



Science Forum (Journal of Pure and Applied Sciences)



Journal Homepage: <https://atbuscienceforum.com.ng/index.php/jpas>

A Non-Homogeneous Semi-Markov Model for the Management of Continuous Blood Glucose Level in Diabetes Patient in Nigeria

Mohammed Abdullahi¹ Lawal Adamu² Hassan Bukar¹

¹Department of Mathematics, Nigerian Army University Bui, Nigeria

²Department of Mathematics, Federal University of Technology, Minna

Abstract

This study develops a non-homogeneous semi-Markov model (NH-SMM) with five clinically defined latent states to characterize the progression and management of blood glucose levels in diabetic patients. The model incorporates time-dependent transition probabilities and variable sojourn times, allowing it to capture the effects of treatment interventions, lifestyle modifications, and underlying disease dynamics. Effective regulation of blood glucose is critical for minimizing diabetes-related complications. Simulation results indicate that treatment yields only marginal reductions in glycemic levels within the first day under both 50% and 90% effectiveness scenarios. However, more substantial reductions are observed after approximately 40 days, particularly under higher treatment efficacy, highlighting the importance of sustained and intensive therapeutic interventions for improved patient outcomes. The interval transition probability $\phi_{12}(n)$ records the largest decreases, while $\phi_{23}(n)$, $\phi_{34}(n)$, and $\phi_{45}(n)$ shows moderate reductions and $\phi_{13}(n)$, $\phi_{24}(n)$, and $\phi_{35}(n)$ exhibit smaller long-term effects. The results further reveal that transition probabilities between glycemic states increase progressively over time across all modeled scenarios, with the most rapid escalation observed in the absence of treatment. This trend reflects the natural progression of uncontrolled diabetes and the associated instability in blood glucose dynamics. Conversely, increased treatment intensity significantly attenuates these transitions, promoting greater stabilization of patients' glycemic levels. The findings demonstrate that both higher treatment effectiveness and sustained intervention duration are critical for achieving improved clinical outcomes. An illustrative application based on five clinically relevant glycemic states highlights the capacity of the model to support treatment optimization and evidence-based policy planning. Additionally, the predictive outputs enhance patient monitoring, surveillance, and the implementation of individualized management strategies in diabetes care.

Keywords

Diabetes,
Interval Transition,
Probability,
Non-homogeneous,
Semi-Markov process

ISSN 1119-4618



1119-4618

JPAS



— Faculty of Science, ATBU Bauchi —

1. Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. It is among the most urgent worldwide public health issues of the twenty-first century. According to the International Diabetes Federation (IDF), approximately 537 million adults were living with diabetes worldwide in 2021, with projections indicating a continued increase, particularly in low and middle-income countries (International Diabetes Federation [IDF], 2021). Sub-Saharan Africa, has witnessed one of the fastest growing rates of diabetes prevalence, and Nigeria, being the most populous country in Africa, bears a substantial share of this burden.

Due to fast urbanization, changes in lifestyle, population growth, and restricted access to preventative healthcare services, diabetes prevalence has consistently increased in Nigeria over the past few decades (Oguoma et al., 2017). Acute complications like hypoglycemia and hyperglycemia, as well as long-term microvascular and macrovascular complications like nephropathy, neuropathy, retinopathy, and cardiovascular diseases, are all linked to poor glycaemic control (American Diabetes Association [ADA], 2023). Morbidity, mortality, and medical expenses are all greatly increased by these consequences.

Maintaining blood glucose levels within suggested goal ranges is essential for the effective management of diabetes. Conventional self-monitoring of blood glucose (SMBG) offers sporadic readings and could miss abrupt changes in blood sugar levels. However, real-time, high-frequency measurements of glucose dynamics are now possible because to developments in Continuous Glucose Monitoring (CGM) technology, offering comprehensive longitudinal data on glycaemic variability (Battelino et al., 2019). The analytical use of CGM data is still restricted in Nigeria, despite its promise.

Over the past three decades, diabetes has become much more common in Nigeria. According to a systematic review by Oguoma et al. (2017), the national prevalence can vary from 3% to 10%, depending on population segment and diagnostic criteria. Due in large part to changes in lifestyle, such as decreased physical activity and greater consumption of processed foods, urban inhabitants have higher rates than rural communities.

Inadequate access to contemporary glucose monitoring devices, high out-of-pocket costs, and a lack of healthcare infrastructure all hinder Nigerians' ability to receive diabetes care. As a result, many patients have inadequate glycaemic control and delayed consequences (Uloko et al., 2018). The significance of analytical techniques that can maximize treatment choices utilizing accessible glucose data is highlighted by these systemic issues.

Interstitial glucose levels are often measured, typically every five to fifteen minutes, by Continuous Glucose Monitoring (CGM) devices. Time in range (TIR), glycaemic variability, and patterns of hypo and hyperglycemia are all comprehensively shown by CGM (Battelino et al., 2019). The American diabetic Association (2023) highlights glycaemic variability and TIR as important markers of successful diabetic care.

Markov models have long been used in medical decision-making and chronic disease modelling (Sonnenberg and Beck, 1993). These models assume the Markov property, which asserts that future states are solely dependent on the current state, and explain transitions between discrete health states with fixed transition probabilities. Standard Markov models are helpful, but they require exponentially distributed sojourn times, which suggests memoryless behavior. This assumption is frequently inaccurate in the context of glucose dynamics because the amount of time spent in a hypo or hyperglycemic state may affect the probability of transitioning to a

different state. Additionally, by permitting alternative sojourn time distributions, semi-Markov models expand the Markov framework (Limnios and Oprisan, 2001). Because of their adaptability, they are especially well-suited for simulating the course of chronic illnesses and biological processes where duration dependence has therapeutic significance.

Panagiota (2024) used a non-homogeneous semi-Markov model to study HIV. In his study he analyzed both the sojourn times as well as the transition probabilities in the four-state model and also introduced an eight-state model and applied the same theory. The results of the study confirm that the non-homogeneous semi-Markov model hypothesis is appropriate to describe the complexity of the disease. Also shows that the hypothesis of linear transition probabilities is inappropriate and causes several problems. To overcome the problems, he proposed the logit transformation to solve the technical problem. However, the logit transition probabilities seem to be limiting in the case of the eight-state model. The perplexity of the eight-state model requires a more robust and advanced technique in order to draw the appropriate inferences about the evolution of the disease.

Latent states in glucose prediction models are closely linked to the underlying physiological condition of a patient. A patient's physiological state is influenced by several behavioral and biological factors, including physical activity, insulin administration and its absorption dynamics, sleep cycle, carbohydrate intake, and stress levels (American Diabetes Association, 2024; Dalla Man et al., 2007). These factors independently affect blood glucose dynamics and therefore influence readings obtained from continuous glucose monitoring (CGM) systems. For instance, carbohydrate consumption typically increases

blood glucose levels due to the digestion and absorption of glucose into the bloodstream, whereas insulin lowers glucose concentrations by facilitating the uptake of glucose into body cells where it is utilized for energy production (Dalla Man et al., 2007). Similarly, physical activity can lead to a reduction in glucose levels because muscles utilize circulating glucose as a source of energy during exercise (Colberg et al., 2016).

This study suggests the use of a non-homogeneous semi-Markov model for managing continuous blood glucose levels in diabetic patients in Nigeria. By modelling transitions among latent glycaemic states, the approach aims to provide improved understanding of glucose dynamics and support data driven clinical decision-making within the Nigerian healthcare context.

2. Materials and Methods

As glucose levels change, physiological behavior also changes, so we are characterizing our latent states through potential physiological mechanisms associated with varying glucose levels. Based on this process, we let the glucose level be classified into five latent states as,

Latent State 1: Hypoglycaemia (dangerously low) glucose values $G < 15$ th percentile

Latent State 2: Low-normal glucose values 15 th percentile $\leq G < 37.5$ th percentile

Latent State 3: Euglycaemia (target range) glucose values 37.5 th percentile $\leq G < 62.5$ th percentile

Latent State 4: Normal-high glucose values 62.5 th percentile $\leq G < 85$ th percentile

Latent State 5: Hyperglycaemia (dangerously high) glucose values $G \geq 85$ th percentile

The possible transitions between the latent states of the diabetic patients above are

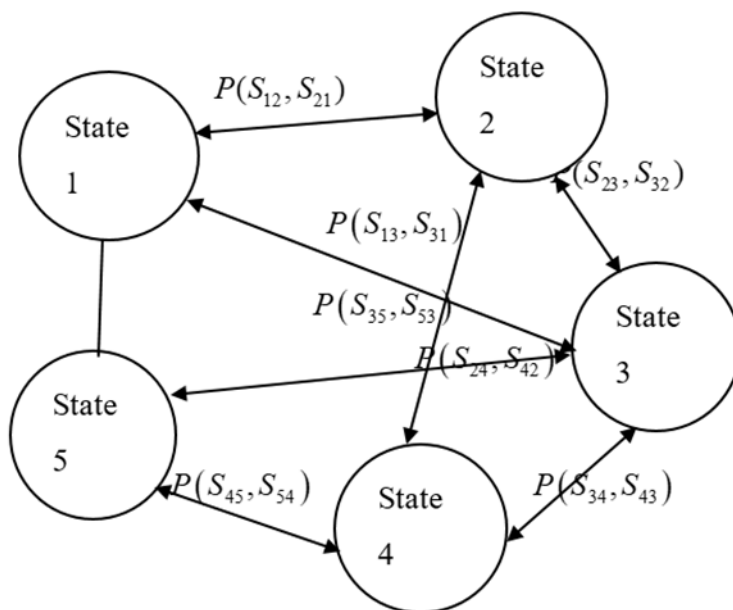


Figure 1. The transition diagram for the diabetic patient deterioration

From figure 1, we record the transition probability matrix P for the process as shown in Equation 1.

$$P = \begin{pmatrix} p_{11} & p_{12} & p_{13} & 0 & 0 \\ p_{21} & p_{22} & p_{23} & p_{24} & 0 \\ 0 & p_{32} & p_{33} & p_{34} & p_{35} \\ 0 & p_{42} & p_{43} & p_{44} & p_{45} \\ 0 & 0 & p_{53} & p_{54} & p_{55} \end{pmatrix} \quad (1)$$

Let (P_{ij}) be the probability that the diabetes patient in its last transition will enter the latent state j on its next transition $i, j = 1, 2, 3, 4, 5$. The transition probabilities must satisfy the followings:

$$P_{ij} \geq 0, \quad i, j = 1, 2, 3, 4, 5 \text{ and} \\ \int_{ij} P_{ij} = 1 \quad i = 1, 2, 3, 4, 5. \quad (2)$$

For the non-homogeneous semi-Markov chain, the transition probabilities are

$$P_{ij}(t) = P(\text{Is the next transition for a diabetic patient who entered state } i \text{ at time } t \text{ is state } j) \\ = f_{ij}(t) + P_{i(k+1)}(t) + P_{0j}(t) \quad (3)$$

Where

$$P_{ij}(t) \geq 0 \text{ and } \sum_j P_{ij}(t) = 1$$

$f_{ij}(t)$ is the probability that a diabetic patient makes a transition to state j given that it entered state i at time t ..

$P_{i(k+1)}(t)$ is the probability of a diabetic patient leaving the system from state i given that it entered the specific state at time t .

$P_{0j}(t)$ is the probability that a diabetic patient will replace a system client in state i , given that the client entered the system's final state at time t .

Whenever the diabetes patient enters the latent state i , the client remains there for a time T_{ij} in state i before making a transition to latent state j . T_{ij} is called the holding time in state i . The holding times are positive integer-valued random variables each governed by a probability distribution density function $f_{ij}(t)$ called the holding time distribution function for a transition from latent state i to latent state j (Howard 1971).

The interval transition probability of the Non-Homogeneous Semi-Markov Model (NHSMM) can be defined as

$$\varphi_{ij}(t, x) = \alpha_{ij}(s, t) + \sum_{l=1, l \neq i}^5 \int_0^5 P_{il}(t) f_{il}(u) \varphi_{li}(t+u, x-u) du \quad (4) \quad *$$

Where:

$\alpha_{i,j}(s, t) = \delta_{i,j} \cdot S_i(s, t)$ and it is the probability of remaining in state i at time t , without any change from time s is called the holding time in state i .

Another expression for the equation (4) is the following

$$\varphi_{ij}(t, x) = \alpha_{ij}(s, t) + \sum_{l=1, l \neq i}^5 \int_0^5 C_{il}(t, u) \varphi_{li}(t+u, x-u) du \quad (5)$$

$$\varphi_{ij}(t, 0) = \begin{cases} 0, & \text{if } j=i \\ 1, & \text{otherwise} \end{cases} \quad i, j = 1, 2, 3, 4, 5 \quad t = 1, 2, 3, 4, 5 \quad (6)$$

Where $C_{il}(t, u)$ is the product of $P_{il} f_{il}$.

This is the interval transition probability from state i to state j in the interval $(0, n]$

3 The Management of the Diabetes

When a diabetic patient undergoes treatment or disease control, it is expected that such intervention will produce a measurable effect on the progression and outcome of the disease. The treatment or control measures typically involve a combination of insulin administration, adherence to a regulated dietary plan, and engagement in regular physical exercise. These therapeutic interventions are intended to improve the patient's health condition by increasing the probability of recovery while simultaneously reducing the probabilities of mortality and disease relapse. Consequently, the effectiveness of the treatment or control strategy can be quantitatively assessed using the following expression.

$$\phi_{ij}(n, k) = \int_0^n P_{ij}(u, k) f_i(u, k) du \quad (7)$$

Where:

$P_{ij}(t, k)$ is the probability of selecting state j as the next state after leaving state i at duration u under treatment k .

$f_i(u, k)$ is the density of the sojourn time in state i under treatment k

K is positive real number in the interval $[0, 1)$ and $i, j = 1, 2, 3, 4, 5$

4 Application

The data used in this research paper were collected from General Hospital Minna Niger state, Nigeria. The data consisted of glucose values recorded daily for 50 patients comprised of 35 male and 15 female patients with the help of Dexcom G6 CGM devices. The device measures glucose using the interstitial fluids.

The transition probability Matrix is then estimated from the data collected of the diabetic clients and are presented as follows:

$$A = \begin{bmatrix} 0.445 & 0.505 & 0.050 & 0.000 & 0.000 \\ 0.163 & 0.500 & 0.330 & 0.007 & 0.000 \\ 0.000 & 0.250 & 0.500 & 0.247 & 0.003 \\ 0.000 & 0.002 & 0.210 & 0.612 & 0.176 \\ 0.000 & 0.000 & 0.014 & 0.486 & 0.500 \end{bmatrix} \quad (16)$$

Exponential Holding Time in States

Suppose that the holding times in each state before making a transition to another state follows the exponential distribution with parameter λ . This implies that the mean holding time in each state is $\frac{1}{\lambda}$ (a day). The mean holding time in each state is shown in table below.

Table 1: Mean Holding Time in the States

Mean Holding Time				
STATE 1	STATE 2	STATE 3	STATE 4	STATE 5
35.52	76.50	63.35	85.05	41.58

The mean holding time in each latent state is presented in Table 1. It shows that Diabetes clients recorded the highest mean holding time in latent state 4 then followed by latent state 2, state 3, state 5 and state 1 respectively.

5 Results

Using the maple software, we obtained the following Tables

Table 2: Interval Transition Probabilities from State 1 to State 2

S/N	$\phi_{12}(n)$		
	$K = 0$	$K = 0.5$	$K = 0.9$
0	0.000000000	0.000000000	0.000000000
1	0.0139424492	0.0069719374	0.00139438748
2	0.0274999639	0.0137513682	0.00275027364
3	0.0406831717	0.0203436078	0.00406872157
4	0.053502469	0.0267538250	0.00659740911
5	0.0659677183	0.0329870458	0.00780963135
6	0.0780888772	0.0390481567	0.00898838215
7	0.0898753854	0.0449419107	0.01013458571
8	0.1013364821	0.0506729286	0.01124914073
.	.	.	.

.	.	.	.
.	.	.	.
40	0.3402287037	0.1701143519	0.03402287037

Table 2 presents the interval transition probabilities from state 1 (Hypoglycaemia glucose) to state 2 (Low-normal glucose). $\phi_{12}(n)$ $n = 1, 2, 3, \dots, 40$. $\phi_{12}(n)$ is the probability that a diabetic patient will be in the state of Low-normal glucose value in day n given that he was under treatment in the day zero. In other words, $\phi_{12}(n)$ is the probability of recovery from treatment at time n given that the patient started treatment at time zero.

Table 3: Interval Transition Probabilities from State 1 to State 3

S/N	$\phi_{13}(n)$		
	$K = 0$	$K = 0.5$	$K = 0.9$
0	0.00000000	0.00000000	0.00000000
1	0.00138044051	0.00069029083	0.000138058166
2	0.0027227687	0.0013615260	0.000272304320
3	0.00402803680	0.00201421860	0.000402843720
4	0.00529726801	0.00264889356	0.000529778712
5	0.00653145726	0.00326604412	0.000653208823
6	0.00773157200	0.00386615413	0.000773230826
7	0.0088955306	0.00444969413	0.000889938826
8	0.01003332506	0.00501712164	0.001003424328
.	.	.	.
.	.	.	.
40	.	.	.
	0.02841259376	0.01684300514	0.003368601027

Table 3 presents the interval transition probabilities. $\phi_{13}(n)$ is the probability that a patient will be a Normal Target/Euglycaemia glucose values in day n given that the patient was under treatment in day zero. It also represents the probability that a diabetic patient develops a resistance to the drug

Table 4: Interval Transition Probabilities from State 2 to State 3

S/N	$\phi_{23}(n)$		
	$K = 0$	$K = 0.5$	$K = 0.9$
0	0.0000000000	0.0000000000	0.0000000000
1	0.0042623354	0.0021311177	0.00042622354

2	0.0084694204	0.0042347102	0.00084694204
3	0.0126222660	0.0063111330	0.00126222660
4	0.0167214740	0.0083607370	0.00167214740
5	0.0207677371	0.0103838685	0.00207677371
6	0.0247617393	0.0123808696	0.00247617393
7	0.0287041554	0.0143520777	0.00287041554
8	0.0325956519	0.0162978259	0.00325956519
9	0.0364368862	0.0182184431	0.00364368862
.	.	.	.
.	.	.	.
.	.	.	.
40	0.1338082192	0.06690410958	0.01338082192

Table 4 shows the interval transition probabilities $\phi_{23}(n)$ $n = 1, 2, 3, \dots, 40$. $\phi_{23}(n)$ is the probability that a diabetic patient will be a Normal Target/Euglycaemia glucose values in day n given that the patient was under treatment in day zero. It also represents the probability that a diabetic patient develops a resistance to the drug

Table 5: Interval Transition Probabilities from State 2 to State 5

S/N	$\phi_{24}(n)$		
	$K = 0$	$K = 0.5$	$K = 0.9$
0	0.0000000000	0.0000000000	0.0000000000
1	0.000090411055	0.000045205528	0.0000090411055
2	0.000179654373	0.00008927186	0.0000179654373
3	0.000267745036	0.000133872518	0.0000267745036
4	0.000354697932	0.000177348966	0.0000354697932
5	0.0004405277756	0.000220263878	0.0000440527756
6	0.000525249014	0.00026264507	0.0000525249014
7	0.000608876024	0.000304438012	0.0000608876024
8	0.000691422918	0.000345711459	0.0000691422918
9	0.000772903648	0.000386451824	0.0000772903648
.	.	.	.
.	.	.	.
.	.	.	.
40	0.002838356164	0.001419178082	0.0002838356164

Table 5 shows the interval transition probabilities $\phi_{24}(n)$ $n = 1, 2, 3, \dots, 40$. $\phi_{24}(n)$ is the probability that a diabetic patient will be a Normal-high glucose values in day n given that the patient was under treatment in day zero

Table 6: Interval Transition Probabilities from State 3 to State 4

S/N	$\phi_{34}(n)$		
	$K = 0$	$K = 0.5$	$K = 0.9$

0	0.000000000	0.000000000	0.000000000
1	0.0039205519	0.0019602760	0.00039205519
2	0.0077788742	0.0038894371	0.0007778742
3	0.0115759546	0.005787977	0.00115759546
4	0.0153127651	0.0076563826	0.00153127651
5	0.018902624	0.0094951312	0.00189902624
6	0.0226093880	0.013046940	0.00226093880
7	0.0261710684	0.0130855342	0.00261710684
8	0.0296762154	0.0148381077	0.00296762154
9	0.0331257262	0.0165628631	0.00331257262
10	0.0036504841	0.0182602421	0.00365204841
.	.	.	.
.	.	.	.
.	.	.	.
40	0.1167587713	0.05837938564	0.01167587713

Table 6: presents the interval transition probabilities $\phi_{34}(n)$ $n=1,2,3,\dots,40$. $\phi_{34}(n)$ is the probability that a patient will be a Normal-high glucose values in day n given that the patient was under treatment in day zero.

Table 7: Interval Transition Probabilities from State 3 to State 5

B	ϕ_{35}		
S/N	$K = 0$	$K = 0.5$	$K = 0.9$
0	0.000000000	0.000000000	0.000000000
1	0.000047618040	0.000023809020	0.00000476
2	0.000094480254	0.00004724127	0.000009448
3	0.000140598639	0.000070299319	0.0000140598
4	0.000185985002	0.000092992501	0.0000185985
5	0.000230650961	0.000115325480	0.000023065
6	0.000274607952	0.000137303976	0.000027460
7	0.000317867228	0.000158933614	0.0000317867228
8	0.000360439863	0.000180219931	0.0000360439863
9	0.000402336756	0.000201168378	0.0000402336756
10	0.000443568633	0.000221784316	0.0000443568653
.	.	.	.
.	.	.	.
.	.	.	.
40	0.001418122728	0.0007090613640	0.0001418122728

Table 7: presents the interval transition probabilities $\phi_{35}(n)$, $n=1,2,3,\dots,40$. $\phi_{35}(n)$ is the probability that a diabetic patient will be a Hyperglycaemia (dangerously high) glucose values in day n given that the patient was under treatment in day zero.

Table 8: Interval Transition Probabilities from State 4 to State 5

	$\phi_{45}(n)$		
S/N	$K = 0$	$K = 0.5$	$K = 0.9$

0	0.0000000000	0.0000000000	0.000000000000
1	0.0041500008	0.00104968926	0.0000993785
2	0.0061879486	0.00208685754	0.00041737151
3	0.0082015873	0.00311165417	0.00062233083
4	0.0101912066	0.00412422674	0.00082484535
5	0.0121570932	0.00512472104	0.0010249444
6	0.0140995302	0.00611328117	0.00122265623
7	0.0160187972	0.00709004946	0.00141800989
8	0.0179151706	0.00805516658	0.00161103332
9	0.0197889236	0.00900877152	0.00180175430
10	0.0216403259	0.0099100157	0.00199020031
.	.	.	.
.	.	.	.
40	.	.	.
	0.0667129064	0.03354706152	0.00670941230

Table 8: Shows the interval transition probabilities $\phi_{45}(n)$, $n=1,2,3,\dots,40$. $\phi_{45}(n)$ is the probability that a patient will be a Hyperglycaemia (dangerously high) glucose in day n given that the patient was under treatment in day zero.

From the above Tables, we have the following Graphs

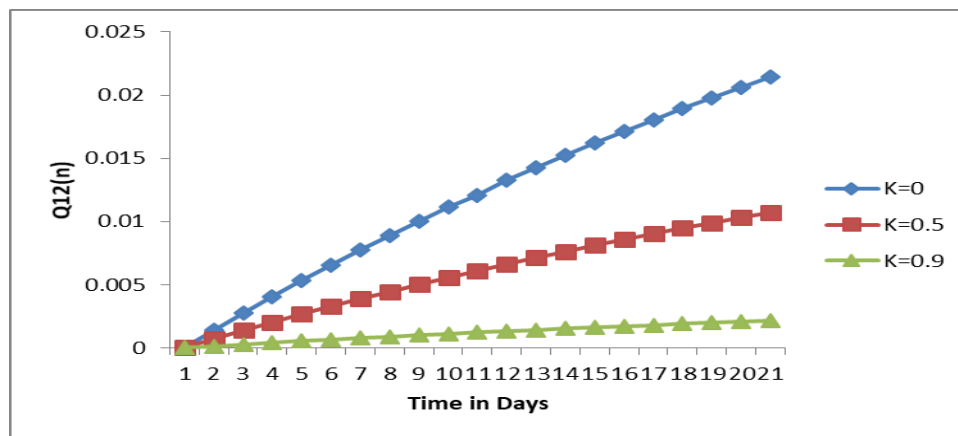


Figure 2: The Graph of Interval Transition Probabilities from State 1 (Hypoglycaemia glucose) to state 2 (Low-normal glucose) and the Effectiveness of the Treatment for Exponential Distribution in Continuous Time

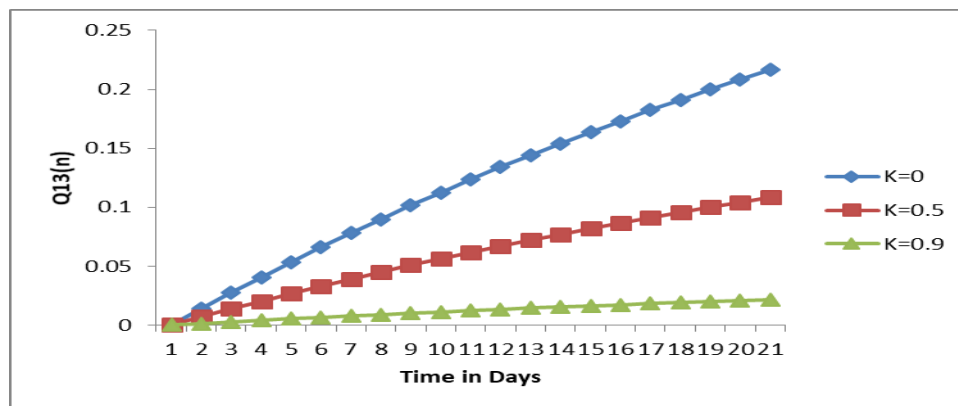


Figure 3: The Graph of Interval Transition Probabilities from State 1 (Hypoglycaemia glucose) to state 3 (Normal Target/Euglycaemia glucose) and the Effectiveness of the Treatment for Exponential Distribution in Continuous Time

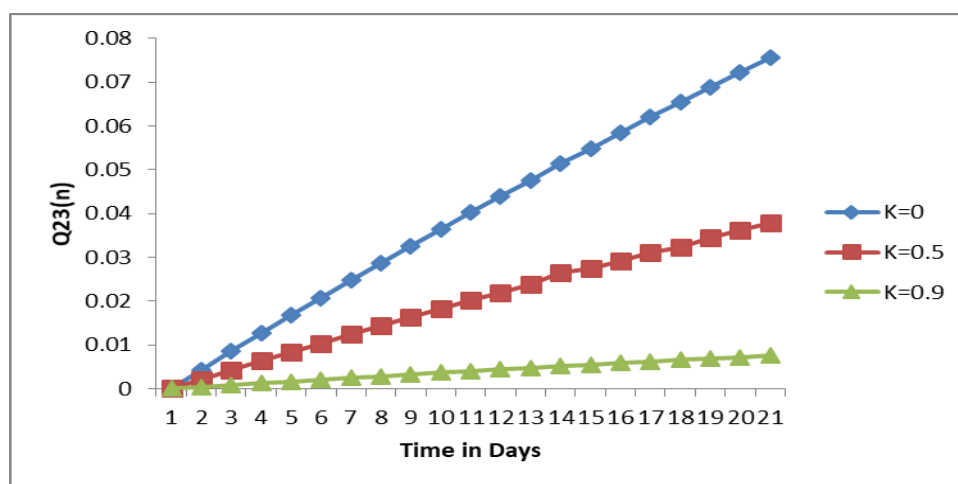


Figure 4: The Graph of Interval Transition Probabilities from State 2 (Low-normal glucose) 3 (Normal Target/Euglycaemia glucose) and the Effectiveness of the Treatment for Exponential Distribution in Continuous Time

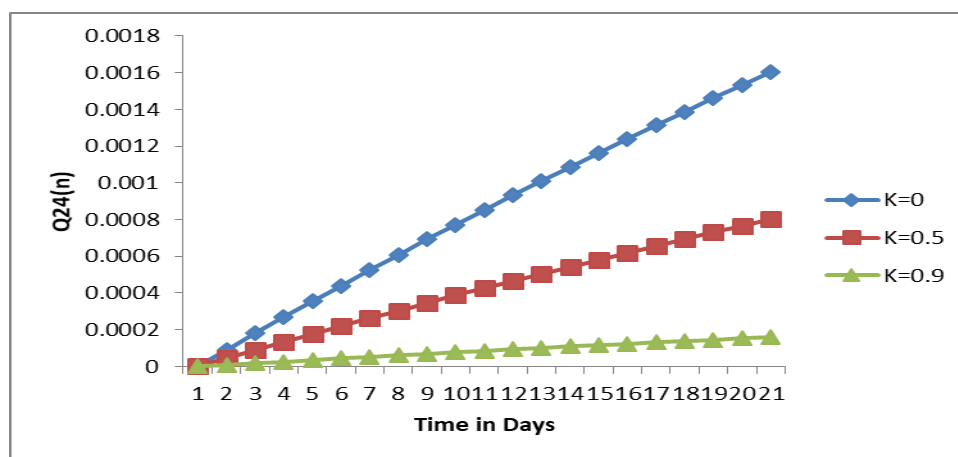


Figure 5: The Graph of Interval Transition Probabilities from State 2 (Low-normal glucose) to State 4 (Normal-high glucose) and the Effectiveness of the Treatment for Exponential Distribution in Continuous Time

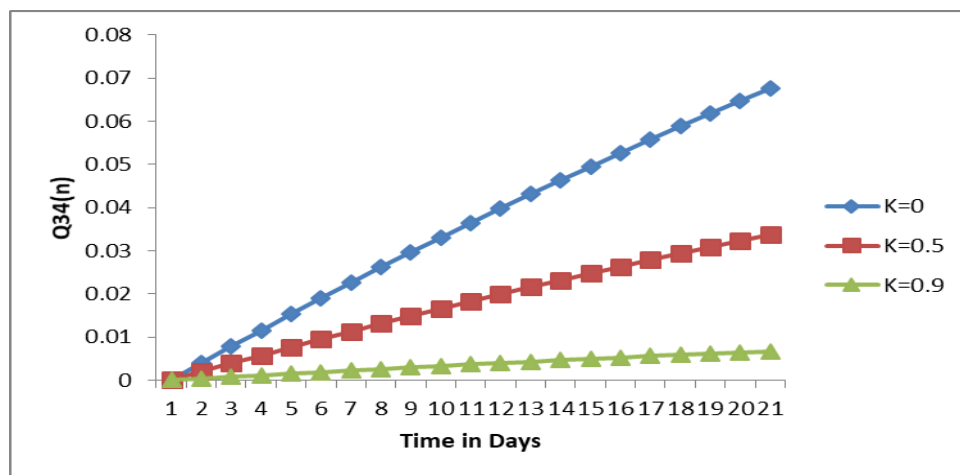


Figure 6: The Graph of Interval Transition Probabilities from State 3 (Normal Target/Euglycaemia glucose) to State 4 (Normal-high glucose) and the Effectiveness of the Treatment for Exponential Distribution in Continuous Time

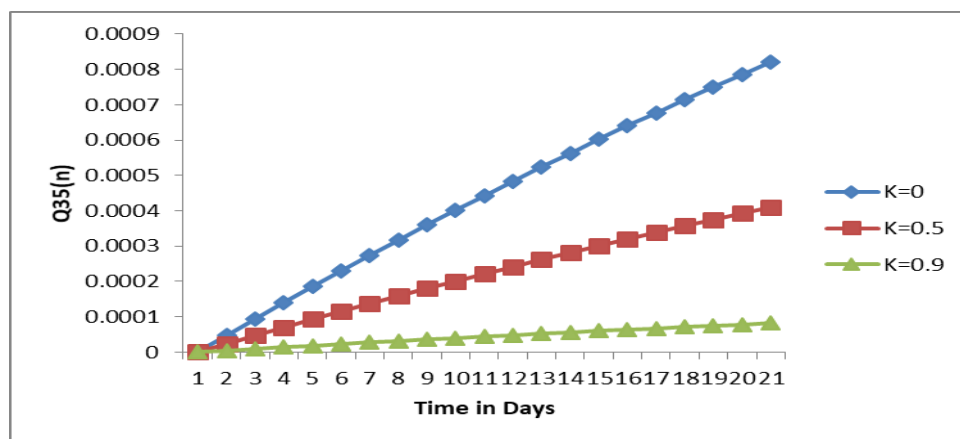


Figure 7: The Graph of Interval Transition Probabilities from State 3 (Normal Target/Euglycaemia glucose) to State 5 (Hyperglycaemia (dangerously high) glucose) and the Effectiveness of the Treatment for Exponential Distribution in Continuous Time

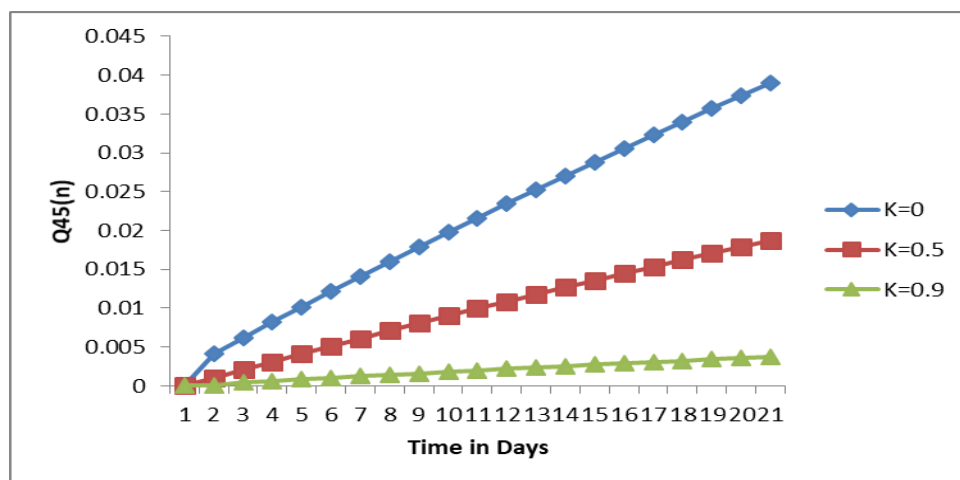


Figure 8: The Graph of Interval Transition Probabilities from State 4 (Normal-high glucose) to State 5 (Hyperglycaemia (dangerously high) glucose) and the Effectiveness of the Treatment for Exponential Distribution in Continuous Time

Discussion

This paper presented a Non-homogeneous Semi- Markov model (NH-SMM) to examine the effect of the treatment on diabetes patient in Nigeria. From the empirical analysis of the collected data, the results indicate that there is no transition of diabetic patient within a day from stage 1 to stage 4 and 5, state 2 to state 5, state 3 to state 1, state 4 to state 1, state 5 to state 1 and state 5 to state 2: that is $\phi_{14}(n) = 0$, $\phi_{15}(n) = 0$, $\phi_{25}(n) = 0$, $\phi_{31}(n) = 0$, $\phi_{41}(n) = 0$, $\phi_{51}(n) = 0$, and $\phi_{52}(n) = 0$. This applies to the n^{th} period under consideration. The holding time in each stage is presented in Table 1. It shows that Diabetic patient clients recorded the highest mean holding time in stage 4 then followed by stage 2, stage 3, stage 5 and stage 1 respectively.

From the Tables 2 to 8, the treatment results in small reductions on the first day for both 50% and 90% effectiveness possibilities, generally below 1.3%, with some tables showing negligible initial changes. After 40 days, the reductions become more pronounced, especially under the 90% effectiveness assumption. The results also show that in Table 2 recorded the highest decreases of about 17% and 30.6% for the 40 days when the treatment is assumed to be 50% and 90% effective respectively, followed by moderate reductions in Tables 4, 6, and 8 for the 40 days when the treatment is assumed to be 50% and 90% effective respectively. In contrast, Tables 3, 5, and 7 show relatively smaller long-term effects for the 40 days when the treatment is assumed to be 50% and 90% effective respectively. Overall, higher treatment effectiveness and longer duration lead to greater reductions.

The graphs illustrates the interval transition probabilities

$\phi_{12}(n)$, $\phi_{13}(n)$, $\phi_{23}(n)$, $\phi_{24}(n)$, $\phi_{34}(n)$, $\phi_{35}(n)$ and $\phi_{45}(n)$ for diabetic patients moving from state 1 (hypoglycemia dangerously low blood glucose level) to state 2 (low-normal glucose level), from state 1 (hypoglycemia dangerously low blood glucose level) to state 3 (Euglycaemia (target range) glucose), from state 2 (low-normal glucose level) to state 3 (Euglycaemia (target range) glucose), from state 2 (low-normal glucose level) to state 4 (Normal-high glucose level), from state 3 (Euglycaemia (target range) glucose) to state 4 (Normal-high glucose level), from state 3 (Euglycaemia (target range) glucose) to state 5 (Hyperglycaemia (dangerously high) glucose values) and from state 4 (Normal-high glucose level) to state 5 (Normal-high glucose level) over a period of 21 days. The parameter K represents the level of treatment intervention, where $K = 0$ denotes to no treatment, $K = 0.5$ represents moderate treatment, and $K = 0.9$ denotes high treatment intensity. The horizontal axis shows time in days, while the vertical axis represents the transition probability $\phi_{ij}(n)$, $i, j = 1, 2, 3, 4, 5$.

Figures 2 to 8 demonstrates that the transition probabilities from latent state i to latent state j for $i, j = 1, 2, 3, 4, 5$ increases with time under all treatment scenarios. However, the rate and magnitude of this increases differ significantly depending on the treatment intensity. In the case of treatment ($K = 0$), the probability of transitioning from latent state i to latent state j for $i, j = 1, 2, 3, 4, 5$ increases most rapidly, reaching the highest values by day 21. This indicates that when no treatment is administered, patients are more likely to move out of the one state to another within the observed period.

For the moderate treatment case ($K = 0.5$), the transition probability also increases steadily over time, but at a considerably slower rate compared to the untreated cases. Over period of 21 day, the probability remains notably lower than that of no treatment. This indicates that moderate treatment reduces the likelihood or speed of transitioning from hypoglycemia to the low-normal glucose state and the same to other states.

In the case of high treatment intensity ($K = 0.9$), the transition probability increases only slightly across the time horizon and remains the lowest among all three scenarios. Even after 21 days, the probability is substantially smaller than in both the untreated and moderately treated cases. This suggests that intensive treatment significantly suppresses or stabilizes transitions of the diabetic patients from one state to another, possibly by tightly controlling glucose fluctuations and preventing rapid shifts between the glucose states.

Conclusion

In conclusion, a non-homogeneous semi-Markov model effectively captures the progression of diabetic patients across different glucose level states and highlights the role of treatment intervention in controlling these diabetic patient transitions. The findings reveal that no direct transition occurs from the hypoglycemic state to the normal-high or hyperglycemic states within a day, while patients tend to remain longest in the normal-high glucose state. The results further demonstrate that treatment effects are initially small but become more substantial over time, with higher treatment effectiveness producing greater reductions. The result also indicates that, from a medical point of view, increased treatment of the diabetic patient intensity significantly slows

transition probabilities between glucose level states, suggesting that sustained and intensive treatment can enhance stability in patients' glucose levels. The prediction model information could be useful in the tracking, surveillance and management of diabetic patient individual undergoing treatment.

References

- American Diabetes Association. (2023). Standards of Care in Diabetes 2023. *Diabetes Care*, 46(Suppl. 1), S1-S291.
- American Diabetes Association. (2024). Standards of care in diabetes—2024. *Diabetes Care*, 47(Supplement 1), S1-S350. <https://doi.org/10.2337/dc24-Sint>
- Battelino, T., Danne, T., Bergenstal, R. M., et al. (2019). Clinical targets for Continuous glucose Monitoring Data Interpretation: Recommendations from the International Consensus on Time in Range. *Diabetes Care*, 42(8), 1593-1603.
- Colberg, S. R., Sigal, R. J., Yardley, J. E., Riddell, M. C., Dunstan, D. W., Dempsey, P. C., Tate, D. F. (2016). Physical activity/exercise and diabetes: A position statement of the American Diabetes Association. *Diabetes Care*, 39(11), 2065-2079. <https://doi.org/10.2337/dc16-1728>
- Dalla Man, C., Rizza, R. A., & Cobelli, C. (2007). Meal Simulation Model of the Glucose- Insulin System. *IEEE Transactions on Biomedical Engineering*, 54(10), 1740-1749. <https://doi.org/10.1109/TBME.2007.893506>
- Howard R. A (1971). *Dynamic Probabilistic Systems*, John Wiley, New York Vol 1and 2,
- International Diabetes Federation. (2021). *IDF Diabetes Atlas (10th ed.)*. Brussels, Belgium: IDF.

Janssen, J., & Manca, R. (2006). *Applied Semi-Markov processes*. Springer.

Limnios, N., & Oprisan, G. (2001). *Semi-Markov Processes and Reliability*. Birkhäuser.

Oguoma, V. M., et al. (2017). Prevalence of Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. *BMJ Open*, 7(5), e015424.

Panagiota K. (2024) *Non-Homogeneous Semi-Markov Processes with Application to HIV*. Master Research Work Submitted to National and Kapodistrian University of Athens. Department of Mathematics

Sonnenberg, F. A., & Beck, J. R. (1993). Markov Models in Medical Decision Making. *Medical Decision Making*, 13(4), 322-338.

Uloko, A. E., et al. (2018). Prevalence and Risk Factors for Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. *Diabetes Therapy*, 9(3), 1307-1316.