

**Impact of Anxiety on HIV Care Continuum: A
Mathematical Modelling Study**

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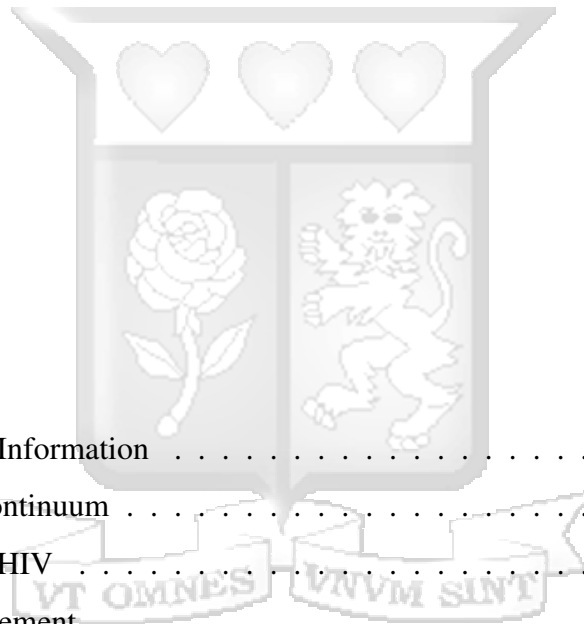
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Abstract

Human Immunodeficiency Virus (HIV)/AIDS is a significant global health issue, ranking as the second leading infectious disease worldwide. At the end of 2023, approximately 39.9 million people were living with HIV/AIDs with between 500,000 and 820,000 deaths occurring due to the infection globally. Anxiety, defined as a pervasive sense of fear and nervousness without a specific trigger, is a significant mental health disorder. Mental health conditions are critical stressors that complicate the care for people living with HIV/AIDs. In this study, we employed mathematical compartmental modeling of HIV with the impact of anxiety among clients across the care cascade in Kenya. The effective reproduction number was calculated using the next-generation matrix and results indicate the continuous presence of the disease in the population. The numerical results indicate that severe cases of anxiety increase the number of diagnosed populations in the care continuum with an increase of 47% among the population diagnosed as a contribution of anxiety. The impact of anxiety to treatment records a 25% decrease among population receiving ART treatment as a result of severe anxiety. There is a positive impact of anxiety treatment on virally suppressed population with 19% increase as a result of minimal or no anxiety within the population. The study shows that intensified integration of anxiety care within the HIV/AIDs care continuum has a positive outcome. The results provide significant insights to policymakers on the most effective ways of improving the HIV/AIDs care continuum in Kenya.

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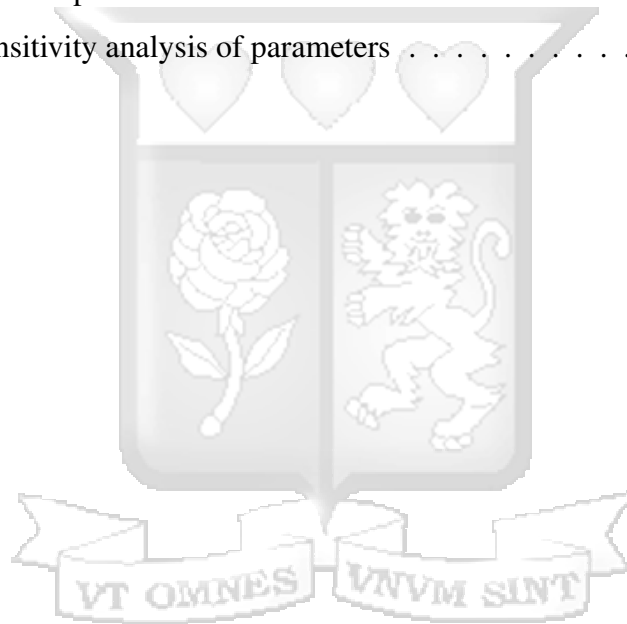


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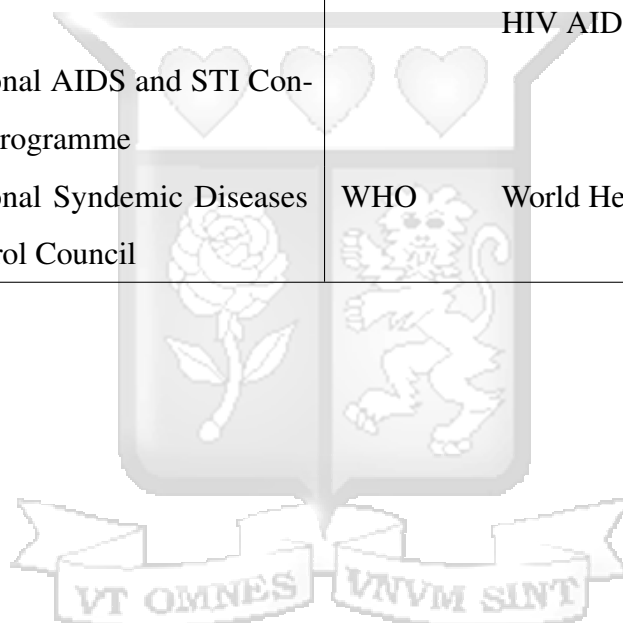
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List of Abbreviations

AIDS	Acquired Immunodeficiency Syndrome	PLWHA	People Living with HIV/AIDS
ART	Antiretroviral therapy	SSA	Sub-Saharan Africa
CDC	Center for Disease Control and Prevention	MoH	Ministry of Health
HIV	Human Immunodeficiency Virus	UNAIDS	Joint United Nations Program on HIV AIDS
NASCOP	National AIDS and STI Control Programme		
NSDCC	National Syndemic Diseases Control Council	WHO	World Health Organization



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Chapter 1

Introduction

The section entails: background information, problem statement, the objectives, scope and importance of carrying out the study.

1.1 Background Information

Human Immunodeficiency Virus (HIV) attacks the human immune system, namely the CD4 cells, which are the cells distinguishing feature against viral invasion of the body. Upon entry and manifestation, the infection develops into Acquired Immune Deficiency Syndrome (AIDS). Since HIV appeared in 1980, the disease has manifested to become a global pandemic. By the end of the year 2023, approximately 39.9 million people were living with HIV/AIDs among which 38.6 million were adults, 1.4 million were children less than 15 years of age, and 53% comprised of women across the globe ([Nachega et al., 2023](#)). Additionally, there were 1.3 million new infections at the end of 2023 of the disease globally, this marked a 39% decline in the number of new infections since the data from 2010 ([Nachega et al., 2023](#)).

HIV/AIDs transmission remains to be well defined since the avenue of acquiring the disease have been identified and various mitigation mechanisms have been employed to try and prevent its spread among key populations who are at higher risk of acquiring the disease ([Tian et al., 2023](#)). Having unprotected sex with an infected partner again remains the main transmission method of the disease. Oral sex, vaginal sex, and in recent times men having sex with men have been on the rise which exacerbates the spread of HIV/AIDs ([Mwaniki et al., 2023](#)).

1.2 HIV Care Continuum

The HIV care continuum, according to the Centers for Disease Control and Prevention (CDC), is the course that an individual with HIV takes from diagnosis to treatment, which ultimately results in the viral load being reduced to an undetectable level (Jaurette et al., 2023). Each phase of the continuum is marked by an estimated proportion of the population that has achieved it. The phases include: receiving an HIV diagnosis; being linked to healthcare; beginning antiretroviral therapy (ART); adhering to the treatment plan; and, ultimately, achieving viral suppression to undetectable levels in the blood.

The Joint United Nations Programme on HIV/AIDS (UNAIDS) has set a target for 2025, known as the 95-95-95 goals: 95% of people with HIV should be diagnosed, 95% of those diagnosed should receive ART, and 95% of those on ART should achieve viral suppression (Onyango et al., 2022). As of 2023, global data from UNAIDS showed progress towards these targets, with rates at 86%, 76%, and 71% respectively. Government and Non-governmental organization interventions have demonstrated positive impacts, indicating progress toward achieving the UNAIDS targets by 2025. In Kenya, these interventions have resulted in 90% of newly diagnosed HIV patients being initiated into the care continuum. Of these individuals, 82% are linked to care and receive ART treatment. Among those linked to care, 92% achieve viral load suppression, clearly indicating clients' adherence to the ART regimen.

1.3 Anxiety and HIV

According to the American Psychological Association, anxiety is a mood that manifests as tension, concerned thoughts, and physical symptoms like elevated blood pressure (Association et al., 2015). There exist anxiety feeling and anxiety disorder and the diagnosis is determined from the Diagnostic Statistical Manual Mental Health Disorders (DSM-5) (American Psychiatric Association et al., 2013). Anxiety encompasses general mixed feeling of a perceived or real threat which affects the cognitive, physical and behavioural conditions. These anxiety-inducing responses, known as the fight-or-flight response, are triggered when

the brain releases the hormone and chemical messenger adrenaline in reaction to real or perceived danger. Some people may experience this reaction in socially unpleasant situations or when they are going through important decisions or events. Anxiety disorder has symptoms identified as; restlessness, an uncontrollable feeling of worry, an increased irritability and some people might have sleeping difficulties ([Association et al., 2015](#)).

According to the DSM-5, anxiety is categorized into various types with Generalized Anxiety Disorder (GAD) being characterized by excessive, persistent worry and concern about general life events, things, and circumstances, and it remains the most common anxiety disorder. Another type is panic disorder, defined by brief or abrupt episodes of extreme fear and anxiety, which can result in shaking, disorientation, lightheadedness, nausea, and difficulty breathing. Specific phobia is the fear and aversion of a specific thing or circumstance. Other types of anxiety disorders include agoraphobia, which is the fear of situations where escape might be difficult or help unavailable during a panic attack; Children with selective mutism, which is characterized by the inability to talk in some social contexts but the ability to speak in others, are frequently affected ; social anxiety disorder, marked by a fear of judgment from the public; and separation anxiety disorder, which occurs as a result of separation from places or people to whom the individual is attached ([American Psychiatric Association et al., 2013](#)).

Mental health has been at the center of discussion when addressing the HIV care continuum, with depression and anxiety marked as the main mental health condition that develops in most patients after acquiring the disease ([Nyongesa et al., 2021](#)). Data from the literature opines that at the end of 2023, the prevalence of depression in sub-Saharan Africa among PLWHA was in the range of (6 – 59)%, while on the other hand, the prevalence of anxiety was in the range of (3 – 21)%. The prevalence of depression was 18.2% and anxiety at a prevalence rate of 11.7% among patients living with HIV ([Mwangala et al., 2022](#)).

1.4 Problem Statement

Currently, HIV/AIDS is the second leading infectious disease worldwide, with an estimated 39 million people living with the virus and 510,000 to 860,000 deaths attributed to the

infection in 2023 (World Health Organization [WHO], (2023). Anxiety and depression are the most prevalent mental health disorders among people living with HIV/AIDS (PLWHA), acting as significant stressors throughout the care continuum. Anxiety, often overlooked among PLWHA, is a widespread mental health issue affecting populations across regions. According to the WHO (2022), the global prevalence of anxiety is rising, with an estimated 3.6% of the population affected. This translates to approximately 264 million people experiencing anxiety worldwide. Kenya, like many countries in Sub-Saharan Africa (SSA), faces a prominent threat of anxiety (Mwangala et al., 2022). This research work aims to develop a mathematical compartmental model that explores the impact of anxiety on the HIV care continuum, specifically focusing on achieving the UNAIDS 95-95-95 treatment target. By bridging this knowledge gap, the model can inform interventions to improve the health outcomes of PLWHA experiencing anxiety.

1.5 Research Objectives

1.5.1 General Objective

The general objective of this study is to examine the impact of anxiety on the HIV/AIDS care continuum by the use of mathematical modeling.

1.5.2 Specific Objectives

1. To develop a mathematical model which explain the relationship between anxiety and HIV care continuum.
2. To determine the influence of anxiety on key stages of the HIV/AIDS care continuum through mathematical analysis.
3. To explore potential interventions or strategies within the mathematical model that could mitigate the negative effects of anxiety on HIV/AIDS care continuum outcomes.

1.6 Significance of the Study

In the HIV care cascade, the major threat to treatment is poor adherence to medication and treatment failure among PLWHA, this pose a hindrance to the achievement of the 95-95-95 target. Mental illness is cormobid conditions that affects PLWHA and again yields a threat to medication adherence. This study provides insights into the HIV/AIDS dynamics including medication adherence patterns and the impact of anxiety on the care continuum. These insights will provide relevant treatment mechanisms including psychotherapy inclusion in the care cascade.

The results from this study may elicit effective responses from the relevant National AIDS and STI Control Programme (NASCOP), disease contention institutions such as the Centers for Disease Control and Prevention (CDC) and the Ministry of Health of Kenya (MOH).

1.7 Scope of the Study

In the wake of impacts associated with HIV/AIDS, mental health has surfaced as a salient concern which has drawn attention in the current fields of medical research. The past research work has been focused on the impact of mental health; depression and anxiety on the well-being of victims living with HIV putting less attention to the impact anxiety has in different stages of the HIV/AIDS care continuum.

This study aim was to bridge the gap in the analysis of the impact of anxiety on the HIV care continuum in Kenya. Through the application of a compartmental mathematical model, the study utilized given proportions and rates from literature work and statistics to inform the interaction between the two diseases.

Chapter 2

Literature review

2.1 Introduction

This chapter gives insights of previous research on mathematical modelling of HIV in addition to the impact of anxiety as mental health co-morbid.

2.2 HIV and Anxiety

According to CDC, anxiety disorder is different from anxious feeling since the latter has been experienced mostly among PLWHA ([Jaurette et al., 2023](#)). [Ji et al. \(2024\)](#) claims that there is a strong link between individuals with HIV/AIDS and high prevalence anxiety cases because his study found that 15.5% of HIV/AIDS patients had anxiety problems. Compared to males, the prevalence was higher in females (20.8%). In these included studies, the average age of PLWHA with anxiety disorders was 46.58 ± 11.15 years. Non-heterosexuals had a significantly greater prevalence (32.1%), according to the subgroup analysis.

Kenya is among countries in the Sub Saharan Africa and it is not left out in the impact of anxiety among people living HIV. According to [Mwangala et al. \(2022\)](#), the burden of mental health disorders among people living with HIV in Kenya has been neglected and through empirical research, they opined prevalence rates of anxiety among older adults living with HIV to be at 11.7%. Youths living with HIV forms another age category of people who are at risk of developing anxiety. The research work conducted by [Nyongesa et al. \(2021\)](#), utilized a patient health questionnaire (9-item) and generalized anxiety disorder scale (7-item) to assess their sample and the results from their study provides a rate of 19% anxiety prevalence within

category of youths living with HIV in comparison to those without the disease. Additionally, the prevalence rate of co-morbid of anxiety and depressive disorder was found to be 16%, registering a staggering difference with the uninfected peers.

The case of HIV with anxiety and depression as commodities is still ravaging major parts of SSA since the youths and young adults are also battling the condition. In a similar research [Too et al. \(2021\)](#) presented findings from their work with a rate between 2.2% and 25% for anxiety symptoms.

2.3 Anxiety and HIV Care Continuum

Different common mental health disorders (CMD) significantly impact the care of people living with HIV. Conditions such as depression and anxiety have particularly drawn the attention of the World Health Organization, which emphasizes the need to understand how these mental health issues affect the care continuum for people living with HIV. Proper identification and screening of mental health conditions are essential for achieving better treatment outcomes.

Upon being diagnosed with HIV, it is normal for individuals to experience feelings of anxiety, largely due to the widespread misconception that HIV/AIDS is incurable. However, while a certain level of anxiety is expected, it can sometimes escalate into an anxiety disorder, significantly impacting psychological well-being. It is crucial to understand that HIV itself does not cause anxiety; rather, anxiety develops as a psychological response to the diagnosis. Anxiety problems are more common among HIV-positive individuals than in the general population ([Ji et al., 2024](#)). Furthermore, disclosing an HIV-positive status has been identified as a significant contributor to anxiety.

In the care continuum for patients diagnosed with HIV, the ultimate goal is to retain patients in care and achieve the UNAIDS target of viral load suppression. Start of antiretroviral therapy (ART) among people infected with HIV has been identified as another cause of anxiety disorders. The fear of taking medications regularly, coupled with the stigma surrounding

ART, can overwhelm patients, leading to anxiety. [Dhaliwal et al. \(2022\)](#) conducted a study on Asian cohort groups in care centers, where clients receive routine treatment and care. The study found that anxiety negatively impacts best practices for maintaining good health among people diagnosed and put in care. The impact of anxiety on people living with HIV/AIDS (PLWHA) spans the entire care continuum, affecting stages from initiation into care to retention and maintenance of viral load at low detectable levels (LDL).

The impact of anxiety within the three stages of treatment—initiation, retention in care, and achieving low detectable levels (LDL) of the virus—is multifaceted. People living with HIV/AIDS (PLWHA) can develop anxiety at any stage, as highlighted by UNAIDS and the WHO. Anxiety often results in compromised treatment outcomes and overall disease management, particularly within the Kenyan context, People Living with HIV/AIDS are put on treatment of ART which comprises of varying regimen states, the stage of any given ART regimen is determined by the health status of the infected individual and stage of treatment. According to the research conducted by [Kechine et al. \(2022\)](#) in Southern Ethiopia documents the impact of anxiety on clients receiving Highly Active Antiretroviral Therapy (HAART). The study conducted a cross-sectional study among public hospitals providing care for close to 830 patients, at 95% C.I [1.32, 7.97] with 25.6% prevalence rate. It is of significance to note that the research determined that a quarter of their sample receiving HAART were affected by anxiety.

Previous research have also identified the impact of anxiety on retaining HIV+ clients receiving care. Lost to follow up is a common occurrence among client put in HIV care for ART. According to Center for Disease Control and Pretensions (CDC), client lost in retention leads to worse cases of HIV spread and containment measure have been coined to determined the primary cause of losing client in care. According to [Rooks-Peck et al. \(2018\)](#), anxiety among other mental health disorder like depression as the potential cause of clients dropping out of care continuum. Through meta analysis of previous research, the authors opined on the actual status which pointed to mental health condition as a barrier to retention in care.

The main aim of interventions by the World Health Organization is to ensure that people living with HIV maintain viral load suppression at low detectable levels (LDL). However,

non-adherence to ART treatment has been observed among clients with anxiety. Anxiety, as a psychological disorder, can lead to emotional detachment from daily activities, including medical care and enrollment in HIV ART care (Wykowski et al., 2019). Similarly, the study by Mukui et al. (2016) identified psychological disorders as one of the leading causes of non-adherence to ART treatment in Kenya. The study's results suggest an imminent surge in non-adherence rates due to the mental health status of PLWHA. To address this, the study proposed psycho-social interventions targeting anxiety and depression.

2.4 State of Mental Health Awareness and Treatment in Kenya

According to the World Health Organization (WHO)(Herrman and Jané-Llopis, 2018), perceptions of mental health vary widely, with many people still fearing to share their mental health conditions. Anxiety, a psychological disorder, has received less attention in many Sub-Saharan countries, including Kenya (David-Ferdon, 2016). Kenya ranks fourth in Africa, with a total of 1.9 million people affected by mental health issues (WHO, 2014). The Centers for Disease Control and Prevention proposes raising awareness of mental health through campaigns targeting various age groups and key populations, such as people living with HIV/AIDS (PLWHA). Advances in mental health treatment in Kenya focus on promoting best practices in informal sectors and finding better ways to alleviate mental health conditions (Musyimi et al., 2017).

2.5 Mathematical Models

The application of mathematical models and differential equations have found wide application in the field of disease modelling in determining the most effective and optimal interventions that can be implemented to alleviate the underlying medical problems. Infectious disease modelling is widely understood among many mathematical researchers

who apply the knowledge of linear or non-linear equations, to systems of conventional compartmental modelling or stochastic and optimal analysis. [Omondi et al. \(2019\)](#) utilized compartment models with application of Markov Chain Monte-Carlo in determining HIV infection in two heterosexual age groups in Kenya. Results from this study illustrated the advanced utilization of mathematical models in analysis of HIV transmission between different age groups.

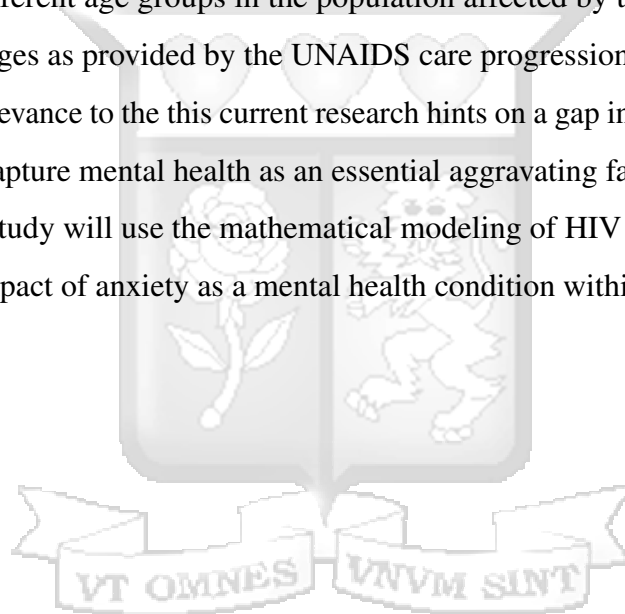
Mathematical modeling involves the use of differential equations which might be Ordinary Differential Equations (ODEs) or Partial Differential Equations (PDEs), in the paper by [De Oliveira et al. \(2022\)](#), the authors used a compartmental model for the analysis of Social Determinants of Health (SDH) in its incorporation to HIV care continuum, the author had four compartments of (S)- the susceptible, (I)- representing HIV+, (A)- individuals with AIDS and (T)- Individuals under treatment. Application of mathematical analysis in determining the infectious disease progression within certain populations involves getting stability analysis of the Disease Free Equilibrium and respective reproduction number. In the paper by To ascertain the reproduction number about the influence of depression on the HIV care cascade in Kenya, the authors employed ODEs and a next-generation matrix([Chemutai et al., 2024](#)). Additionally, the authors utilized Runge Kutta technique of order four in performing numerical simulation for seamless approximations of the Initial Value Problems (IVP).

Epidemiology and mathematical modelling involves the analysis of co-infections which occurs when a host develop a secondary infection as a result of a primary infection such the case of HIV with anxiety and TB. In the article by [Chukwu et al. \(2022\)](#), the author presented mathematical analysis and sensitive assessment of HIV and Listeriosis as co-infection, in the mathematical analysis, author calculated two different reproduction numbers representing the manifestation of the two related disease within the same host using the method of Next Generation matrix approach.

According to the work done by [De Oliveira et al. \(2022\)](#), there is a notable gap in mathematical analysis of social determinants of health and their relationship with the HIV care continuum. The authors discuss various social factors related to management of HIV/AIDS, including

psychological determinants, but fail to illustrate these factors in a model diagram representing the care continuum. Additionally, they did not perform mathematical analyses to determine the impact of different variables on the population. The study aims to address this gap by applying mathematical modeling to examine the impact of anxiety on the HIV care continuum, incorporating distinct compartments for co-infection states.

Additionally, in the study done by [Schnure et al. \(2022\)](#), compartmental mathematical modelling is presented as a tool in the forecast analysis of HIV and targeted intervention among different age groups in Kenya. The study highlights vital components of developing a mathematical model for an infectious disease like HIV with a strong focus on the HIV care continuum thus different age groups in the population affected by the disease and the care continuum stages as provided by the UNAIDS care progression guide. Justification of the study and its relevance to the this current research hints on a gap in the commodities since the paper did not capture mental health as an essential aggravating factor in the care of HIV. As a solution this study will use the mathematical modeling of HIV care continuum taking into account the impact of anxiety as a mental health condition within the care continuum.



Chapter 3

Methodology

3.1 Introduction

In this chapter, the method used to answer the aforementioned research question was developed to address various dynamics of the impact of anxiety on the HIV care continuum. Within the chapter also exists the mathematical formulation techniques and the use of Ordinary Differential Equations to understand the mechanisms of the disease treatment and relative outcome.

3.2 Source of Data

In this research, the data used was primarily obtained from previous literature work. The study applied a vast search of the parameter estimates from evidence-based research work to help with the mathematical simulation in the analysis. Additionally, the research used data from clinical trials previously held in Kenya and data from the Ministry of Health database.

3.3 Model Description

The model represents HIV care continuum with prominent impact of anxiety. The compartmental model has the human population divided into nine compartments of the susceptible individuals not having HIV and not anxious $S(t)$, the undiagnosed HIV positive population $P(t)$. The population of HIV-positive individuals who are affected by anxiety $Pa(t)$, infected individuals who have been diagnosed with HIV and confirmed to be positive $I(t)$. The class

of people who tested positive for HIV and are diagnosed with anxiety $A(t)$. Individuals diagnosed with HIV but lack anxiety $T(t)$, thus are put on ART treatment. The compartment $Ta(t)$ represents the group of people with anxiety receiving anxiety therapy at the same time as ART treatment. $Va(t)$ represents the group of individuals who have attained viral load suppression but still experiencing anxiety. $V(t)$ is the final class of both individuals who attained viral load suppression and did not have anxiety together with those who had anxiety and are now free of anxious feelings, additionally, they have attained viral load suppression. Thus the total population N is given by;

$$N(t) = S(t) + P(t) + Pa(t) + I(t) + A(t) + T(t) + Ta(t) + Va(t) + V(t).$$

One major assumption of the model is that all parameters remain constant. Parameter Λ represents the recruitment rate of new individuals into the population through the development maturity and immigration of people. Upon recruitment, individuals become infected at a rate denoted by β , subsequently joining the population of undiagnosed HIV cases. The parameter ω_1 signifies the testing rate among individuals not affected by anxiety, transitioning them to the diagnosed HIV-positive group. Similarly, λ_1 denotes the rate at which undiagnosed HIV-positive individuals develop anxiety, becoming part of the HIV-positive anxious group without diagnosis. ω_2 represents the rate at which individuals from the HIV-positive anxious group undergo testing for both HIV and anxiety diagnosis. θ_1 and θ_2 are the rates at which diagnosed HIV-positive individuals, with and without anxiety, respectively, commence ART treatment. λ_2 indicates the rate at which individuals initially on ART treatment alone develop anxiety. ψ_1 represents the transition rate for individuals leaving anxiety therapy to undergo ART therapy alone. Adherence rates to ART treatment are denoted by δ_1 and δ_2 for those on ART alone and those undergoing anxiety therapy alongside ART, respectively. ψ_2 signifies the effectiveness rate of recovering from anxiety to join the virally suppressed group without anxiety. κ represents the non-adherence rate leading to relapse to a state of high viral load. Additionally, the model assumes that all compartments experience natural death at a rate of μ , with diagnosed individuals and those on ART treatment experiencing additional disease-induced death at a rate denoted by α .

The force of infection is the relative effectiveness of transmission per contact rate β from

the population of infectious individuals among the classes; P, I, P_a, A . An assumption is that individuals receiving ART treatment have reduced viral load hence a low propensity of being infectious. Additionally, individuals who have achieved viral load suppression are non-infectious. Another assumption is that there is minimal time difference between diagnosis and initiation of treatment hence there is no relationship between the diagnosed classes. Concerning the general population under consideration, the force of infection is given by;

$$\beta_v(t) = \frac{(\beta \varepsilon_1 P + \beta \varepsilon_2 P_a + \beta \varepsilon_3 I + \beta \varepsilon_4 A)S}{N} \quad (3.1)$$

where $\beta \varepsilon_1 > \beta \varepsilon_2 > \beta \varepsilon_3 > \beta \varepsilon_4$.

3.4 Additional Model Assumptions

1. Anxiety increases the risk of morbidity in the HIV diagnosed people.
2. Attaining Viral Load Suppression (VLS) is a success in the management of anxiety and HIV/AIDS.
3. No other deaths due to other diseases in the population.

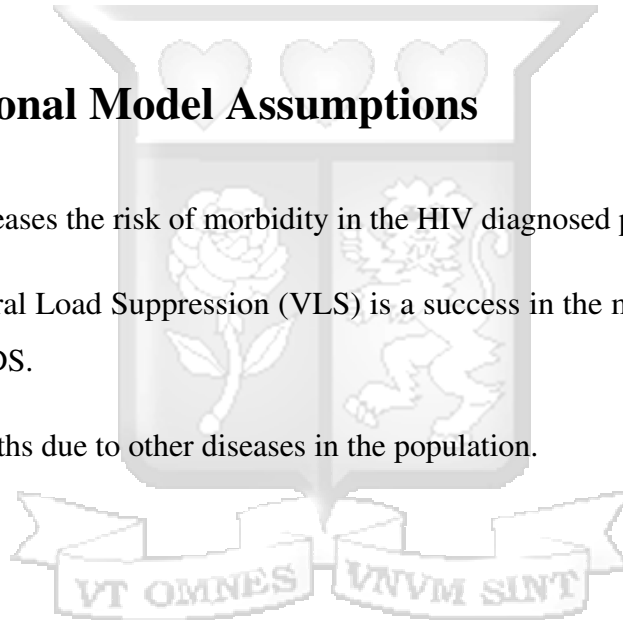
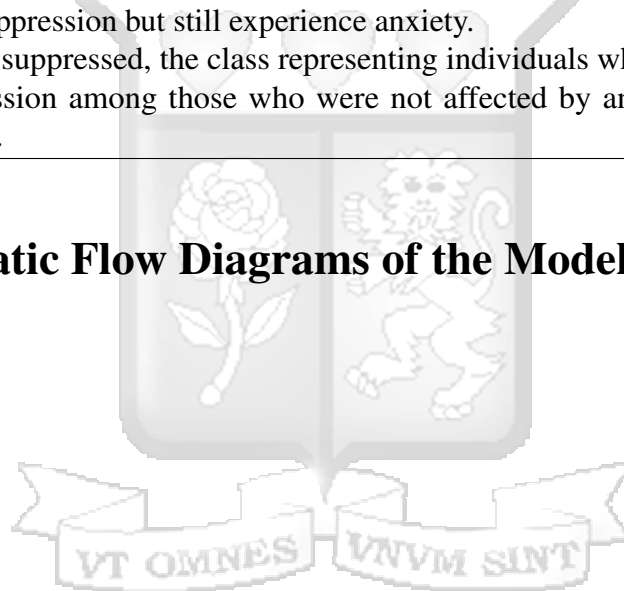


Table 3.1: Table of model variables

Symbol	Description
S	State of HIV-negative susceptible group of people free of HIV and anxiety.
P	HIV-positive class representing individuals who are HIV positive but have not been diagnosed with HIV and anxiety.
Pa	HIV-positive class with anxiety, representing individuals who are HIV positive, affected by anxiety but not yet diagnosed with either HIV or anxiety.
I	HIV-positive diagnosed class, group of individuals who have tested positive for HIV.
A	HIV-positive diagnosed and anxiety diagnosed, a group of individuals positively diagnosed with HIV and also anxiety.
T	HIV-positive on treatment, the class of those taking ART treatment alone.
Ta	HIV-positive receiving ART treatment and anxiety therapy, this is the class of those who are in both treatments for HIV and anxiety.
Va	Virally suppressed but still anxious, the group of individuals who have attained viral load suppression but still experience anxiety.
V	Virally suppressed, the class representing individuals who have attained viral load suppression among those who were not affected by anxiety and those who had anxiety.

3.5 Schematic Flow Diagrams of the Models



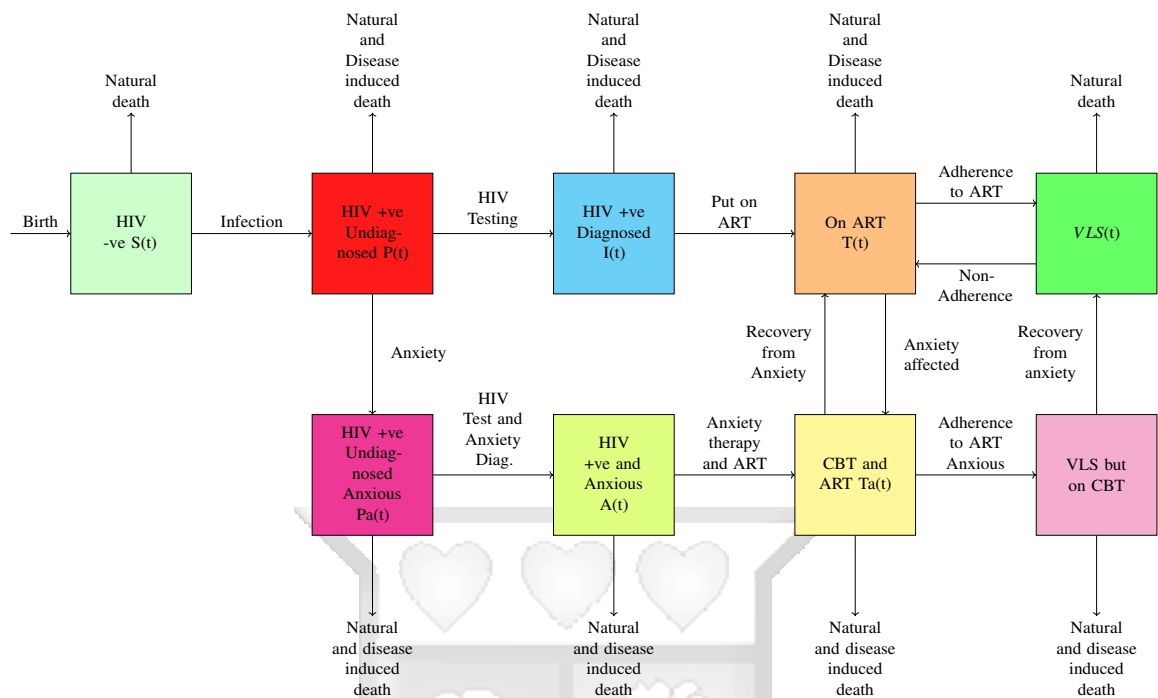


Figure 3.1: Model diagram: HIV and anxiety compartmental model

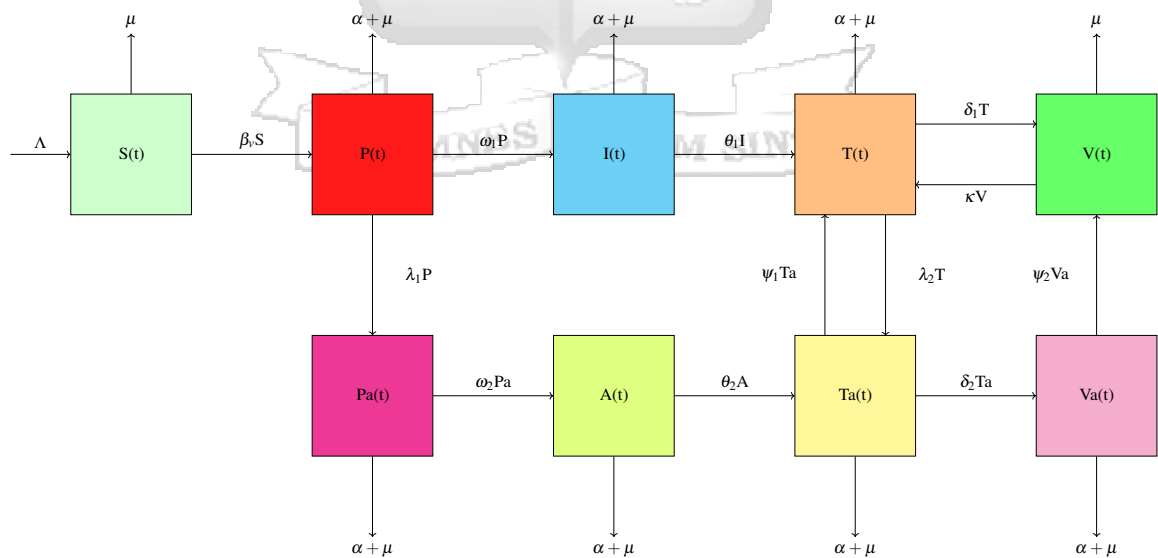


Figure 3.2: Model diagram: HIV and anxiety parameterized model

Table 3.2: Table of model parameters

Parameter	Description
Λ	Recruitment rate.
β	HIV infection rate.
λ_1	Rate at which the infected undiagnosed acquire anxiety.
ω_1	HIV testing rate of the infected undiagnosed group.
ω_2	Rate at which HIV-infected unorganized group affected by anxiety get to be tested and diagnosed of anxiety.
θ_1	Rate at which HIV +ve individuals get to be put on (ART) treatment.
θ_2	Rate of acquiring ART treatment and anxiety therapy among HIV +ve anxiety affected group.
δ_1	Adherence rate among the group put on ART treatment alone.
δ_2	Adherence rate among anxious group who still have anxiety.
ψ_1	Recovery rate from anxiety to be put on ART treatment alone.
λ_2	Rate of acquiring anxiety among individuals who are receiving anxiety treatment alone.
ψ_2	Recovery rate from anxiety among the group who were still anxious to move to the virally suppressed group who do not have anxiety.
κ	Non-adherence rate and respective relapse of high VL.
α	Disease induced death.
μ	Natural death within the population.



3.6 Model Equations

The following entails the systems of differential equations;

$$\begin{aligned}
 \frac{dS}{dt} &= \Lambda - (\mu + \beta_v)S, \\
 \frac{dP}{dt} &= \beta_v S - (\alpha + \mu + \omega_1 + \lambda_1)P, \\
 \frac{dP_a}{dt} &= \lambda_1 P - (\alpha + \mu + \omega_2)P_a, \\
 \frac{dI}{dt} &= \omega_1 P - (\alpha + \mu + \theta_1)I, \\
 \frac{dA}{dt} &= \omega_2 P_a - (\alpha + \mu + \theta_2)A, \\
 \frac{dT}{dt} &= \theta_1 I + \psi_1 T_a + \kappa V - (\alpha + \mu + \lambda_2 + \delta_1)T, \\
 \frac{dT_a}{dt} &= \theta_2 A + \lambda_2 T - (\alpha + \mu + \delta_2 + \psi_1)T_a, \\
 \frac{dV_a}{dt} &= \delta_2 T_a - (\alpha + \mu + \psi_2)V_a, \\
 \frac{dV}{dt} &= \delta_1 T + \psi_2 V_a - (\mu + \kappa)V,
 \end{aligned} \tag{3.2}$$

where $S(t) > 0, P(t) \geq 0, Pa(t) \geq 0, I(t) \geq 0, A(t) \geq 0, T(t) \geq 0, Ta(t) \geq 0, Va(t) \geq 0, V(t) \geq 0$.

3.6.1 Mathematical Analysis of the Model

The model solutions should be bounded for all $t > 0$ in the positive region. This shows that the model is biologically and epidemiological meaningful.

Boundedness

Theorem 3.1. *All solutions $(S(t), P(t), Pa(t), A(t), T(t), Ta(t), Va(t), V(t)) \in \mathbb{R}^9$ of the model are bounded and there exist a biologically feasible region of the model given by:*

$$\Gamma = \{(S(t), P(t), P_a(t), A(t), T(t), T_a(t), V_a(t), V(t))$$

$$\in \mathbb{R}^9 \mid S(t) > 0, P(t) \geq 0, P_a(t) \geq 0, I(t) \geq 0, A(t) \geq 0, T(t) \geq 0, T_a(t) \geq 0, V_a(t) \geq 0, V(t) \geq 0\}.$$

Proof. From the total population description, a change of N leads to a respective change in all state variables of the population. Taking all parameters of the model yields:

$$\begin{aligned} \frac{dN}{dt} = & \Lambda - (\mu - \beta_v)S + \beta_v S - (\alpha + \mu + \omega_1 + \lambda_1)P + \lambda_1 P - (\alpha + \mu + \omega_2)P_a + \omega_1 P - (\alpha + \mu + \theta_1)I \\ & + \omega_2 P_a - (\alpha + \mu + \theta_2)A + \theta_1 I + \psi_1 T_a + \kappa V - (\alpha + \mu + \lambda_2 + \delta_1)T \\ & + \theta_2 A + \lambda_2 T - (\alpha + \mu + \delta_2 + \psi_1)T_a \\ & + \delta_2 T_a - (\alpha + \mu + \psi_2)V_a + \delta_1 T + \psi_2 V_a - (\mu + \kappa)V. \end{aligned} \quad (3.3)$$

From the above system of equations, the expanded system reduces to;

$$\begin{aligned} \frac{dN}{dt} = & \Lambda - \mu S - (\alpha + \mu)P - (\alpha + \mu)P_a - (\alpha + \mu)I - (\alpha + \mu)A - (\alpha + \mu)T - (\alpha + \mu)T_a \\ & - (\alpha + \mu)V_a - \mu V. \end{aligned} \quad (3.4)$$

But in the absence of the disease, ($P=P_a=I=A=T=T_a=V_a=V=0$)

$$\frac{dN}{dt} = \Lambda - \mu S(t) - \mu(P + P_a + I + A + T + T_a + V_a + V).$$

Hence, the model reduces to a bounded model of the form shown below where $S=N$ when the number of susceptible is equal to the total number of the population

$$\frac{dN}{dt} \leq \Lambda - \mu N(t).$$

To qualify for boundedness, the following equation has to stand for the total population

$$\frac{dN}{dt} \leq \Lambda - \mu N(t).$$

Applying the method of integration by an integrating factor;

$$\frac{d}{dt} [e^{\mu t} N(t)] \leq e^{\alpha t} \Lambda. \quad (3.5)$$

Using the initial condition of the model when $t=0$, the inequality results to;

$$N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\alpha} (1 - e^{-\mu t}).$$

As $t \rightarrow \infty$ we have;

$$N(t) \leq \frac{\Lambda}{\mu}. \quad (3.6)$$

This implies that $0 < N(t) \leq \frac{\Lambda}{\mu}$ shows that the model is bounded to the region Γ thus satisfying the proof. □

Positivity

Using the non-negative initial conditions, the solutions of the model will remain non-negative for all $t \geq 0$. This leads to the following theorem.

Theorem 3.2. *Let the initial value of the system in the equation be represented as*

$$\{S(t) > 0, P(t) \geq 0, Pa(t) \geq 0, I(t) \geq 0, A(t) \geq 0, T(t) \geq 0, Ta(t) \geq 0, Va(t) \geq 0, V(t) \geq 0\} \in \Gamma.$$

The solution set $\{S(t), P(t), Pa(t), I(t), A(t), T(t), Ta(t), Va(t), V(t)\}$ from the equation is positive for all $t > 0$

Proof. From the first equation in (3.2) in the model,

$$\frac{dS}{dt} = \Lambda - (\mu + \beta_v)S, \quad (3.7)$$

which simplifies to;

$$\frac{dS}{dt} \geq -(\mu + \beta_v)S. \quad (3.8)$$

Integrating equation (3.8) by the method of separation of variables and using the initial conditions (when $t=0$, $S = S(0)$), yields;

$$S(t) \geq S(0)e^{-(\mu + \beta_v)t}. \quad (3.9)$$

Since $e^{-(\mu + \beta_v)t} \geq 0$ and $S(0) > 0$, $S(t)$ is positive for all $t \geq 0$.

Again, from the second equation in the model system (3.2),

$$\frac{dP}{dt} = \beta_v S - (\alpha + \mu + \omega_1 + \lambda_1)P. \quad (3.10)$$

By letter $a_1 = (\alpha + \mu + \omega_1 + \lambda_1)$,

$$\frac{dP}{dt} = \beta_v S - a_1 P, \quad (3.11)$$

which can be simplified as;

$$\frac{dP}{dt} \geq -a_1 P, \quad (3.12)$$

$$P(t) \geq P(0)e^{-a_1 t} \geq 0. \quad (3.13)$$

The above solution procedure can be applied to all the remaining equations in the model system (3.2), yielding the following results:

$$\begin{aligned}
P_a(t) &\geq P_a(0)e^{-a_2t} \geq 0, I(t) \geq I(0)e^{-a_3t} \geq 0, A(t) \geq A(0)e^{-a_4t} \geq 0, T(t) \geq T(0)e^{-a_5t} \geq 0, \\
T_a(t) &\geq T_a(0)e^{-a_6t} \geq 0, V_a(t) \geq V_a(0)e^{-a_5t} \geq 0, V(t) \geq V(0)e^{-(\mu+\kappa)t} \geq 0.
\end{aligned}
\tag{3.14}$$

□

3.7 Stability Analysis at Disease-free Equilibrium and Effective Reproduction Number

3.7.1 Disease-free Equilibrium

Disease-free equilibrium is a state of the absence of infection in the population. Thus, other than the susceptible, all the variables are set to zero i.e. $P = P_a = I = A = T = T_a = V_a = V = 0$.

From the first equation from the system (3.2). The Susceptible class reduces to: $S(\mu - \beta_v) = \Lambda$ or $S = \frac{\Lambda}{\mu + \beta_v}$.

Since β_v is the force of infection and at DFE it is zero, hence the value of S reduces to: $S = \frac{\Lambda}{\mu}$

Thus, the disease-free equilibrium D_0 is given by;

$$D_0 = (S, P, P_a, I, A, T, T_a, V_a, V) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0 \right).$$

3.7.2 Effective Reproduction Number

The basic reproduction number (R_v) is the number of secondary infections, that an average infectious person can cause in a population within which every member of the population is susceptible to the infection. The effective reproduction number is obtained using the method of next-generation matrix thus through the solution of matrix approach. (R_v) is the spectral

radius of the next generation matrix FV^{-1} where, where F represents new infections in infected compartments and V represent transitivity of the infection. From the system of differential equations, there exist six classes of infection that are to be considered in the determination of effective reproduction numbers.

From the force of infection:

$$\beta_v(t) = \frac{(\beta\varepsilon_1P + \beta\varepsilon_2P_a + \beta\varepsilon_3I + \beta\varepsilon_4A)S}{N}, \quad (3.15)$$

where $P, P_a, I,$ and A are chosen are the infectious classes then using the next generation matrix, The matrices of $F_{(x)}$ and $V_{(x)}$ are given as;

$$F_{(x)} = \begin{pmatrix} \frac{(\beta\varepsilon_1P + \beta\varepsilon_2P_a + \beta\varepsilon_3I + \beta\varepsilon_4A)S}{N} \\ 0 \\ 0 \\ 0 \end{pmatrix} \text{ and } V_{(x)} = \begin{pmatrix} (\alpha + \mu + \omega_1 + \lambda_1)P \\ -\lambda P + (\alpha + \mu + \omega_2)P_a \\ -\omega P + (\alpha + \mu + \theta_1)I \\ -\omega_2 P_a + (\alpha + \mu + \theta_2)A \end{pmatrix}.$$

The resulting Jacobian Matrices of the matrices above at disease-free equilibrium (DFE) are given below, obtained by partial derivative with respect to P, P_a, I and A respectively;

$$F_{D^0} = \begin{pmatrix} \beta\varepsilon_1 & \beta\varepsilon_2 & \beta\varepsilon_3 & \beta\varepsilon_4 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V_{D^0} = \begin{pmatrix} \alpha + \mu + \omega_1 + \lambda_1 & 0 & 0 & 0 \\ -\lambda_1 & \alpha + \mu + \omega_2 & 0 & 0 \\ -\omega_1 & 0 & \alpha + \mu + \theta_1 & 0 \\ 0 & -\omega_2 & 0 & \alpha + \mu + \theta_2 \end{pmatrix}.$$

The inverse of Matrix V at D^0 is given by;

$$V^{-1} = \begin{pmatrix} \frac{1}{\alpha + \lambda_1 + \mu + \omega_1} & 0 & 0 & 0 \\ \frac{\lambda_1}{(\alpha + \mu + \omega_2)(\alpha + \lambda_1 + \mu + \omega_1)} & \frac{1}{\alpha + \mu + \omega_2} & 0 & 0 \\ \frac{\omega_1}{(\alpha + \theta_1 + \mu)(\alpha + \lambda_1 + \mu + \omega_1)} & 0 & \frac{1}{\alpha + \theta_1 + \mu} & 0 \\ \frac{\lambda_1 \omega_2}{(\alpha + \theta_2 + \mu)(\alpha + \mu + \omega_2)(\alpha + \lambda_1 + \mu + \omega_1)} & \frac{\omega_2}{(\alpha + \theta_2 + \mu)(\alpha + \mu + \omega_2)} & 0 & \frac{1}{\alpha + \theta_2 + \mu} \end{pmatrix}.$$

The matrix product between F and V^{-1} is as shown below;

$$FV^{-1} = \begin{pmatrix} M_1 \frac{\beta \omega_2 \varepsilon_4}{(\alpha + \theta_2 + \mu)(\alpha + \mu + \omega_2)} + \frac{\beta \varepsilon_2}{\alpha + \mu + \omega_2} & \frac{\beta \varepsilon_3}{\alpha + \theta_1 + \mu} & \frac{\beta \varepsilon_4}{\alpha + \theta_2 + \mu} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

where M_1 is the largest eigenvalue of the upper triangular matrix and the values are presented as follows;

$$R_v = M_1 = Z_1 + Z_2 + Z_3 + Z_4,$$

$$Z_1 = \frac{\beta \omega_1 \varepsilon_3}{(\alpha + \theta_1 + \mu)(\alpha + \lambda_1 + \mu + \omega_1)}, Z_2 = \frac{\beta \lambda_1 \omega_2 \varepsilon_4}{(\alpha + \theta_2 + \mu)(\alpha + \mu + \omega_2)(\alpha + \lambda_1 + \mu + \omega_1)},$$

$$Z_3 = \frac{\beta \varepsilon_1}{\alpha + \lambda_1 + \mu + \omega_1},$$

$$Z_4 = \frac{\beta \lambda_1 \varepsilon_2}{(\alpha + \mu + \omega_2)(\alpha + \lambda_1 + \mu + \omega_1)}.$$

The proportion of R_v indicates the progression of the HIV-anxiety co-infections in the population. When $R_v < 1$ it means the disease state is cleared from the population. If $R_v > 1$ this informs that the containment of the disease and the co-infection remains unstable. The stability is further analyzed in the following to decipher the impact of the treatment of anxiety.

3.7.3 Local Stability of the Disease-free Equilibrium

Theorem 3.3. *The disease free equilibrium D_0 is locally asymptotically stable in Γ if $R_v < 1$ and unstable otherwise for all parameters.*

Proof. The Jacobian matrix of the entire system (3.2) at DFE is given by;

$$D^0 = \begin{pmatrix} -Q_1 & -\beta\varepsilon_1 & -\beta\varepsilon_2 & \beta\varepsilon_3 & -\beta\varepsilon_4 & 0 & 0 & 0 & 0 \\ 0 & \beta\varepsilon_1 - Q_2 & \beta\varepsilon_2 & \beta\varepsilon_3 & \beta\varepsilon_4 & 0 & 0 & 0 & 0 \\ 0 & \lambda_1 & -Q_3 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \omega_1 & 0 & -Q_4 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \omega_2 & 0 & -Q_5 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \theta_1 & 0 & -Q_6 & \psi_1 & 0 & \kappa \\ 0 & 0 & 0 & 0 & \theta_2 & \lambda_2 & -Q_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \delta_2 & -Q_8 & 0 \\ 0 & 0 & 0 & 0 & 0 & \delta_1 & 0 & \psi_2 & -Q_9 \end{pmatrix},$$

where; $Q_1 = \mu$; $Q_2 = (\alpha + \mu + \omega_1 + \lambda_1)$; $Q_3 = (\alpha + \mu + \omega_2)$; $Q_4 = (\alpha + \mu + \theta)$; $Q_5 = (\alpha + \mu + \theta_2)$; $Q_6 = (\alpha + \mu + \lambda_2 + \delta_1)$; $Q_7 = (\alpha + \mu + \delta_2 + \psi_1)$; $Q_8 = (\alpha + \mu + \psi_2)$; $Q_9 = (\mu + \kappa)$.

The Jacobin matrix is well-posed since the sum of its columns yields only removable parameters from the model.

To find the eigenvalues, for the Jacobian matrix in D_0 we perform; $|J - \lambda I|$ and this yields;

$$\mathbb{J} = \begin{pmatrix} -\mu - \lambda & -\beta\varepsilon_1 & -\beta\varepsilon_2 & -\beta\varepsilon_3 & -\beta\varepsilon_4 & 0 & 0 & 0 & 0 \\ 0 & \beta\varepsilon_1 - Q_2 - \lambda & \beta\varepsilon_2 & \beta\varepsilon_3 & \beta\varepsilon_4 & 0 & 0 & 0 & 0 \\ 0 & \lambda_1 & -Q_3 - \lambda & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \omega_1 & 0 & -Q_4 - \lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \omega_2 & 0 & -Q_5 - \lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \theta_1 & 0 & -Q_6 - \lambda & \psi_1 & 0 & \kappa \\ 0 & 0 & 0 & 0 & \theta_2 & \lambda_2 & -Q_7 - \lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \delta_2 & -Q_8 - \lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & \delta_1 & 0 & \psi_2 & -(\mu + \kappa) - \lambda \end{pmatrix}$$

By inspection of the Jacobian matrix, the eigenvalues are derived as follows;

The last two columns and rows yield a lower triangular matrix

$$J = \begin{pmatrix} -Q_8 - \lambda & 0 \\ \psi_2 & -(\mu + \kappa) - \lambda \end{pmatrix}.$$

This gives the first and second eigenvalues; $\lambda_1 = -(\mu + \kappa)$ and $\lambda_2 = -(\alpha + \mu + \psi_2)$ Deleting the two rows and the two columns leaves a 7x7 matrix.

$$\begin{pmatrix} -\mu & -\beta\varepsilon_1 & -\beta\varepsilon_2 & -\beta\varepsilon_3 & -\beta\varepsilon_4 & 0 & 0 \\ 0 & \beta\varepsilon_1 - (\alpha + \mu + \omega_1 + \lambda_1) & \beta\varepsilon_2 & \beta\varepsilon_3 & \beta\varepsilon_4 & 0 & 0 \\ 0 & \lambda_1 & -(\alpha + \mu + \omega_2) & 0 & 0 & 0 & 0 \\ 0 & \omega_1 & 0 & -(\alpha + \mu + \omega_1) & 0 & 0 & 0 \\ 0 & 0 & \omega_2 & 0 & -(\alpha + \mu + \theta_2) & 0 & 0 \\ 0 & 0 & 0 & \theta_1 & 0 & -(\alpha + \mu + \lambda_2 + \delta_1) & \psi_1 \\ 0 & 0 & 0 & 0 & \theta_2 & \lambda_2 & -(\alpha + \mu + \delta_2 + \psi_1) \end{pmatrix}.$$

Again by inspection, the two last rows and columns yield the third and fourth eigenvalues; $\lambda_3 = -(\alpha + \mu + \delta_2 + \psi_1)$ and $\lambda_4 = -(\alpha + \mu + \lambda_2 + \delta_1)$. The matrix reduces to a 5x5 matrix given by;

$$J = \begin{pmatrix} -\mu - \lambda & \beta\varepsilon_1 & \beta\varepsilon_2 & \beta\varepsilon_3 & \beta\varepsilon_4 \\ 0 & \beta\varepsilon_1 - (\alpha + \mu + \omega_1 + \lambda_1) - \lambda & 0 & 0 & 0 \\ 0 & \lambda_1 & -(\alpha + \mu + \omega_2) - \lambda & 0 & 0 \\ 0 & \omega_1 & 0 & -(\alpha + \mu + \omega_1) - \lambda & 0 \\ 0 & 0 & \omega_2 & 0 & -(\alpha + \mu + \theta_2) - \lambda \end{pmatrix}.$$

The reduced Jacobian is a lower triangular matrix with the following eigenvalues;

$\lambda_5 = -(\alpha + \mu + \theta_2)$; $\lambda_6 = -(\alpha + \mu + \omega_1)$; $\lambda_7 = -(\alpha + \mu + \omega_2)$; $\lambda_8 = \beta\varepsilon_1 - (\alpha + \mu + \omega_1 + \lambda_1)$ and $\lambda_9 = -\mu$.

Since all the eigenvalues have negative real parts, D^0 is locally asymptotically stable. \square

3.7.4 Global Stability

Theorem: The disease-free equilibrium D_0 of the system (1) is globally asymptotically stable if $R_0 < 1$ and unstable otherwise.

Using the Lyapunov theorem of stability, if \exists a function $V : \mathbb{R}^n \implies \mathbb{R}$ which satisfies the equations:

- (i) $V(x) = 0$ when $X = x$

$$(ii) V(X) > 0, \forall X \neq x$$

$$(iii) V'(X) \leq 0, \forall X$$

Thus if $V'(X) \leq 0$ then x is said to be a Lyapunov stable and if $V'(X) < 0$ hence the x is said to be globally asymptotically stable.

Considering the infectious variables of model equation (5.1) we have:

$$\begin{aligned} \frac{dP}{dt} &= \beta_v S - (\alpha + \mu + \omega_1 + \lambda_1)P, \\ \frac{dP_a}{dt} &= \lambda_1 P - (\alpha + \mu + \omega_2)P_a, \\ \frac{dI}{dt} &= \omega_1 P - (\alpha + \mu + \theta_1)I, \\ \frac{dA}{dt} &= \omega_2 P_a - (\alpha + \mu + \theta_2)A. \end{aligned} \tag{3.16}$$

Given that the disease-free equilibrium D_0 is:

$$D_0 = (S, P, P_a, I, A, T, T_a, V_a, V) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0 \right)$$

where by Lyapunov theorem, $V_{P,P_a,I,A} = aP, bP_a, cI, dA$: where $a, b, c, d \in \mathbb{R}_+$.

$$(i) V_{(0,0,0,0)} = 0,$$

$$(ii) V_{P,P_a,I,A} = \forall P,P_a,I,A \neq 0,$$

$$(iii) V' = \frac{dv}{dt} = a \frac{dP}{dt} + b \frac{dP_a}{dt} + c \frac{dI}{dt} + d \frac{dA}{dt}.$$

The first theorem can be proved by subjecting all the variables in equation (3.16) to zero which yields a value of zero, additionally, the second theorem is satisfied from the model since each variable represents a given proportion of the entire population thus it does not lead to zero. It is important to provide proof of the third theorem of the derivative of the functions V . From the force of infection:

$$\beta_v(t) = \frac{(\beta \varepsilon_1 P + \beta \varepsilon_2 P_a + \beta \varepsilon_3 I + \beta \varepsilon_4 A)S}{N}. \tag{3.17}$$

From the third equation of the theorem applying the differential equations from the infectious classes yields.

$$\begin{aligned} \frac{dv}{dt} = & a[\beta_v S - (\alpha + \mu + \omega_1)P] + b[\lambda_1 P - (\alpha + \mu + \omega_2)P_a] \\ & + c[\omega_1 P - (\alpha + \mu + \theta_1)I] + d[\omega_2 P - (\alpha + \mu + \theta_2)A]. \end{aligned} \quad (3.18)$$

Expanding equation (3.18) yields:

$$\begin{aligned} \frac{dv}{dt} \leq & a\beta_v S - a(\alpha + \mu + \omega_1)P + b\lambda_1 P - b(\alpha + \mu + \omega_2)P_a \\ & + c\omega_1 P - c(\alpha + \mu + \theta_1)I + d\omega_2 P_a - d(\alpha + \mu + \theta_2)A. \end{aligned} \quad (3.19)$$

Replacing S from the DFE and β_v yields

$$\begin{aligned} \frac{dv}{dt} = & a \frac{\Lambda (\beta \varepsilon_1 P + \beta \varepsilon_2 P_a + \beta \varepsilon_3 I + \beta \varepsilon_4 A) \Lambda}{\mu N} \\ & [b\lambda_1 - a(\alpha + \mu + \omega_1) + c\omega_1]P \\ & + [d\omega_2 + b(\alpha + \mu + \omega_2)]P_a \\ & + [-c(\alpha + \mu + \theta_1)]I \\ & + [-d(\alpha + \mu + \theta_2)]A. \end{aligned} \quad (3.20)$$

From subjecting the other variables in the infectious classless to zero except the population of the infected people affected by anxiety. Applying the infectiousness rate into the equation yields.

$$\begin{aligned} \frac{dv}{dt} = & a \frac{\Lambda}{\mu} \beta \varepsilon_1 [b\lambda_1 - a(\alpha + \mu + \omega_1 + \lambda_1) + (\alpha + \mu + \theta_1)\omega_1] \\ & + \beta \varepsilon_2 [(\alpha + \mu + \omega_2)\omega_2 - \omega_2(\alpha + \mu + \omega_2)] \\ & + \beta \varepsilon_3 [-(\alpha + \mu + \theta_1)] \\ & + \beta \varepsilon_4 [-(\alpha + \mu + \omega_2) + (\alpha + \mu + \theta_2)]. \end{aligned} \quad (3.21)$$

Solving for the value of a yields:

$a = (\alpha + \lambda_1 + \mu + \omega_1)(\alpha + \theta_2 + \mu)$. Applying the value of a into equation (3.21) yields;

$$\begin{aligned} \frac{dv}{dt} = & (\alpha + \lambda_1 + \mu + \omega_1)(\alpha + \theta_2 + \mu) \left[\frac{\beta \varepsilon_1}{\alpha + \mu + \omega_1} + \frac{\beta \lambda_1 \varepsilon_2}{(\alpha + \mu + \omega_2)(\alpha + \lambda_1 + \mu + \omega_1)} \right. \\ & \left. + \frac{\beta \varepsilon_3 + \omega_3}{(\alpha + \theta_1 + \mu)(\alpha + \lambda_1 + \mu + \omega_1)} + \frac{\beta \lambda_1 \omega_2 \varepsilon_4}{(\alpha + \theta_2 + \mu)(\alpha + \mu + \omega_2)(\alpha + \lambda_1 + \mu + \omega_1)} - 1 \right]. \end{aligned} \quad (3.22)$$

The system is evident in showing the value of R_v which is illustrated as follows;

$$\frac{dv}{dt} = (\alpha + \lambda_1 + \mu + \omega_1)(\alpha + \theta_2 + \mu)[R_v - 1]P. \quad (3.23)$$

When the value of $R_v < 1$ then $\frac{dv}{dt} < 0$. This implies that the disease-free equilibrium will be globally asymptotically stable.

3.7.5 Endemic Equilibrium

If $R_v > 1$, the system has a unique endemic equilibrium given by:

$$\mathcal{D}_1 = [S^*, P^*, P_a^*, I^*, A^*, T^*, T_a^*, V_a^*, V^*].$$

where,

$$\begin{aligned} S^* &= \frac{\Lambda}{\mu + \beta_v}, P^* = \frac{\beta_v \Lambda}{(\mu + \beta_v)(\alpha + \mu + \omega_1 + \lambda_1)}, P_a^* = \frac{\lambda_1 \beta_v \Lambda}{(\mu + \beta_v)(\alpha + \mu + \omega_1 + \lambda_1)(\alpha + \mu + \omega_2)}, \\ I^* &= \frac{\omega_1 \beta_v \Lambda}{(\mu + \beta_v)(\alpha + \mu + \omega_1 + \lambda_1)(\alpha + \mu + \theta_1)}, A^* = \frac{\omega_2 \lambda_1 \beta_v \Lambda}{(\mu + \beta_v)(\alpha + \mu + \omega_1 + \lambda_1)(\alpha + \mu + \omega_2)}, \\ T^* &= \frac{\theta_1 \omega_1 \beta_v \Lambda}{(\mu + \beta_v)(\alpha + \mu + \omega_1 + \lambda_1)(\alpha + \mu + \theta_1)} + \frac{\psi T_a^*}{(\alpha + \mu + \lambda_2 + \delta_1)} + \frac{\kappa V^*}{(\alpha + \mu + \lambda_2 + \delta_1)}, \\ T_a^* &= \frac{\theta_2 A^*}{(\alpha + \mu + \delta_2 + \psi_1)} + \frac{\lambda_2 T^*}{(\alpha + \mu + \delta_2 + \psi_1)}, V_a^* = \frac{\delta_2 T_a^*}{(\alpha + \mu + \psi_2)}, \\ V^* &= \frac{\delta_1 T^*}{(\mu + \kappa)} + \frac{\psi_2 V_a^*}{(\mu + \kappa)}. \end{aligned} \quad (3.24)$$

The system of the solutions in (3.24) using the infectious variables and the relative force of infection shows relative disease presence in the population when $R_v > 1$. The endemic equilibrium D_1 is locally asymptotically stable when the value of R_v is less than unity.

Chapter 4

Sensitivity Analysis and Numerical Simulations

4.1 Sensitivity Analysis

Sensitivity analysis is a mathematical method used to determine how sensitive a model is to changes in the values of its parameters. The model structure is made up of variables and parameters. The parameters determine the impact each variable has on the model structure hence it is vital to determine how sensitive the model can be to the changes in parameter values.

This study utilized the Normalized Forward Sensitivity Index which is applied to the effective reproduction number and the relative parameters involved in the R_v . The Normalized Forward Sensitivity Index (F.S.I) is computed on R_v based on the following formula where the parameter η represents the parametric change on the variable of interest concerning R_v :

$$F.S.I = \frac{\partial R_v}{\partial \eta} * \frac{\eta}{R_v}. \quad (4.1)$$

The following are some of the parameters involved in the force of infection and how their F.S.I solution is represented.

$$\beta \varepsilon_1^* = \frac{\beta_{\varepsilon_1}}{\frac{\lambda_1 \left(\frac{\omega_2 \beta_{\varepsilon_4}}{\alpha + \theta_2 + \mu} + \beta_{\varepsilon_2} \right)}{\alpha + \mu + \omega_2} + \frac{\omega_1 \beta_{\varepsilon_3}}{\alpha + \theta_1 + \mu} + \beta_{\varepsilon_1}} \quad (4.2)$$

$$\beta \varepsilon_2^* = \frac{\lambda_1 \beta_{\varepsilon_2}}{(\alpha + \mu + \omega_2) \left(\frac{\lambda_1 \left(\frac{\omega_2 \beta_{\varepsilon_4}}{\alpha + \theta_2 + \mu} + \beta_{\varepsilon_2} \right)}{\alpha + \mu + \omega_2} + \frac{\omega_1 \beta_{\varepsilon_3}}{\alpha + \theta_1 + \mu} + \beta_{\varepsilon_1} \right)}, \quad (4.3)$$

$$\beta \varepsilon_3^* = \frac{\omega_1 \beta \varepsilon_3}{(\alpha + \theta_1 + \mu) \left(\frac{\lambda_1 \left(\frac{\omega_2 \beta \varepsilon_4}{\alpha + \theta_2 + \mu} + \beta \varepsilon_2 \right)}{\alpha + \mu + \omega_2} + \frac{\omega_1 \beta \varepsilon_3}{\alpha + \theta_1 + \mu} + \beta \varepsilon_1 \right)}, \quad (4.4)$$

$$\beta \varepsilon_4^* = \frac{\lambda_1 \omega_2 \beta \varepsilon_4}{(\alpha + \theta_2 + \mu) (\alpha + \mu + \omega_2) \left(\frac{\lambda_1 \left(\frac{\omega_2 \beta \varepsilon_4}{\alpha + \theta_2 + \mu} + \beta \varepsilon_2 \right)}{\alpha + \mu + \omega_2} + \frac{\omega_1 \beta \varepsilon_3}{\alpha + \theta_1 + \mu} + \beta \varepsilon_1 \right)}. \quad (4.5)$$

Inserting numerical values of the parameters shown in Table 4.1 we obtain the values of the sensitivities of the parameters as shown in Table 4.2.

The results of the sensitivity indices from Table 4.2 indicate λ_1 , λ_2 , α , and the effectiveness of infection from the force of infection β and ε_4 are more sensitive to the model while μ and effective rate of infection ε_1 are less sensitive to the model. The high value in sensitivity of λ_1 and λ_2 indicates the real effect of anxiety in the population of those living with HIV. However, since the objective is to assess the impact of anxiety on the HIV/AIDS care cascade, the following simulations give more insights into the impact anxiety has on the key stages of the HIV/AIDS care continuum.



Table 4.1: Table of parameter values

Parameter	Description	Value	Source
Λ	Recruitment rate.	0.2422	World Bank
β	HIV infection rate.	0.037	NSDCC
ε_1	Relative HIV infectiousness for positive undiagnosed person	1.4	Varied
ε_2	Relative HIV infectious of HIV+ person with anxiety undiagnosed	1.5	Varied
ε_3	Relative HIV infectiousness of infected diagnosed persons	1.6	Varied
ε_4	Relative HIV infectiousness of HIV+ and anxious persons	1.7	Varied
λ_1	Rate at which the infected undiagnosed acquire anxiety.	0.1117	Nyongesa et al. (2021)
λ_2	Rate of acquiring anxiety among individual who are receiving anxiety treatment alone.	0.08	Nyongesa et al. (2021)
ω_1	HIV testing rate of the infected undiagnosed group.	0.56	Waruiru et al. (2014)
ω_2	Rate at which HIV-infected undiagnosed group affected by anxiety get to be tested and diagnosed of HIV and anxiety.	0.25*	Assumed
θ_1	Rate at which HIV +ve individuals get to be put on (ART) treatment.	0.0094	UNAIDS
θ_2	Rate of acquiring ART treatment and anxiety therapy among HIV +ve anxiety-affected group.	0.005	Nyongesa et al. (2021)
ψ_1	Recovery rate from anxiety to be put on ART treatment alone.	0.0045*	Assumed
ψ_2	Recovery rate from anxiety among the group who were still anxious to move to the virally suppressed group who do not have anxiety.	0.009*	Assumed
δ_1	Adherence rate among the group put on ART treatment alone.	0.908	KENPHIA
δ_2	Adherence rate among anxious group who still have anxiety.	0.0041	Wykowski et al. (2019)
α	Disease induced death.	0.00148572	NSDCC
μ	Natural death within the population.	0.00783	World Bank
κ	Non-adherence rate and respective relapse of high VL.	0.091	KENPHIA

Table 4.2: Sensitivity analysis of parameters

Parameter	Sensitivity Index
β	1.00000
ε_1	0.04993
ε_2	0.41408
ε_3	0.02272
ε_4	0.60817
λ_1	0.82534
λ_2	0.75804
θ_1	-0.11538
θ_2	-0.08978
ω_1	0.01298
ω_2	-0.00641
α	-0.14319
μ	-0.12269

4.2 Numerical Simulations

The parameters utilized in the numerical simulation for the system of equations in the model (3.2) are detailed in Table 4.1. These parameter values were sourced from existing literature and government repositories, reflecting an estimated total population of 47,564,296, as reported in the 2019 Kenya Population and Housing Census (KNBS, 2019). Anxiety severity rates of minimal anxiety (0-4), mild anxiety (5-9), moderate (10-14) and severe anxiety (>15), used with regards to the Generalized Anxiety Disorder scale (GAD-7) to inform the variations of anxiety in the classes. Numerical simulations were conducted using MATLAB software through the help of Runge Kutta fourth order.

4.2.1 Impact of Anxiety on HIV/AIDS Diagnosis

Mental health has become a growing concern, as it significantly impacts key stages of care for HIV/AIDS in the country, with anxiety playing a major role in disease dynamics. The development of anxiety among individuals infected with HIV leads to a combination of physiological and psychological changes due to the fear of the infection and the possible emergence of symptoms. As a result of this fear, the majority of individuals tend to seek testing to confirm their status. The illustration in Figure 4.1 demonstrates the impact of

anxiety on different levels of severity—mild anxiety, minimal/no anxiety, and severe anxiety represented by the parameter λ_1 and λ_2 with different values of 0.11 and 0.08 (Nyongesa et al., 2021).

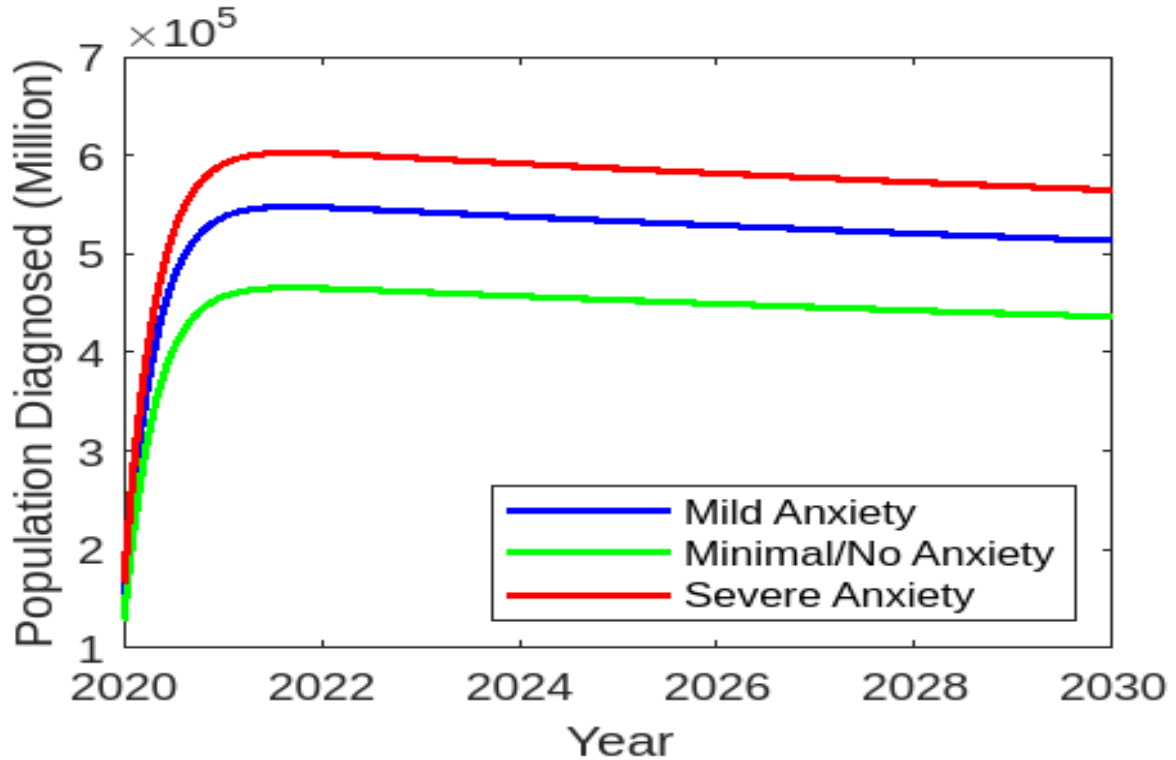


Figure 4.1: Comparative analysis of the impact of anxiety on HIV diagnosis. Different intensities of anxiety in the population have a relative impact on the diagnosis rates with more people getting to be diagnosed with severe instances of anxiety compared to minimal or no anxiety. Anxiety rates based on score; (Minimal anxiety (0-4), Mild anxiety (5-9), Severe anxiety (>15)).

The red line represents increase in number of diagnoses resulting from severe anxiety. Conversely, when there is minimal or no anxiety in the population, as shown by the green line, the number of diagnosed cases remains low. This illustration highlights the positive correlation between severe anxiety and increased diagnosis rates. Analysis is simulated with respect to the years ranging from 2020 through 2030 indicating the potential effect of anxiety among people living HIV across the years with a stabilized state incurred from 2024 up to 2030

4.2.2 Anxiety Impact on Population Receiving ART

Anxiety disorders among people living with HIV/AIDS (PLWHA) can have significant ramifications on the care continuum, with a major impact observed among individuals actively receiving antiretroviral therapy (ART). Anxiety has a profound effect on medication adherence, often leading individuals to default from care. In the HIV/AIDS care cascade, retaining PLWHA in treatment is essential, as it is one of the most effective strategies for reducing viral transmission. Severe anxiety can cause both psychological and physical changes that affect an individual's willingness to remain adherent to ART. Figure 4.2 illustrates the decline in the population receiving ART due to severe anxiety, represented by the red line. Minimal anxiety results in a lower dropout rate, while mild anxiety, represented by the blue line, closely follows the trend of severe anxiety in terms of treatment discontinuation from care. The initial rise in the ART population in the first few months is due to the immediate initiation of newly diagnosed individuals into care. However, in the following years, the population drops and stabilizes, reflecting the dynamics presented in the Figure 4.2.

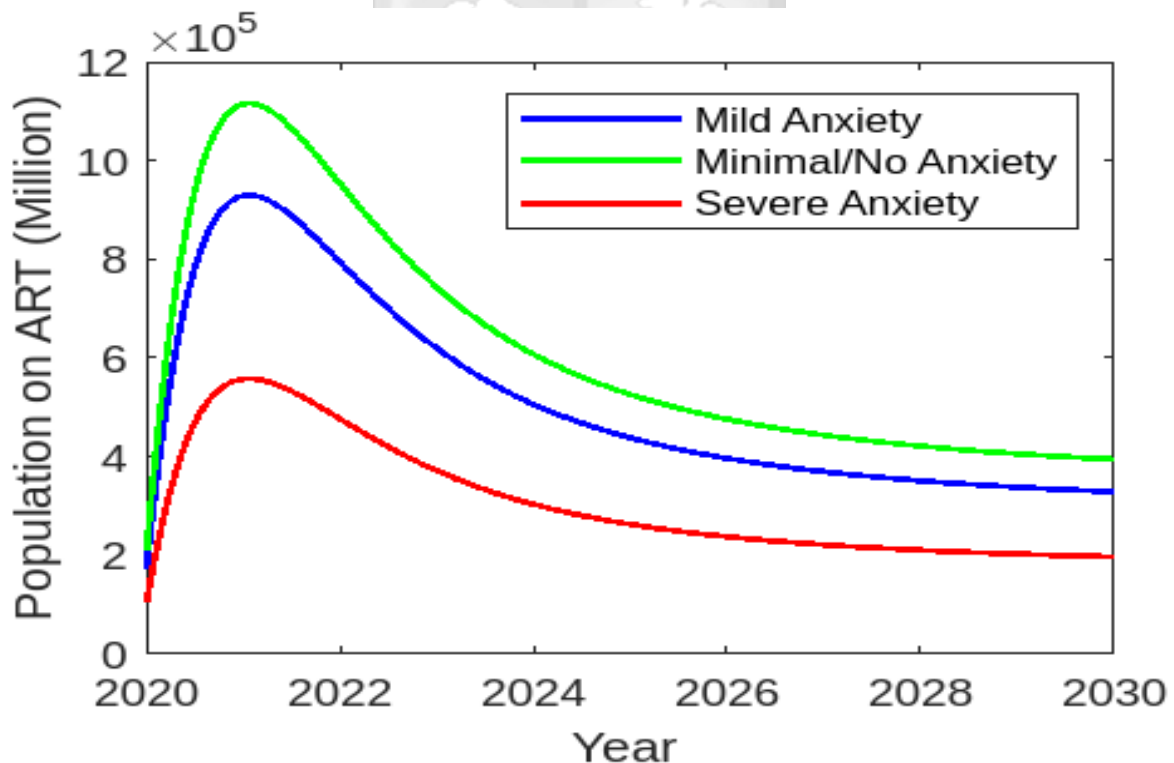


Figure 4.2: The dynamics of the impact of anxiety on the population undergoing ART therapy shows that there is a significantly lower number of individuals adhering to ART due to severe cases of anxiety (>15), compared to when anxiety is minimal or absent (0-4).

4.2.3 Impact of Anxiety Treatment on Viral Load Suppression

The UNAIDS 95:95:95 target for eradicating HIV infection can only be achieved when PLWHA achieves viral load suppression below detectable levels. Anxiety can significantly impact this target by reducing the proportion of the population who are virally suppressed compared to those not affected by anxiety. The illustration from the study, shown in Figure 4.3, demonstrates impact of incorporating effective anxiety treatment (cognitive behavioral therapy and medication) among individuals receiving ART and its effect on the population with suppressed viral load over time period shown. The initial time point is at the year 2020, and the intervals in months, approximately equivalent to 2 years, project the prospects toward the year 2030, which is the target year set by UNAIDS for HIV/AIDS eradication in the country. In Figure 4.3, minimal or no anxiety represents the effectiveness of incorporating anxiety treatment into care, leading to a high number of individuals with suppressed viral load, as indicated by the green line. Individuals moderately recovering from anxiety are represented by the blue line, while those who are not receiving or not responding to treatment are shown by the red line, which continues to reflect a low proportion of virally suppressed individuals. The severity of anxiety rates in the population of those living with HIV/AIDS is synonymous with failure to adhere to ART, and a majority of the population is affected by an increase in viral load, which impacts the CD4 cell count in the blood. The result is a failed viral load suppression (VLS), which jeopardizes efforts to reduce the spread of infection. The current treatment method for anxiety thus pharmacological and non-pharmacological indicates a stabilized population on ART over the period of 2024 through 2030 with a slightly increasing population close to 850,000 patient achieving their viral load suppression.

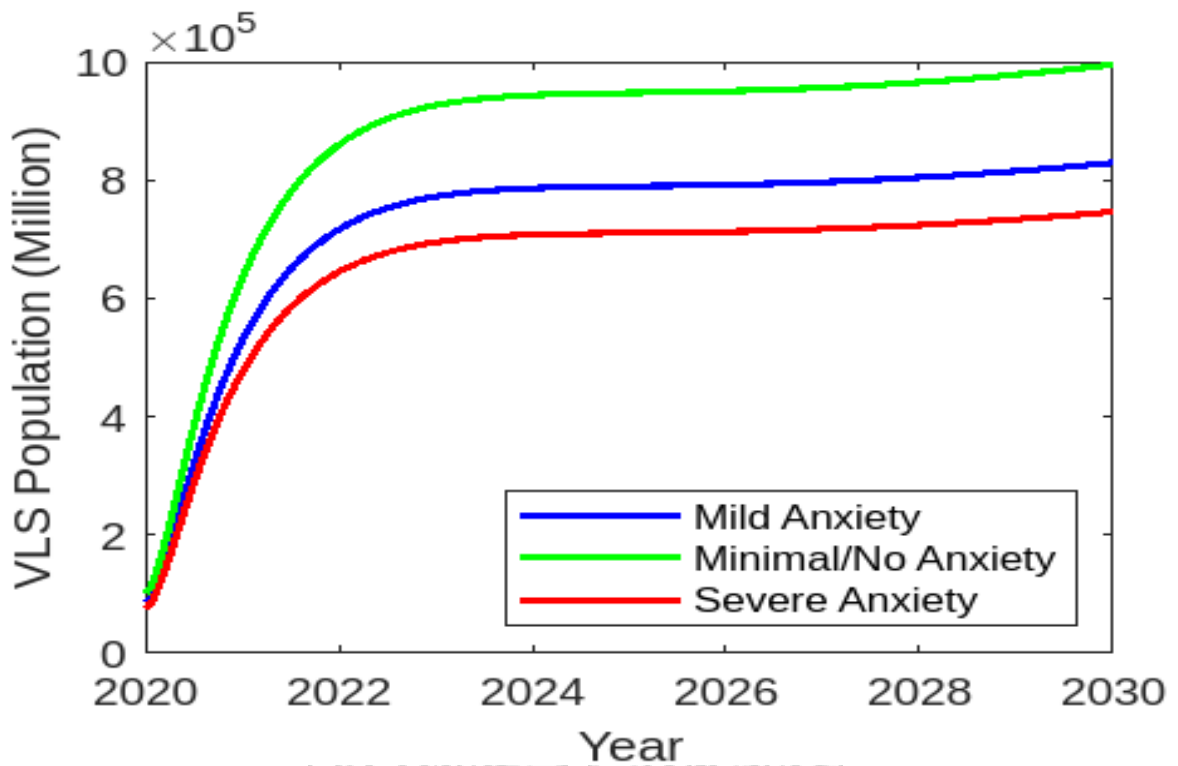


Figure 4.3: Comparison of the virally suppressed population receiving anxiety treatment in different states of anxiety. The figure shows a steadily higher number of virally suppressed individuals with minimal to no anxiety (0-4), indicating the positive effects of anxiety treatment.

Chapter 5

Conclusion and Recommendations

5.1 Conclusion

This study considered the use of a deterministic compartmental model to assess the impact of anxiety on the HIV/AIDS care continuum in Kenya. In addition to the development of the model, this model was analyzed for well-posedness. The Next Generation matrix was utilized to determine the effective reproduction number R_v . The model at disease free equilibrium turned out to be locally asymptotically stable with the contentious presence of the disease in the population as represented by $R_v > 1$. Global stability was determined using Lyapunov theorem of stability analysis and the results opine the disease free equilibrium remains to be globally asymptotically stable. The disease remains to exist in the population hence the endemic equilibrium was unity with the effective reproduction number.

The results from the numerical analysis resonates to previous assumption of the negative impacts of anxiety to the care and maintenance of HIV/AIDS in the country. However, anxiety presence on the contrary leads to an increased rates of diagnoses of the disease. Utilization of the model in understanding the major impediments to the success of eradicating HIV/AIDS in the country gives insights to the significance of initiating testing of anxiety among PLWHA since it is a major mental health concern which impedes the success of achieving the 95:95:95 UNAIDS target. Adherence and remaining to be faithful to ART highly depends on the physical and psychological status of the individuals under care for the disease hence reduction of the severity of anxiety among the population under care has a great positive impact in the population who remains to the adherent to ART care.

The results from this study shows that incorporation of anxiety treatment reduces the severity level to minimal or no anxiety which conveniently leads to better adherence to ART treatment. Higher rates of ART adherence remains to be the main aim towards increasing the population under treatment and care who have viral load suppressed. Retaining the recommended levels of viral load suppression can only be a success when the healthcare team understand the need of screening for the mental health disorders among people living with HIV/AIDS and

create and awareness of the better ways they can overcome the mental health problem of anxiety through seeing guidance to the care. The study explored the integration of screening for both anxiety and testing for HIV and the results indicate a success in the management of anxiety an initial stage before incurring a great impact in the care continuum which can result from anxiety disorder occurring as an impediment to ART care and attaining viral load suppression. One of the greatest challenges which might be experienced during the screening of anxiety is the subjectivity of the screening tools, the individuals screened for the mental health disorder are at a higher chance of giving false response which can greatly impact the care continuum. In order to solve the problem of false and subjective results, the study indicates a continuous screening for anxiety across the care continuum for anxiety to be certain of the mental health study of the population of interest.

5.2 Recommendations

Mental health continues to grow as a burden in the world and it affects majority of the population who are having underlying medical conditions such as HIV/AIDs. The study gives informative insights to the impact of anxiety on care continuum of HIV/AIDs which is intended to provide proven results for the Government of Kenya through the Ministry of Health and other bodies to implement the screening and and initiation of care for anxiety among PLWHA. The joint United Nations target for 2025 states that into the aforementioned year, there should be 95% of the population who are infected getting tested for the disease, 95% of those tested should be linked into care and the 95% of those linked to care are attaining viral load suppression. The success of this target can be made possible if the population of the PLWHA are screened for anxiety disorder and treatment therapy initiated successfully. The study results shows a proven need for increasing psychosocial training centers for the population under care for HIV/AIDS to incorporate the coping techniques and training to reduce impact of anxiety. An implementation of the suggested recommendations could see the country leading in the eradication of HIV/AIDS into the year 2030 as shown by the results from the study.

5.3 Future Research

The study is an eye-opener to potential future research in the field of modelling the mental health impact to care continuum of HIV/AIDS. Anxiety disorder is a single mental health disorder and there are other common mental health disorder such as depression and post-traumatic stress disorder (PTSD), obsessive compulsive disorder and bipolar disorder. It is possible for future research to look into the disorder in relation to the HIV/AIDS care continuum. HIV/AIDS care has proven to be costly over the period, advancing the research in understanding the frugality of managing the HIV comorbidities is an opportune area for future research. Anxiety disorder can be treated either through pharmacological or non-pharmacological methods, developing a research on the most effective treatment method among PLWHA is a great area for future research.



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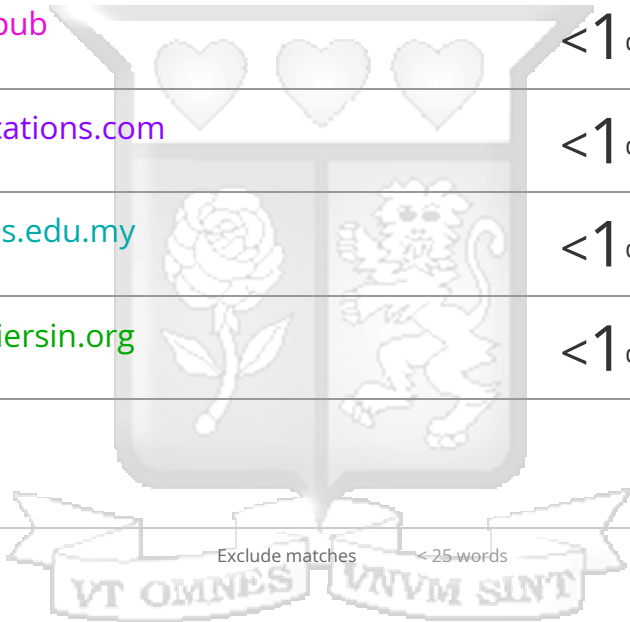
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Appendix B: Ethical approval certificate



5th December 2024

Mr Ogutu Kennedy,
kennedy.ogutu@strathmore.edu

Dear Mr Ogutu,

RE: Impact of Anxiety on HIV Care Continuum: A Mathematical Modelling Study

This is to inform you that SU-ISERC has reviewed and **approved** your above **SU-masters** proposal. Your application reference number is **SU-ISERC2440/24**. The approval period is from **5th December 2024 to 4th December 2025**.

This approval is subject to compliance with the following requirements:

- i. Only approved documents including (informed consents, study instruments, MTA) will be used.
- ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by SU-ISERC.
- iii. Death and life-threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to SU-ISERC within 72 hours of notification.
- iv. Any changes anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to SU-ISERC within 72 hours.
- v. Clearance for the export of biological specimens must be obtained from relevant institutions.
- vi. Submission of a request for renewal of approval at least 60 days prior to the expiry of the approval period. Attach a comprehensive progress report to support the renewal.
- vii. Submission of an executive summary report within 90 days of completion of the study to SU-ISERC.

Before commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology, and Innovation (NACOSTI) <https://research-portal.nacosti.go.ke/> and obtain other clearances needed.

Yours sincerely,

Mr Ambrose Rachier,
Chairperson; SU-ISERC