	7	5.34
4,4	40	30.53
4,5	3	2.29
4,8	2	1.53
5,4	5	3.82
5,5	5	3.82
5,6	1	0.76
6,6	1	0.76
6,7	1	0.76
7,7	1	0.76
Total	131	100

Source:(Research, 2025)

Table 4: Transition Matrix of the Health State of Patients from 2022-2023

STATES	1	2	3	4	5	6	7	8	TOTAL
1	0	1	0	1	0	0	0	2	4
2	1	16	5	6	3	0	0	0	31
3	0	4	0	14	1	0	0	0	19
4	2	9	7	40	3	0	0	2	63
5	0	0	0	5	5	1	0	0	11
6	0	0	0	0	0	1	1	0	2
7	0	0	0	0	0	0	1	0	1
8	0	0	0	0	0	0	0	0	0
TOTAL	3	30	12	66	12	2	2	4	131

Source: (Researcher's Construct, 2025)

From Table 4, the majority of patients (63.5%) classified under high FBS level (state 4) neither regressed nor progressed, while 11% and 14.3% transitioned to moderate and normal FBS levels, respectively, indicating an improvement in their condition. Additionally, 52% of patients in State 2 (normal FBS level) remained in the same state. Furthermore, the condition of those in State 3 (moderate FBS level) worsened, as 74% transitioned to a diabetic state. Only 21% moved to a normal FBS level, showing an improvement. Among patients with foot numbness, 50% of them condition either improved or worsen. Patients in state 6 (ulcers) either remained in that state or progressed to state 7 (amputation), indicating a higher risk of limb amputation. Patients who started in State 7, all remained in that state throughout the 12 months; none transitioned to another state, which signifies an absorbing state. Refer to Appendix A for the calculations presented in Table 5.

Table 5: Transition Probability Matrix of T2DM Patients from 2022-2023

STATES	1	2	3	4	5	6	7	8
1	0	0.25	0	0.25	0	0	0	0.5
2	0.032	0.52	0.161	0.193	0.094	0	0	0
3	0	0.211	0	0.737	0.052	0	0	0
4	0.032	0.142	0.111	0.635	0.047	0	0	0.033
5	0	0	0	0.455	0.455	0.090	0	0
6	0	0	0	0	0	0.5	0.5	0
7	0	0	0	0	0	0	1	0
8	0	0	0	0	0	0	0	1

Source: (Researcher’s construct, 2025)

The transition probability matrix in Table 5 indicates that diabetes patients who suffered from low FBS levels (State 1) have a 0.25 probability of either having a normal FBS level or a high FBS level within the year. In addition, patients in this same state have a 0.5 probability of dying within the year. State 2 consists of patients whose FBS levels are normal and are between 3.9mmol/L - 5.7mmol/L; these patients have a 0.03 probability of their FBS levels falling below the normal FBS level within the year and a 0.52 likelihood that they will still have a normal FBS level. They also have 0.16 and 0.19 probabilities of moving to FBS levels between 5.8mmol/L - 6.9mmol/L (moderate FBS) and above 7mmol/L (high FBS), respectively. Also, they have a 0.10 probability of developing numbness within the year. The likelihood of developing ulcers, having their limbs amputated, and dying within the year is zero.

On the other hand, patients whose FBS levels are between 5.8mmol/L - 6.9mmol/L (moderate FBS level) have a 0.21 probability of transitioning to a normal FBS state and a 0.74 probability of their FBS levels going up above 7mmol/L(high). They also have a 0.05 probability of developing numbness within the year. Furthermore, patients in this state have a zero probability of developing ulcers, getting their limbs amputated, or dying within the year. Patients whose FBS levels are above 7mmol/L (high FBS level), have a 0.03 probability of transitioning to a low FBS level state, and a 0.14 probability of transitioning to a normal FBS state (3.9mmol/L – 5.7mmol/L). They also have a 0.11 probability of transitioning into moderate FBS levels within the year, a 0.64 probability that their FBS levels will remain the same, and a 0.05

probability of experiencing numbness. They also have a 0.03 probability of dying within the year.

Patients with hyperglycaemia who experience numbness in the limbs (mostly their feet) have a 0.455 probability of either recovering from numbness or continuing to stay in that same state with the same condition. These patients also have a 0.09 probability of developing ulcers within the year. Those who have developed ulcers have a 0.50 probability of remaining in the same state or moving to the next state, which is amputation (State 7).

Lastly, those whose legs have been amputated have a 100% chance of remaining in their condition within the year.

Transition Diagram

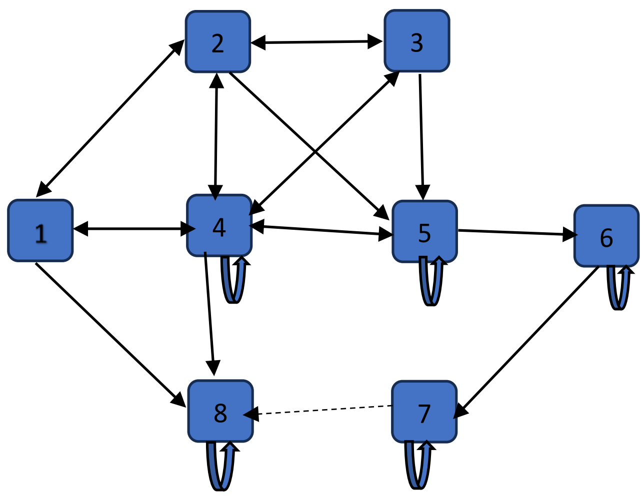

Figure 4: Transition diagram of the movement of T2DM patients within states (Researcher's construct, 2025)

The transition diagram in Figure 4 indicates the movement of patients from one state to another state. The line with double arrows shows that the two states communicate with each other. That is if a patient leaves his/her state and moves to a particular state, the patient can move back to his/her original state. The line with one arrow indicates only a forward movement; that is, if a patient leaves his or her original state and enters the next state, the patient cannot return to that state. The curved arrow shows that a patient remains in his original state within the year without moving to any other state.

State 7 (amputation of limbs) is the last state of the neuropathy progression, and when patients enter that state, they remain there till they die. However, patients can die in any of the states before they get to the last state, which is amputation. So, states 7 and 8 are considered absorbed states. This model is not a sickness-to-death model; hence amputation, which is the last stage of neuropathy progression, is viewed as an absorbed state together with death. There was no movement from amputation to death in this study.

Projection of the Health State of Patients

Table 6: Projected Transition Probabilities of T2DM Patients for 3 years

STATES	1	2	3	4	5	6	7	8
1	0.012	0.133	0.050	0.234	0.04	0.003	0	0.523
2	0.023	0.257	0.098	0.449	0.108	0.015	0.004	0.046
3	0.024	0.218	0.094	0.508	0.088	0.01	0.002	0.055
4	0.024	0.204	0.092	0.490	0.082	0.009	0.002	0.097
5	0.018	0.119	0.066	0.472	0.136	0.064	0.089	0.037
6	0	0	0	0	0	0.125	0.875	0
7	0	0	0	0	0	0	1	0
8	0	0	0	0	0	0	0	1

Source: (Researcher's Construct, 2025)

In three years, patients, irrespective of their state of condition, begin to develop complications gradually. Patients who have hypoglycaemia (low FBS) have about 0.0458 and 0.003 probabilities of developing numbness and ulcers, respectively. Their risk of dying will also increase from 0.5 to 0.522 in three years. Patients who have normal FBS levels (3.9mmol/L-5.7mmol/L) in the next three years have a 0.11 and a 0.02 probability of developing numbness and ulcers, respectively. Their risk of dying will move from 0% to 5% in three years. Patients whose blood sugar levels are between 5.8mmol/L- 6.9mmol/L (moderate FBS) have a 0.5 probability of their blood sugar level going above 7mmol/L(high) in three years, and also, 0.09 and 0.01 probabilities of developing numbness and ulcers, respectively. They also have a 0.06 probability of dying.

Again, patients who have high FBS levels have a 0.49 probability of remaining in that condition in the next three years, and their risk of dying will increase from 0.03 to 0.1. For patients who have developed numbness, they have a 0.47 probability of their condition getting better, and a 0.14 probability that their condition will not change.

Generally, the health state of patients in the next three years shows that the probability of their health improving reduces minimally across all states, and the probability of their condition deteriorating increases gradually across all states.

Table 7: Projected Transition Probabilities of T2DM Patients for 5 years

STATES	1	2	3	4	5	6	7	8
1	0.011	0.106	0.045	0.231	0.046	0.007	0.005	0.549
2	0.022	0.206	0.087	0.455	0.094	0.018	0.020	0.098
3	0.022	0.203	0.088	0.460	0.089	0.015	0.014	0.110
4	0.021	0.193	0.084	0.440	0.085	0.014	0.012	0.150
5	0.019	0.158	0.072	0.408	0.084	0.031	0.143	0.084
6	0	0	0	0	0	0.031	0.969	0
7	0	0	0	0	0	0	1	0
8	0	0	0	0	0	0	0	1

Source: (Researcher's Construct, 2025)

The projected probability matrix for the next 5 years shows a gradual increase in the risk of developing complications from the normal FBS, Moderate FBS, and high FBS states, except the low FBS state, where patients have a 54.91% chance of dying.

The Average Time Spent in Each State of the Transition

The transition probability matrix in Table 3 is partitioned into the canonical form:

$$\pi = \left[\begin{array}{c|c} Q & R \\ \hline O & I \end{array}\right] \tag{18}$$

Where Q is a transition from a transient state to another transient state, and is a 6 by 6 matrix, R is a transition from a transient state to an absorbed state; and a 6 by 2 matrix. O is a zero matrix and I is the identity matrix.

$$\begin{array}{c} \\ 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \\ 7 \\ 8 \end{array}
\begin{array}{c}
\begin{array}{cccccccc} 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 \end{array} \\
\left[\begin{array}{cccccc|cc}
0 & 0.25 & 0 & 0.25 & 0 & 0 & 0 & 0.5 \\
0.032 & 0.516 & 0.161 & 0.194 & 0.097 & 0 & 0 & 0 \\
0 & 0.211 & 0 & 0.737 & 0.052 & 0 & 0 & 0 \\
0.032 & 0.143 & 0.111 & 0.635 & 0.048 & 0 & 0 & 0.031 \\
0 & 0 & 0 & 0.455 & 0.455 & 0.090 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0.5 & 0.5 & 0 \\
\hline
0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1
\end{array}\right]
\end{array}$$

$$Q = \begin{bmatrix} 0 & 0.25 & 0 & 0.25 & 0 & 0 \\ 0.032 & 0.516 & 0.161 & 0.194 & 0.097 & 0 \\ 0 & 0.211 & 0 & 0.737 & 0.053 & 0 \\ 0.032 & 0.143 & 0.111 & 0.635 & 0.048 & 0 \\ 0 & 0 & 0 & 0.455 & 0.455 & 0.091 \\ 0 & 0 & 0 & 0 & 0 & 0.5 \end{bmatrix} \tag{19}$$

$$R = \begin{bmatrix} 0 & 0.5 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0.032 \\ 0 & 0 \\ 0.5 & 0 \end{bmatrix} \tag{20}$$

$$I = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} \tag{21}$$

$$O = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \tag{22}$$

The expected time spent in each state of the transient process; W is given as:

$$W = (I - Q)^{-1} \tag{23}$$

$$(I - Q) = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} - \begin{bmatrix} 0 & 0.25 & 0 & 0.25 & 0 & 0 \\ 0.0323 & 0.5161 & 0.1613 & 0.1935 & 0.0968 & 0 \\ 0 & 0.2105 & 0 & 0.7368 & 0.0526 & 0 \\ 0.0317 & 0.1429 & 0.1111 & 0.6349 & 0.0476 & 0 \\ 0 & 0 & 0 & 0.4545 & 0.4545 & 0.0909 \\ 0 & 0 & 0 & 0 & 0 & 0.5 \end{bmatrix} \tag{24}$$

$(I - Q) =$

$$\begin{bmatrix} 1 & -0.25 & 0 & -0.25 & 0 & 0 \\ -0.323 & 0.4839 & -0.1613 & -0.1935 & -0.0968 & 0 \\ 0 & -0.2105 & 1 & -0.7363 & -0.0526 & 0 \\ -0.0317 & -0.1429 & 0.1111 & 0.3651 & -0.0476 & 0 \\ 0 & 0 & 0 & -0.4545 & 0.5455 & -0.0909 \\ 0 & 0 & 0 & 0 & 0 & 0.5 \end{bmatrix}$$

(25)

$W = (I - Q)^{-1} =$

$$\begin{bmatrix} 1.3241 & 3.2793 & 1.2936 & 6.8826 & 1.3072 & 0.2377 \\ 0.6605 & 7.4748 & 2.6743 & 13.2189 & 2.7378 & 0.4977 \\ 0.6354 & 5.9780 & 3.5146 & 13.9544 & 2.6174 & 0.4758 \\ 0.6359 & 5.6424 & 2.5001 & 14.3113 & 2.4911 & 0.4529 \\ 0.5298 & 4.7011 & 2.0830 & 11.9239 & 3.9089 & 0.7106 \\ 0 & 0 & 0 & 0 & 0 & 2 \end{bmatrix} \quad (26)$$

The expected time spent in the transient process of each state is projected in years since the data was collected within one year. Patients in State 1(low FBS) are expected to stay in that condition for about a year before moving to the next state in the transient states. If the patient transitioned from a low FBS state to a normal FBS state, he/she is expected to stay in that condition for about three years before moving to the next state. However, if the patient transitioned from a low FBS state to either a moderate or high FBS state, the patient is expected to stay in these states for one year and seven years, respectively, before moving to the next state. Patients who transitioned from a low FBS state to a numbness state will continue to experience numbness for one year in that state of their condition. A patient who transitions from a low FBS state to an ulcer state is expected to stay in that state for only two years before s/he enters the absorbed states, that is, amputation of limbs or death.

Also, a patient classified in State 2 (normal FBS) is expected to continue to have a normal FBS level for about eight years before transitioning to any other state. After that, if the patient transitions to a moderate FBS level or a high FBS level, the patient is expected to stay in these states for about three years and thirteen years, respectively. However, if the patient transitions from a normal FBS state to a numbness state or ulcer state, s/he is expected to stay in these states for about three years and less than a year, respectively. Again, if a patient transitions to a low FBS level, the patient is expected to stay there for less than a year

In addition, if a patient was classified in State 3 (moderate FBS) at the beginning of the process, the patient is expected to stay in that state for about four years before transitioning to any other state in the transient states. But if the patient transitioned to either a normal FBS state, or a low FBS state, s/he is expected to spend about six years or less than a year, respectively in these states. Nevertheless, if the patient transitions to either the high FBS or numbness states, s/he is expected to stay in these states for fourteen years or about three years, respectively. However, if the patient enters the ulcer state, s/he is expected to spend less than a year in that state before being absorbed.

Again, a patient who started with a high FBS level has a maximum of fourteen years to stay in that state before transitioning to any other state in the transient states. After that, if the patient transitioned to either a normal FBS state or a low FBS state, s/he is expected to stay in these conditions for about five years or six months, respectively in these states. But, if the patient transitioned to either a moderate FBS or a numbness state, the patient is expected to stay in these states for about three years or two years, respectively in these states. Patients who entered State 6 (ulcer) are expected to spend less than a year in this state before being amputated or dying.

Similarly, a patient classified in State 5 (numbness), the patient is expected to stay in this state for four years before transitioning to any other state in the transient states. After the 4 years, if the patient transitions to a moderate or a high FBS state, s/he can stay in these states for two years or 12 years, respectively. The patient has less than a year's stay period if s/he transitions to the low FBS state. However, if the patient transitions to a normal FBS state or an ulcer state, then the patient can stay in these states for about five years or less than a year, respectively.

Lastly, if a patient started in State 6 (ulcer), s/he does not have a chance of transitioning into any state in transient states but will remain in his/her current state for two years before getting amputated or dying.

Total Time Spent in Transient States before Absorption

Let W_t be the total time spent in the transient state before being absorbed.

where $t = 1,2\ 3,4,5,6$

Let N be a matrix of ones:

$$N = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} \tag{27}$$

$$W_t = WN \tag{28}$$

W_t=

$$\begin{bmatrix} 1.3241 & 3.2793 & 1.2936 & 6.8826 & 1.3072 & 0.2377 \\ 0.6605 & 7.4748 & 2.6743 & 13.2189 & 2.7378 & 0.4977 \\ 0.6354 & 5.9780 & 3.5146 & 13.9544 & 2.6174 & 0.4758 \\ 0.6359 & 5.6424 & 2.5001 & 14.3113 & 2.4911 & 0.4529 \\ 0.5298 & 4.7011 & 2.0830 & 11.9239 & 3.9089 & 0.7106 \\ 0 & 0 & 0 & 0 & 0 & 2 \end{bmatrix} \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix}$$

(29)

$$W_t = \begin{bmatrix} 14.3244 \\ 27.2639 \\ 27.1756 \\ 26.0337 \\ 23.8572 \\ 2 \end{bmatrix} \tag{30}$$

From equation 30, the mean sojourn time spent in transient states for patients classified under a low FBS state before they got absorbed (amputation of limbs or death) is 14 years. Patients who were classified in a normal FBS state and a moderate FBS state have a mean sojourn time of 27 years each in transient states before they either get their limbs amputated or die from their condition. Patients who were in a high FBS state have a mean sojourn time of 26 years in transient states before they enter the absorbed states, where their limbs are either amputated (as a result of slow-healing ulcers spreading to other parts of the body) or die from the disease. Furthermore, patients who have developed numbness in their feet or hands have a mean sojourn time of 24 years in transient states before entering the absorbed states. These patients, after 24 years, will either have their limbs amputated or die because of T2DM complications.

Lastly, patients who have already developed diabetic ulcers have a mean sojourn time of two years in a transient state before entering an absorbed state. Their condition is expected to worsen in two years; hence they will be amputated of their condition.

Absorption Probability

The expected absorption probability (EAP) when a patient gets absorbed in an absorbing state S_j from a transient state S_i is given as:

$$EAP = WR \tag{31}$$

$$EAP = \begin{bmatrix} 1.3241 & 3.2793 & 1.2936 & 6.8826 & 1.3072 & 0.2377 \\ 0.6605 & 7.4748 & 2.6743 & 13.2189 & 2.7378 & 0.4977 \\ 0.6354 & 5.9780 & 3.5146 & 13.9544 & 2.6174 & 0.4758 \\ 0.6359 & 5.6424 & 2.5001 & 14.3113 & 2.4911 & 0.4529 \\ 0.5298 & 4.7011 & 2.0830 & 11.9239 & 3.9089 & 0.7106 \\ 0 & 0 & 0 & 0 & 0 & 2 \end{bmatrix} \begin{bmatrix} 0 & 0.5 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0.0317 \\ 0 & 0 \\ 0.5 & 0 \end{bmatrix}$$

$$EAP = \begin{bmatrix} 0.1188 & 0.8802 \\ 0.2489 & 0.7493 \\ 0.2379 & 0.7601 \\ 0.2264 & 0.7716 \\ 0.3553 & 0.6429 \\ 1 & 0 \end{bmatrix} \tag{32}$$

From the expected absorption probabilities in equation 15, the likelihood that a patient with low FBS level will have his or her limbs amputated in the absorbed state is 0.1188 and the likelihood that the patient will die in the absorbed state is 0.8802. The probability that patients with normal FBS levels will have their limbs amputated in the absorbed state is 0.2489, and the likelihood that they will die in the absorbed state is 0.7493. Patients who have moderate and high FBS levels have 0.2379 and 0.2264 probabilities of their limbs being amputated in the absorbed state, respectively, and 0.7601 and 0.7716 probabilities of dying in the absorbed state, respectively.

Again, patients who have developed numbness of the feet and hands have a 0.3553 probability of their limbs being amputated, and a 0.6429 probability of dying in the absorbed state, whilst patients who have developed diabetes ulcers have a 100% chance of their limbs being amputated and a zero chance of dying in the absorbed state.

Generally, the probability of patients dying in the absorbed state is higher than the probability of patients having their limbs amputated, except for patients who have developed diabetic ulcers.

Output of Multinomial Logistic Regression Using SPSS

Table 8: Case Processing Summary

	Transition 2022 to 2023	N	Marginal Percentage
	1,2	1	0.80%
	1,4	1	0.80%
	1,8	2	1.50%
	2,1	1	0.80%
	2,2	16	12.20%
	2,3	5	3.80%
	2,4	6	4.60%
	2,5	3	2.30%
	3,2	4	3.10%
	3,4	14	10.70%
	3,5	1	0.80%
	4,1	2	1.50%
	4,2	9	6.90%
	4,3	7	5.30%
	4,4	40	30.50%
	4,5	3	2.30%
	4,8	2	1.50%
	5,4	5	3.80%
	5,5	5	3.80%
	5,6	1	0.80%
	6,6	1	0.80%
	6,7	1	0.80%

	7,7	1	0.80%
Sex	F	111	84.70%
	M	20	15.30%
Hypertension	NO	4	3.10%
	YES	127	96.90%
Valid		131	100.00%
Missing		0	
Total		131	
Subpopulation		58a	

Source: (Researcher's Construct, 2025)

Table 8 gives a summary of the data with 23 transition categories, which are the response categories and three predictor variables: age, sex, and hypertension. The total number of respondents in the study was 131, comprising 111 females and 20 males. Also, 127 of the respondents are hypertensive.

Table 9: Step Summary

Model	Action	Effect(s)	Model Fitting Criteria -2Log Likelihood	Effect Selection Tests Chi-Square
0	Entered	Intercept, Age, Hypertension, Sex	465.725	.

Source: (Researcher's Construct, 2025)

The step summary in Table 8 did not include the interaction terms, indicating that there is no interaction between age, sex, and hypertension.

Table 10: Model Fitting Information

Model	Model Fitting Criteria	Likelihood Ratio Tests		
	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	516.894			
Final	465.725	51.169	66	0.91

Source: (Researcher's Construct, 2025)

The model is not statistically significant since the p-value (0.91) is greater than the alpha value of 0.05. This indicates that the predictor variables age, sex, and hypertension, though associated factors of T2DM, do not have any statistically significant influence on the transition of patients from one state to the other. Transition depends on FBS levels, and these factors, though risk factors of getting diabetes, do not determine a patient's movement from one state to another, but rather depend on the FBS levels.

Table 11: Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	834.722	1188	1
Deviance	367.91	1188	1

Source: (Researcher's Construct, 2025)

The goodness-of-fit table shows that both the Pearson and deviance are not statistically significant because they both have p-values greater than the alpha value of 0.05, which suggests that the model, though not statistically significant, is a good fit for the data.

Table 12: Overall Model Fit

Pseudo R-Square	
Cox and Snell	0.323
Nagelkerke	0.326
McFadden	0.079

Source: (Researcher's Construct, 2025)

The Cox and Snell, Nagelkerke, and McFadden all have smaller values less than 1, which means that the overall model is not a good fit.

Table 13: Likelihood Ratio Test

Effect	Model Fitting Criteria -2 Log Likelihood of Reduced Model	Chi-Square	df	Sig.
Intercept	465.725a	0	0	.
Age	486.582b	20.856	22	0.53
Hypertension	461.075	.	22	.
Sex	472.835b	7.11	22	0.999

Source: (Researcher's Construct, 2025)

The likelihood ratio test in Table 13 indicates that none of the predictor variables are statistically significant because they all have p-values greater than the alpha value of 0.05. This means that they do not have any statistically significant influence on the transition of patients from one state to another. The other output tables are in Appendix B.

Discussion

T2DM is a chronic metabolic disorder that is characterised by high levels of sugar in the blood, which causes serious damage to the kidneys, heart, blood vessels, eyes, and nerves. Some of the factors associated with T2DM include: overweight, advanced age, female gender, urban environment, and educational level (Motala, 2014). In this study, the majority of participants were females, representing 84.7%, which indicates that more females reported to the facility than their male counterparts. The mean age of participants is 61.5 years, which is in line with a similar study conducted by (Liu et al., 2010) in China, where the mean age was 63.3 ± 12.2 years. Another study in India, conducted by Senthilvel et al. (2012), also arrived at a similar mean age of 58.83 ± 10.53 years. However, Senthilvel *et al*. (2012), reported more males (63%) than females 37% in their study.

The majority of the participants in this study fall within the age bracket of 50 to 79 years, and this is in consonance with Gatimu et al. (2016) who also reported an increase of 3.95% in diabetes among adults aged 50 years and above. The study also identified hypertension as a major factor associated with T2DM since 96% of participants were hypertensive, and this is consistent with Ekoru et al.'s (2019) study, where they identified hypertension, hyperlipidaemia, and obesity as the most common complications or comorbidities in T2DM patients, in which hypertension constituted 71% of the cases.

The transition of patients from moderate FBS levels (prediabetes) to high FBS levels (diabetes) was high (73.68%) within one year. Most patients with normal and high FBS levels remained in the same states within the year. Low FBS (hypoglycaemia) is a serious condition among T2DM since 50% of patients in that state die within the year. The projected probabilities of patients' state of health in the next three and five years show a gradual increase in patients' risk of developing neuropathy complications such as numbness of feet and hands, diabetic ulcers, amputation of limbs, and an increased risk of dying. This suggests that in the long term, patients' conditions will worsen rather than improve, and this is in line with Berhe et al. (2023) .

The average time spent in each state of the transient phase shows that patients spend more years in state 4, which is the diabetes state. After that, most of them begin to develop numbness and gradually progress to an ulcer state before entering the absorbed state (amputation of limbs or death). Patients with low FBS levels who enter state 4 can remain there for at least six years before leaving. Those who transition from a normal FBS state or numbness state to the diabetes state spend at least 13 years in each before moving on. Patients entering state 6 (diabetes ulcers) spend less than a year in that state. This stage is characterised by rapid deterioration, and patients are often amputated when they leave that state.

The mean sojourn time for patients in transient states is 14 years for a low FBS state and 27 years for a normal FBS state. Additionally, the mean sojourn times for patients with high FBS levels and those experiencing numbness are 26 and 23 years, respectively, while patients with diabetic ulcers have a mean sojourn time of two years. Patients in the ulcer state have no chance of transitioning to any other state within the transient states. After two years, it is expected that these patients will enter the absorbed state, where their limbs will likely be amputated.

In conclusion, T2DM can be managed to prolong the life span of patients if they adhere to good dietary practices and take their medication regularly. This is evidenced in the mean sojourn time, which shows patients could live with the disease for up to 27 years before they get amputated or die from their condition. This is similar to Srikanth's study on diabetes retinopathy, where the mean sojourn time of T2DM patients in transient states was between 8 to 15 years before they went blind, and even 23 years in the city of Taiwan. Lastly, when patients enter the absorbing states (amputation of limbs and death), they have a higher probability (0.6 to 0.88) of dying than being amputated, except in the ulcer state, where patients have a 100% chance of being amputated.

Chapter Summary

In this chapter, Minitab software application was used for the preliminary analysis of basic statistics and their relationship with T2DM, whilst MATLAB Application software was used for further analysis of the data. The probability matrix for the transition of patients from one state of their condition was established and used to project the health state of patients in the next three to five years. The mean sojourn time spent in the transient states by patients before they were absorbed, and the absorption probability in the absorbed states were also calculated to establish how long patients stayed with the disease before being amputated or dying.

CHAPTER FIVE

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Overview

This chapter gives an overview of the entire study and the conclusions from the analysis of the data. It also presents recommendations for future research on the progression of T2DM and its management and for policymakers to take pragmatic steps to reduce the increasing cases of the disease.

Summary

The objective of this study is to model the neuropathy progression of T2DM cases using the fasting blood sugar (FBS) levels of patients and other complications developed, such as numbness, ulcers, and amputations of limbs. The study also explored the average time patients live with the disease in the progression states before their limbs are amputated or they die. Data were obtained on all T2DM patients who visited the diabetic clinic for medical care in October 2022. The health state of patients' condition was assessed using their fasting blood sugar levels and neuropathy conditions developed at the time of the study and put into groups called states: State 1 consisted of patients with low FBS levels (< 3.9mmol/L), State 2 was made up of patients whose FBS level was normal and within the range of 3.9 – 5.7mmol/L, State 3 are patients whose FBS levels are moderate (5.8 – 6.9mmol/L), State 4 consisted of patients with high FBS levels (≥ 7mmol/L), State 5, patients who experienced numbness of the feet and hands, State 6 consisted of patients who had developed ulcers, State 7, patients who limbs have been amputated and

State 8, patients who died within the study period. (October 2022 - October 2023). The health state of these same patients was assessed in October 2023, and the results were compared with those taken in October 2022. A transition matrix was established, which showed the movement of patients from one state to another within the year. Patients whose information didn't cover the 12 months and those whose diabetic status was unknown were excluded. In all, 131 T2DM patients who were on medication and visited the hospital regularly for review data were used for this analysis.

About 422 million people worldwide live with diabetes, with the majority of these people in the lower and middle-income countries. About 1.5 million people die every year of diabetes (WHO, 2023). The prevalence rate of T2DM cases in Africa has been increasing, and the majority of these patients are aged below 60 years (Motala, 2014). Ghana is also battling with the disease, with 6% of its adult population being affected by T2DM, and this has been attributed to advanced age, female gender, urban environment, high income, and tertiary education (Danquah et al., 2012).

Markov chain, a stochastic model, was used to model the progression of T2DM in patients and to find the average time patients stay with the disease before their limbs are amputated or they die. The model also projected the health state of patients for the next three years and five years using the transition matrix established.

Statistical software such as SPSS and MATLAB was used for the analysis of the data. The preliminary results revealed that 84.7% of patients were females and the remaining 15.3% males. In addition, about 97% of the patients in this study were hypertensive. The majority of T2DM patients fall within the age group 50-59 years. The second age group with the most patients is the age group 60-69 years, followed by the age group 70-79 years.

The transition matrix was established and used to make projections into the future about the state of health of patients. The transition matrix also indicates the movement of patients from one state to another within the year. The mean sojourn time was also computed, which revealed the average time patients spent in the transient states (states 1 to 6) before they entered the absorbed states (amputation of limbs or death). The results further showed that, T2DM patients' condition would worsen in the long term rather than improve since patients' condition in three years and five years showed an increase in the risk of developing numbness of the feet, diabetic ulcer, amputation of the feet, and death. Also, patients who entered the ulcer state have a no chance of regressing to any of the states, but rather have a 50% chance of either remaining in the same condition or progress to the amputation state. Patients who enter the diabetic state (high FBS level) from any other state will stay there for a longer time than any other state.

In addition, patients in a low FBS state have a stay period of 14 years before their limbs are amputated or they die from their condition. Those in normal and moderate FBS states have a stay period of about 27 years before their limbs are amputated or they die from their condition. In addition, patients who are in a high FBS state and a numbness state have a stay period of 26 and 23 years, respectively. However, patients in the ulcer state have about 2 years stay period in that state before their limbs are amputated or they die from their condition.

Conclusions

The study identified seven states of neuropathy progression of T2DM, and death being the last state. States one to six were classified as transient states, while states seven and eight were absorbed states. Patients were expected to progress to the last state, which is amputation; however, some patients died in some of the states before amputation. A patient can die in any of the six states in the transient states.

The study also identifies age, sex, and hypertension as factors associated with T2DM. Females constitute 84.7% of T2DM participants in the research, and 97% of them were hypertensive. In addition, most patients in this study were in the middle age group of 40-49 and 50-59 years.

The study also revealed that when patients develop ulcers on their limbs, they have a 100% chance that they will be amputated in about two years. The study also identifies state 1 (low FBS level) and state 6 (ulcer) as high-risk states, and patients should ensure that they do not enter these states since the risk of dying in state 1 is 50% and the risk of getting amputated in state 6 is 100%.

In addition, the projected probability matrices for the next 3 and 5 years showed a gradual increase in the risk of developing complications from the normal FBS, Moderate FBS, and high FBS states, except the low FBS state, where patients have a 54.91% chance of dying.

Lastly, the average time patients in a low FBS state can live with the disease before they get their limbs amputated or die is 14 years, whilst patients in the normal and pre-diabetes states have an average stay period of 27 years before their limbs are amputated or die of their condition. Patients who are in the moderate or high states have an average stay time of 26 and 24 years, respectively, and patients in the ulcer state have a stay time of 2 years before their limbs are amputated. Patients can manage their condition with adherence to medications and adopt a healthy lifestyle to live long with the disease.

Recommendations

The study recommends the following:

The Bono East health directorate should intensify education on the prevalence of T2DM and the economic burden of the disease within the region.

Diabetes patients who visit the health facility for medical care should be educated on the risks involved in the progression of the disease so that patients will take their medication very seriously and adopt healthy lifestyles to prolong their lives.

Further studies should be done to compare the risks of progression and patients' dietary preferences, including those who do not take their medication regularly.

Women were more exposed to T2DM and should therefore take preventive measures such as exercising and eating a healthy diet to avoid being overweight, since it is one of the major risk factors of T2DM.

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APPENDICES

APPENDIX A

CALCULATION OF TRANSITION PROBABILITIES

The probability of transitioning from state ι to state j is denoted by $P_{\iota j}$.

$P_{\iota j}$ = the number of counts in row ι, column j divided by the total counts in row ι.

$P_{11} = \frac{0}{4}$

$= 0$

$P_{12} = \frac{1}{4}$

$= 0.25$

$P_{13} = \frac{0}{4}$

$= 0$

$P_{14} = \frac{1}{4}$

$= 0.25$

$P_{15} = \frac{0}{4}$

$= 0$

$P_{16} = \frac{0}{4}$

$= 0$

$P_{17} = \frac{0}{4}$

$= 0$

$P_{18} = \frac{2}{4}$

$= 0.5$

$P_{21} = \frac{1}{31}$

$= 0.0323$

$P_{22} = \frac{16}{31}$

$= 0.5161$

$P_{23} = \frac{5}{31}$

$= 0.1613$

$P_{24} = \frac{6}{31}$

$= 0.1935$

$P_{25} = \frac{3}{31}$

$= 0.0968$

$P_{26} = \frac{0}{31}$

$= 0$

$P_{27} = \frac{0}{31}$

$= 0$

$P_{28} = \frac{0}{31}$

$= 0$

$P_{31} = \frac{0}{19}$

$= 0$

$P_{32} = \frac{4}{19}$

$= 0.2105$

$P_{33} = \frac{0}{19}$

$= 0$

$P_{34} = \frac{14}{19}$

$= 0.7368$

$P_{35} = \frac{1}{19}$

$= 0.0526$

$P_{36} = \frac{0}{19}$

$= 0$

$P_{37} = \frac{0}{19}$

$= 0$

$P_{38} = \frac{0}{19}$

$= 0$

$P_{41} = \frac{2}{63}$

$= 0.0317$

$P_{42} = \frac{9}{63}$

$= 0.1429$

$P_{43} = \frac{7}{63}$

$= 0.1111$

$P_{44} = \frac{40}{63}$

$= 0.6349$

$$P_{45} = \frac{3}{63}$$
$$= 0.0476$$

$$P_{46} = \frac{0}{63}$$
$$= 0$$

$$P_{47} = \frac{0}{63}$$
$$= 0$$

$$P_{48} = \frac{2}{63}$$
$$= 0.0317$$

$$P_{51} = \frac{0}{11}$$
$$= 0$$

$$P_{52} = \frac{0}{11}$$
$$= 0$$

$$P_{53} = \frac{0}{11}$$
$$= 0$$

$$P_{54} = \frac{5}{11}$$
$$= 0.4545$$

$$P_{55} = \frac{5}{11}$$
$$= 0.4545$$

$$P_{56} = \frac{1}{11}$$
$$= 0.0909$$

$$P_{57} = \frac{0}{11}$$
$$= 0$$

$$P_{58} = \frac{0}{11}$$
$$= 0$$

$$P_{61} = \frac{0}{2}$$
$$= 0$$

$$P_{62} = \frac{0}{2}$$
$$= 0$$

$P_{63} = \frac{0}{2}$

$= 0$

$P_{64} = \frac{0}{2}$

$= 0$

$P_{65} = \frac{0}{2}$

$= 0$

$P_{66} = \frac{1}{2}$

$= 0.5$

$P_{67} = \frac{0}{2}$

$= 0.5$

$P_{68} = \frac{0}{2}$

$= 0$

$P_{71} = \frac{0}{1}$

$= 0$

$P_{72} = \frac{0}{1}$

$= 0$

$P_{73} = \frac{0}{1}$

$= 0$

$P_{74} = \frac{0}{1}$

$= 0$

$P_{75} = \frac{0}{1}$

$= 0$

$P_{76} = \frac{0}{1}$

$= 0$

$P_{77} = \frac{1}{1}$

$= 1$

$P_{78} = \frac{0}{1}$

$= 0$

P_{81} to P_{87} will all have a probability of zero except P_{88} which will automatically have a probability of 1 since it is an absorbed state. The transition matrix is shown in Table 3.

APPENDIX B

PARAMETER ESTIMATES

Transition 2022to2023a		B	Std. Error	Wald	df	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
								Lower Bound	Upper Bound
1,2	Intercept	-2.861	12.287	0.054	1	0.816			
	Age	0.108	0.159	0.467	1	0.494	1.114	0.817	1.521
	[Hypertension=NO]	2.924	11216.785	0	1	1	18.614	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-5.747	7.711	0.555	1	0.456	0.003	8.72E-10	11698.46
	[Sex=M]	0c	.	.	0	.	.	.	.
1,4	Intercept	-7.32	13.33	0.302	1	0.583			
	Age	0.115	0.141	0.667	1	0.414	1.122	0.851	1.48
	[Hypertension=NO]	0.969	11194.72	0	1	1	2.634	0	.b

	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.279	10.091	0.001	1	0.978	1.322	3.40E-09	513681885.8
	[Sex=M]	0c	.	.	0	.	.	.	.
1,8	Intercept	-11.734	11.739	0.999	1	0.317			
	Age	0.192	0.13	2.163	1	0.141	1.211	0.938	1.563
	[Hypertension=NO]	2.202	8276.86	0	1	1	9.047	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-0.092	8.526	0	1	0.991	0.912	5.04E-08	16516113.76
	[Sex=M]	0c	.	.	0	.	.	.	.
2,1	Intercept	-0.659	13.536	0.002	1	0.961			
	Age	0.011	0.153	0.005	1	0.944	1.011	0.749	1.363
	[Hypertension=NO]	0.082	0	.	1	.	1.086	1.086	1.086
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.051	10.124	0	1	0.996	1.052	2.54E-09	435800716.3
	[Sex=M]	0c	.	.	0	.	.	.	.
2,2	Intercept	3.098	9.754	0.101	1	0.751			

	Age	0.042	0.113	0.139	1	0.709	1.043	0.836	1.302
	[Hypertension=NO]	13.272	5229.606	0	1	0.998	580490.1	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-3.326	7.154	0.216	1	0.642	0.036	2.92E-08	44192.321
	[Sex=M]	0c	.	.	0	.	.	.	.
2,3	Intercept	0.054	10.052	0	1	0.996			
	Age	0.062	0.118	0.274	1	0.601	1.064	0.844	1.341
	[Hypertension=NO]	0.687	6988.329	0	1	1	1.988	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-2.29	7.226	0.1	1	0.751	0.101	7.16E-08	143126.664
	[Sex=M]	0c	.	.	0	.	.	.	.
2,4	Intercept	-1.128	10.334	0.012	1	0.913			
	Age	0.047	0.117	0.164	1	0.686	1.048	0.834	1.317
	[Hypertension=NO]	0.348	6759.186	0	1	1	1.417	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.197	7.728	0.001	1	0.98	1.217	3.22E-07	4604196.861

	[Sex=M]	0c	.	.	0	.	.	.	.
2,5	Intercept	3.427	10.377	0.109	1	0.741			
	Age	0.008	0.127	0.004	1	0.952	1.008	0.786	1.292
	[Hypertension=NO]	0.454	8133.395	0	1	1	1.575	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-3.164	7.243	0.191	1	0.662	0.042	2.89E-08	61864.956
	[Sex=M]	0c	.	.	0	.	.	.	.
3,2	Intercept	-7.13	10.68	0.446	1	0.504			
	Age	0.133	0.119	1.256	1	0.262	1.143	0.905	1.442
	[Hypertension=NO]	1.201	7141.855	0	1	1	3.323	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.239	7.958	0.001	1	0.976	1.27	2.14E-07	7551808.116
	[Sex=M]	0c	.	.	0	.	.	.	.
3,4	Intercept	0.167	9.784	0	1	0.986			
	Age	0.06	0.113	0.285	1	0.593	1.062	0.852	1.324
	[Hypertension=NO]	0.522	5919.745	0	1	1	1.686	0	.b

	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-1.113	7.213	0.024	1	0.877	0.329	2.38E-07	453274.845
	[Sex=M]	0c	.	.	0	.	.	.	.
3,5	Intercept	-9.219	13.327	0.479	1	0.489			
	Age	0.144	0.142	1.031	1	0.31	1.155	0.875	1.524
	[Hypertension=NO]	1.354	10950.8	0	1	1	3.873	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.201	9.976	0	1	0.984	1.223	3.94E-09	379275906.3
	[Sex=M]	0c	.	.	0	.	.	.	.
4,1	Intercept	-0.948	12.131	0.006	1	0.938			
	Age	0.027	0.141	0.036	1	0.85	1.027	0.779	1.354
	[Hypertension=NO]	17.455	5229.603	0	1	0.997	38084168	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-0.555	8.81	0.004	1	0.95	0.574	1.82E-08	18124103.98
	[Sex=M]	0c	.	.	0	.	.	.	.
4,2	Intercept	-1.28	9.869	0.017	1	0.897			

	Age	0.082	0.114	0.519	1	0.471	1.086	0.868	1.358
	[Hypertension=NO]	0.75	6234.922	0	1	1	2.118	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-1.531	7.218	0.045	1	0.832	0.216	1.55E-07	301533.403
	[Sex=M]	0c	.	.	0	.	.	.	.
4,3	Intercept	-6.18	10.016	0.381	1	0.537			
	Age	0.155	0.116	1.785	1	0.182	1.168	0.93	1.467
	[Hypertension=NO]	1.674	6349.96	0	1	1	5.334	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-1.866	7.224	0.067	1	0.796	0.155	1.10E-07	218155.908
	[Sex=M]	0c	.	.	0	.	.	.	.
4,4	Intercept	3.91	9.646	0.164	1	0.685			
	Age	0.026	0.111	0.054	1	0.816	1.026	0.826	1.274
	[Hypertension=NO]	16.506	5229.603	0	1	0.997	14738815	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-1.848	7.151	0.067	1	0.796	0.158	1.29E-07	192386.167

	[Sex=M]	0c	.	.	0	.	.	.	.	
4,5	Intercept	0.359	10.354	0.001	1	0.972				
	Age	0.057	0.125	0.211	1	0.646	1.059	0.829		1.352
	[Hypertension=NO]	0.832	7967.011	0	1	1	2.297	0	.b	
	[Hypertension=YES]	0c	.	.	0	.	.	.	.	
	[Sex=F]	-3.005	7.243	0.172	1	0.678	0.05	3.39E-08		72430.095
	[Sex=M]	0c	.	.	0	.	.	.	.	
4,8	Intercept	-11.093	11.482	0.933	1	0.334				
	Age	0.226	0.14	2.598	1	0.107	1.253	0.952		1.65
	[Hypertension=NO]	3.405	8216.596	0	1	1	30.113	0	.b	
	[Hypertension=YES]	0c	.	.	0	.	.	.	.	
	[Sex=F]	-3.917	7.304	0.288	1	0.592	0.02	1.21E-08		32799.789
	[Sex=M]	0c	.	.	0	.	.	.	.	
5,4	Intercept	-1.849	10.475	0.031	1	0.86				
	Age	0.056	0.118	0.224	1	0.636	1.057	0.84		1.331
	[Hypertension=NO]	0.412	7003.595	0	1	1	1.51	0	.b	

	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.223	7.842	0.001	1	0.977	1.25	2.64E-07	5914910.578
	[Sex=M]	0c	.	.	0	.	.	.	.
5,5	Intercept	-1.504	10.162	0.022	1	0.882			
	Age	0.086	0.12	0.513	1	0.474	1.09	0.861	1.379
	[Hypertension=NO]	15.045	5229.605	0	1	0.998	3419473	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-2.525	7.232	0.122	1	0.727	0.08	5.59E-08	114513.177
	[Sex=M]	0c	.	.	0	.	.	.	.
5,6	Intercept	-5.826	13.363	0.19	1	0.663			
	Age	0.092	0.142	0.424	1	0.515	1.097	0.83	1.449
	[Hypertension=NO]	0.724	0	.	1	.	2.063	2.063	2.063
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.289	10.153	0.001	1	0.977	1.335	3.04E-09	586082441
	[Sex=M]	0c	.	.	0	.	.	.	.
6,6	Intercept	-7.32	13.33	0.302	1	0.583			

	Age	0.115	0.141	0.667	1	0.414	1.122	0.851	1.48
	[Hypertension=NO]	0.969	11194.72	0	1	1	2.634	0	.b
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	0.279	10.091	0.001	1	0.978	1.322	3.40E-09	513681885.8
	[Sex=M]	0c	.	.	0	.	.	.	.
6,7	Intercept	4.304	13.377	0.104	1	0.748			
	Age	-0.073	0.165	0.195	1	0.659	0.93	0.673	1.285
	[Hypertension=NO]	-0.638	0	.	1	.	0.528	0.528	0.528
	[Hypertension=YES]	0c	.	.	0	.	.	.	.
	[Sex=F]	-0.384	9.695	0.002	1	0.968	0.681	3.81E-09	121655757.4
	[Sex=M]	0c	.	.	0	.	.	.	.

Source: (Researcher's Construct, 2025)