TRANSMISSION DYNAMICS OF HUMAN IMMUNODEFICIENCY VIRUS AND HEPATITIS C VIRUS CO-INFECTION MODEL

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DECLARATION

I, **OLUWAKEMI, ELIZABETH ABIODUN,** a Ph.D. student in the Department of Physical Sciences, (Mathematics Programme), Landmark University, Omu-Aran, hereby declare that this thesis entitled "**TRANSMISSION DYNAMICS OF HUMAN IMMUNODEFICIENCY VIRUS AND HEPATITIS C VIRUS COINFECTION MODEL**", submitted by me is based on my original work. Any material(s) obtained from other sources or work done by any other persons or institutions have been duly acknowledged.

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CERTIFICATION

This is to certify that this thesis has been read and approved as meeting the requirements of the Department of Physical Sciences, Landmark University, Omu-Aran, Nigeria, for the Award of Ph.D. Degree.

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ABSTRACT

Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) are co-infected in about 2.3 million people globally. Contrary to HCV mono-infection, HIV co-infection has a negative effect on the course of HCV, leading to increased rates of HCV persistence after acute infection, higher viral levels, and accelerated development of liver fibrosis and end-stage liver disease. The homeostasis of Cluster of Differentiation 4 (CD4+) T cell numbers is severely impacted by HCV co-infection, which also promotes HIV replication and the survival of viral reservoirs. Based on the application of mathematical models, there were significant developments in the understanding of the transmission of epidemic diseases in large populations. Thus, mathematics offers a concise and powerful way to expose exactly the factors that determine the epidemiology of the diseases.

This study developed a new mathematical model for HIV-HCV co-infection and examines the implication of HCV-associated with liver health problem co-infection on HIV disease progression in the setting of antiretroviral therapy (ART) and direct-acting antiviral (DAA). In addition, the consequences of HIV fallout on treatment, children born to infected mothers, those who are unaware of their HIV and HCV status due to stigmatization, the proportion of HCV acutely infected individuals who spontaneously recovered from the virus due to immunity are also investigated.

The positivity and boundedness of each model under investigation were established using well-known theorems and by setting the differential equations to zero, the equilibria were demonstrated. The next generation matrix method was used to create the fundamental reproduction numbers for each model. The models' local and global stabilities were verified using the linearization and Lyapunov function approaches, respectively. For the bifurcation

investigations, the centre manifold theorem was employed, and each model was subjected to a sensitivity analysis to identify any parameters that would have a favourable impact on the models. In order to demonstrate how the parameters affected each model, numerical simulations were carried out on the models. Optimal control assessments were also conducted to demonstrate the significance of control on the activities of the models.

When the threshold parameter is less than one, only the vulnerable individuals exist in the analysis, and all other compartments tend to zero. Furthermore, the increasing incidence of HIV treatment fallout resulted in decline in the HIV on treatment population, but increase in other populations. The findings confirmed that an increase in testing and treatment rates resulted in a drop in HIV unawareness, whereas HIV and AIDS individuals decreased over time. It was discovered that the acute population reduces at a time, t, range of $0 < t\ (months) < 5.8$ while the chronic HCV population declines at a range of $5.8 < t\ (months) < 30$. In dually infected individuals, treating HCV infection first was found to reduce the co-infection reproduction number (R_{ech}) which may reduce the effects of liver cancer.

Treatment and prevention with both ART and condoms are suggested for preventing the spread of HIV-HCV co-infection and helps to reduce the risk of HIV and HCV co-infection. Finally, it is advised that all pregnant women be tested for HIV and HCV, HIV infected people be screened for HCV, and HCV be treated first if tested positive to help with virus management.

DEDICATION

This thesis is dedicated to the great God, the Lord Almighty, the author and the finisher of my faith.

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LIST OF NOMENCLATURE FOR HIV-HCV MODEL

$S(t)$	Susceptible Individuals
$H_U(t)$	Unaware HIV individuals
$H_A(t)$	Aware HIV individuals
$H_T(t)$	HIV on Treatment Individuals
$A_A(t)$	AIDS individual
$I_C(t)$	Acute HCV Individual
$C_C(t)$	Chronic HCV Individuals
$H_{UI}(t)$	Unaware HIV individual co-infected with Acute HCV
$H_{AI}(t)$	Aware HIV individual co-infected with Acute HCV
$H_{TI}(t)$	HIV individual on treatment co-infected with Acute HCV
$H_{UC}(t)$	Unaware HIV individual co-infected with Chronic HCV
$H_{AC}(t)$	Aware HIV individual co-infected with Chronic HCV
$H_{TC}(t)$	HIV individual on treatment co-infected with Chronic HCV
$A_{AI}(t)$	HIV individual showing symptoms of AIDS co-infected with Acute HCV
$A_{AC}(t)$	HIV individual showing symptoms of AIDS co-infected with Chronic HCV

Λ	Recruitment rate
ω	Spontaneous clearance for Acute HCV
η	Progression rate from Acute to Chronic HCV / Non-spontaneous clearance rate
$r_i, i = 1,2, \ldots$	HCV treatment rate for HCV
λ_H	Force of infection associated with HIV infection
λ_C	Force of infection associated with HCV infection
γ	Modification parameter for Acute HCV
τ	Modification parameter for Chronic HCV
$\alpha_1, i = 1,2,3$	HIV testing rate
$\delta_{i,} i = 1,2,, \ldots$	Modification parameter
$\varepsilon_{1,}$	Factor to modify spontaneous clearance of HCV in presence of co-infection
$\varepsilon_{2,}$	Acceleration factor for disease progression of HCV in presence of co-infection
φ	Rate of newborns infected with HIV
$\rho_i, i = 1,2,3$	Progression rate from unaware HIV to AIDS
$\theta_{i,} i = 1,2,3, \ldots$	HIV/ AIDS treatment rate
$\upsilon_{i,} i = 1,2,3$	HIV defaulters from treatment rate (progression rate from aware HIV to AIDS)
μ	Natural Mortality
d_a	Mortality due to AIDS
d_c	Mortality due to HCV
$\frac{1}{\sigma_c}$	Average time an individual infected with HCV remains in a state of acute infection
c_C/c_h	HCV/ HIV contact rate
b_h/b_c	Transmission Coefficient for HIV and HCV
t	Time

LIST OF ACRONYMS

ART	Anti-retroviral Treatment
HAART	Highly Active Anti-retroviral Treatment
DAA	Direct Acting Anti-retroviral
HIV	Human Immunodeficiency Virus
HCV	Hepatitis C Virus
AIDS,	Acquired Immune Deficiency Syndrome
UNIADS	United Nations for AIDS
WHO	World Health Organization
CDC	Center for Disease Control
PrEP	Oral Pre-Exposure prophylaxis
PEP	Oral Post-Exposure prophylaxis
CD4	Cluster of Differentiation 4
MTCT	Mother to Child Transmission
PWID	People who inject drug
PLWH	People Living with HIV

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background to the Study

Disease transmission rates in large populations are among the many topics being investigated by epidemiologists. When most people think about epidemiology, they think of the description of illness cases in terms of the number of people affected per specified number of people, square kilometers, or days. This description might consist of basic bar charts and mapping epidemiology research, among others, to explain the occurrence of transmissible diseases in large populations. Disease rates expressed as a function of population size, geographic location, and/or time period are often connected with traditional epidemiological studies.

In recent years, there have been important advancements in the understanding of the spread of epidemic diseases in large populations based on the use of mathematical models. The insights gained from these models are particularly essential in the formulation of control programs and strategic interventions in developed and developing countries. The majority of human infectious diseases have reasonably well-understood mechanisms of infection, pathogenesis, and symptomatology. This knowledge, however, is not enough to forecast how the diseases will disseminate in a large population.

Mathematics offers adequate tools to explain complex relations in a way that makes it relatively easy to evaluate their consequences. Thus, mathematics provides a clear and powerful technique to disclose exactly the components that determine the epidemiology of the diseases. The

compartmental type of mathematical model is commonly used to depict the dynamics of disease; in these models, the population is segmented into subsets. These sections symbolize the various steps an illness takes as it spreads from infected person to infected person. Transfers of individuals between storage areas may be regarded as a continuous event in populations of very large sizes. Thus, systems of differential equations can be used to mathematically represent the variation of the number of individuals within each compartment "as time goes by."

Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS)

The human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) continue to pose one of the most critical global health and development issues since their discovery in the early 1980s (Ilahi and Nurhalimah, 2019). HIV is a blood-borne illness that can affect anyone at any time and has a highly varied course of disease in people (Mayo Foundation, 2020a). AIDS, the last stage and natural development of HIV, occurs when the CD4 cell count falls below 200 cells per cubic millimeter of blood or when the immune system is impaired. The global HIV epidemic has killed 68 percent people since its peak in 2004 as of 2021. Additionally, fewer people contracted HIV for the first time than at any time before 1990.

According to the latest data update from the World Health Organization and the Joint United Nations Programme on HIV/AIDS (UNAIDS, 2022), in 2021, children [0–14 years] accounted for 1.7 million [1.3–2.1 million] of the estimated 38.4 million [33.9–43.8 million] HIV-positive people worldwide. People with HIV are overwhelmingly concentrated in low and middle-income nations. In 2021, there were reportedly 1.5 million [1.1-2.0 million] new HIV infections (WHO, 2022a; UNAIDS, 2022). Majority of these kids are from sub-Saharan Africa and acquired the virus from their HIV-positive moms during pregnancy, childbirth, or breastfeeding. The highest annual rate of new HIV infections since the epidemic began was nearly five million in 2003 (Mukandavire *et*

al., 2010).

New infections continue to damage communities and disrupt critical socioeconomic infrastructure all across the planet. More people are becoming infected, existing cases are surviving longer, and the population as a whole is growing, all of which contribute to the pandemic's relentless spread. Although there has been an increase in the availability of HIV tests, approximately 21% of these same people do not know they have the virus (UNAIDS, 2021). With 40.1 million [33.6-48.6 million] deaths caused by HIV to date, it is still a significant global public health concern (WHO, 2022a). Based on the global HIV epidemic in 2021 by WHO, globally, 650 000 [510 000–850 000] people died in 2021 as a result of HIV-related causes. In 2021, there were between 110 000 and 230 000 new HIV infections among children worldwide (WHO, 2022a; UNAIDS, 2022).

The global response to AIDS has, unfortunately, neglected HIV-positive youngsters. Only 53% (950 000) of the 1.8 million children living with HIV (aged 0–14 years) worldwide in 2019 were diagnosed and receiving treatment, whereas 68% of adults were (UNAIDS, 2020). The remaining 850,000 children living with HIV have not been diagnosed and are therefore not receiving the potentially life-saving HIV medication that is available. Two-thirds of the missing kids are between the ages of 5 and 14, and they rarely, if ever, visit regular medical clinics. Families and communities affected by HIV/AIDS, TB, and other related diseases must be actively engaged, and family services must be made available, in order to locate and begin treating the missing children (WHO, 2020a). The failure to promptly diagnose HIV in infants and children and link them to effective HIV treatment regimens is a contributing factor to the anticipated 95, 000 child deaths from AIDS-related illnesses in 2019. Untreated, half of infants infected with HIV at or near birth will die before their second birthday (UNAIDS, 2020).

In 2016, for instance, there were roughly 1.8 million new infections, or about 5,000 new infections per day, with over two-thirds of them occurring in sub-Saharan Africa. One third of all new infections globally occur in people aged 15 to 24, suggesting that HIV typically affects people during their prime working years. As of right now, females account for almost half of the adult population with the virus. Unsurprisingly, HIV/AIDS is a major killer of women of childbearing age (WHO, 2017a).

Research and epidemiologic methodologies give reliable, real-time information to better comprehend the global HIV/AIDS pandemic and its accompanying co-morbidities, co-infections, and complications (CCC), advice prevention and treatment strategies, and indicate where research should be undertaken.

Hepatitis C Virus, HCV

Major causes of human morbidity and mortality globally are viral infections. And infection with the hepatitis C virus (HCV) is one of the key factors in this regard (Aston, 2018). The hepatitis C virus causes a potentially fatal liver infection known as hepatitis C Virus (HCV). It is a significant global health issue. It increases the chance of death from fibrosis and cirrhosis liver cancer and can induce both acute and chronic infections (WHO, 2019b). HCV, isolated for the first time in 1989, belongs to the family Flaviviridae, genus Hepacivirus, and is a highly diverse blood-borne virus (Ciplamed, 2016). The virus can stay dormant on environmental surfaces for up to three weeks at room temperature. A website citing the U.S. Centers for Disease Control and Prevention, however, states that HCV can live on environmental surfaces for at least 16 hours but no more than four days at room temperature. This infection has been spreading over the world since its discovery in 1989 (Ciplamed, 2016). Around 1.5 million new cases of the hepatitis C virus are reported each year, with an estimated 58 million people worldwide carrying the infection.

According to estimates, 3.2 million children and adolescents worldwide have chronic hepatitis C infection. According to the WHO, 290 000 people died from hepatitis C in 2019, primarily from cirrhosis and hepatocellular carcinoma (primary liver cancer). Every WHO area has HCV. With 12 million chronically ill persons in each region, the Eastern Mediterranean and European regions have the largest illness burden. An estimated 10 million persons each in the Western Pacific and South-East Asia regions have a chronic infection. In the African region, 9 million persons have a chronic infection, compared to 5 million in the Americas region (WHO, 2022b).

Some individuals who contract HCV for a brief period (up to six months) and subsequently recover on their own have acute Hepatitis C. Hepatitis C causes chronic hepatitis in the majority of patients (American liver foundation (ALF), 2020). By the end of 2019, the World Health Organization (WHO) had released a comprehensive set of hepatitis prevention, testing, treatment, care, costing, and strategic information guidelines and tools to assist country-level hepatitis responses (WHO, 2019b).

HIV and Hepatitis C Virus Co-infection

Both Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) are considered blood-borne viruses because they are spread through contact with the blood of an infected individual. Globally, 2–15% of patients with HIV also have HCV. An estimated 1.3 million of the 2.75 million people infected with HIV/HCV worldwide inject drugs (PWID) (WHO, 2019c1). In 2017, 2.3 million people living with HIV were simultaneously infected with HCV, according to the World Health Organization. Infectious diseases like HIV and HCV have become critical problems in public health around the world. Africa and South and East Asia bear the heaviest brunt of these co-infections (WHO, 2019c2). Co-infection with HIV and another disease usually poses greater dangers and has more dire outcomes for individuals. When HIV is present alongside HCV, the

viral infection advances much more quickly in the latter. If the CD4 count drops below 200 cells/mm3, there is an increased risk of serious liver damage (GAT, 2009). Hepatocellular carcinoma, liver cirrhosis, and liver-related mortality are also more likely to occur (Thein *et al.*, 2008b).

Concerning co-infection, there have been reports of effective HCV drug combinations in treating people who are both HIV positive and HCV positive. Furthermore, the majority of patients with HCV can be successfully treated for HIV (Franciscus, 2015). New antiviral medications have the potential to treat HCV in persons who are HIV-positive and infected with HIV, but additional research is needed to prove their effectiveness.

1.2 Statement of the Problem

HIV and HCV continue to be major problems in Africa and Southeast Asia, as their prevalence and associated mortality continue to rise (UNIADS, 2022). These troubling statistics may jeopardize the Global Health Sector Strategies (GHSS) for HIV 2020-2030 and viral hepatitis 2016-2021, which commit to a 65% and 35.5% decrease in mortality and a 90% and 22.3% decrease in incidence by 2030 (WHO, 2018b; 2022a).

Various researchers have undertaken numerous studies on HIV-HCV co-infection, but there are a few neglected areas of concern that are examined in this study. Some of the areas that have not been given enough attention among others are: death due to HCV on the assumption that it is relatively low (Moualeu *et al.,* 2011); the assumption that AIDS patients dually or singly infected cannot transmit infection due to their health status (Mushayabasa *et al.,* 2012); and non-consideration of HIV treatment due to the relatively low use of antiretroviral drugs (Yovanna *et al.,* 2013).

This study addresses the research gaps noted in the aforementioned articles. Investigations will be conducted on people who are infected but unaware of their status, as well as those who become aware after testing and later seek treatment for HIV and AIDS. Taking into consideration defaulters lost to follow-up who are at risk of developing AIDS, children born to an infected mother are at risk of developing the disease (those who died at birth and those who are recruited into the HIV-infected class). Also taken into account are people who get HCV and get better on their own during the acute phase and people who get treatment during the chronic phase.

1.3 Justification of the Study

Mathematical models have been extensively applied to the study of disease transmission dynamics and extrapolation from epidemiological data for risk prediction. According to the data, a variety of diseases, including HIV/AIDS and HCV, constitute a significant threat and have become a burden on medical professionals and social/health workers. In 2021, about 4,000 people were infected with HIV, including about 1,100 adolescents and young adults (15 to 24 years of age) on a daily basis. Also, if current trends continue, 1,2 million new HIV infections would occur in 2025, which is three times the target of 370 000 new infections for 2025 (UNAIDS, 2022).

To reduce the spread of AIDS pandemic and prevent millions of new HIV infections in this decade, it is necessary to conduct immediate and exhaustive research into the inequities that cause AIDS. Consequently, comprehensive research in this sector is crucial and necessary.

1.4 Aim and Objectives

This research work aim is to investigate the HIV-HCV co-infection model with impact of testing, treatment and the effect of inefficient follow-up.

The specific objectives are to:

i. develop a new mathematical model for the transmission of HIV, HCV and HIV-HCV co-infection model.
ii. examine the existence of the disease-free and endemic equilibria for HCV, HIV and HIV-HCV model.
iii. investigate the local and global stability analysis of the disease-free and endemic equilibria.
iv. construct the basic reproduction number for each of the models using next generation matrix.
v. Study the sensitivity analysis for the model parameters to identify the most influencing parameter.
vi. perform steady bifurcation analysis on the models (either forward or backward).
vii. carry out numerical simulations when there are no optimal controls imposed and after imposing optimal control on the mono-infected model.

1.5 Research Questions

The study focuses to answer the following questions:

i. How do we determine the nature of the outbreak of the disease?
ii. How can the spread of the disease be predicted?
iii. What are the mechanisms behind the spread of the disease?
iv. How can the blow up be prevented through the stability analysis?
v. How effectively can parameter sensitivity determine the nature of spread of the disease?
vi. Which control parameter is most-effective on the models?
vii. How does HCV infection influence HIV patients, and vice versa?

1.6 Scope of the Study

The research seeks to examine the transmission dynamics of HIV-HCV co-infection model with its impact on treatment, the effect of inefficient follow-up and the optimal control strategies to minimize cost and maximize treatment with the removed rate of individuals infected. The study is restricted to the deterministic model. For the numerical simulations, estimated data that has already been published in articles and assumed values are used.

1.7 Significance of the Study

Since this research is based on Goal number 3, "good health and well-being" of the 17 SDGs declared by the UN, the results of this study are expected to benefit the Ministry of Health, the public health sector, the community, NGOs, and other epidemiological end users.

This should aid in policy formulation, planning, budgeting, resource allocation, and disease control by taking treatment and prevention of co-infection into account. It should also improve HIV-HCV outbreak control strategies in communities. The study is expected to add to the body of knowledge on mathematical applications in epidemiology and serve as the basis for further HIV-HCV co-infection research. By critically considering testing and treatment with passive adherence, can help WHO reach its 90-90-90 HIV and HCV elimination and coverage target by 2030.

1.8 Definition of Basic Terms

Model

It can be defined as a condensed illustration of a complicated real-world structure or occurrence, which explain or anticipate the observed events. In the process, learn about the basic mechanisms (the key characteristics) that support the system.

Compartmental Model

This is a model which assigns members of a host population to compartments based on their infection status or other attributes.

Dynamic of a model

The term "dynamic" refers to models in which populations change due to birth, death, and migration, as well as how incidence (the force of infection) changes over time as a result of positive or negative feedback brought on by changes in case counts (i.e., the prevalence of infection), immunity, or differential mortality of high-risk people.

Force of Infection / Transmission rate

This is the probability per unit of time at which susceptible members of the host population are infected.

Transmission probability ($\boldsymbol{\beta}$)

Probability of transmission from an infected host to a vulnerable host during prolonged physical contact.

Contact Rate:

This is the rate at which individuals in a host population interact such that infection could potentially be transmitted.

Equilibrium Points

If the derivative of a function at a given point is zero, the function's value at that moment is not changing, such positions are referred to as equilibrium points in differential equations (or fixed points or constant steady states) (Elmer, 2019).

Disease -free Equilibrium

A time-invariant state with no infection presents in the host population.

Endemic Equilibrium

A time-invariant state with infection presents in the host population.

Epidemic:

This is an event in which an infection sweeps through a population.

Stability of Equilibrium Points

In terms of the solution of a differential equation, a function $f(x)$ is said to be stable if any alternative solution of the problem begins sufficiently close to it at $x = 0$ and remains close to it as x increases. As x rises, the solution is considered asymptotically stable if the difference between the solutions approaches zero. A solution is termed unstable if it lacks one of these characteristics.

Basic Reproduction Number; R_0

This is the anticipated number of secondary cases that a typical infective individual, (Van and Watmough, 2002), will cause in a community that is entirely susceptible. "If $R_0 < 1$, then, on average, over its infectious period, an infected individual generates less than one new infected individual, and the infection cannot grow." If R_0 is greater than one, the disease can spread across the community since each infected person typically produces more than one new infection. Each

current infection results in one new infection if If R_0 is 1. There won't be an outbreak or an epidemic, but the sickness will remain active and steady.

Optimal Control

This is defined as a set of ordinary differential equations describing the path of the control variables that minimizes or maximizes the cost functional (Moore and Okyere, 2020).

Bifurcation

This is simply the co-existence of disease free equilibrium and the endemic equilibrium points.

Simulation

Simulations in a deterministic framework typically refer to models that have been run with various parameter settings (because each simulation provides the same output for a unique set of parameters).output for a unique set of parameters).

Sensitivity analysis

It aids in judging how well the results hold up under varied situations or how well the model's results hold up outside of the simulation environment (i.e., different populations). It can be performed either in a one-way fashion (by changing just one parameter while keeping the rest the same) or through multivariate analysis.

CHAPTER TWO

2.0 REVIEW OF LITERATURE

Numerous studies on Hepatitis C Virus (HCV), HIV/AIDS, and HIV co-infection with HCV have been conducted, and the findings will be summarized in this study. This section provides a review of the methods and mathematical techniques used to control the transmission dynamics of the virus.

2.1 Conceptual Issues

2.1.1 Human Immunodeficiency Virus; HIV Epidemiology

HIV is a member of the genus Lentivirus, family Retroviridae, and subfamily Orthoretrovirinae (ICTV, 2021). This virus's genome, which is made up of two single-stranded ribonucleic acid (RNA) molecules, is contained within a cone-shaped capsid see figure 2.1 (Visual Science, 2010). Before the incorporation of the virus genome into the chromosome of the host cell, retroviruses can convert their RNA genome into a double-stranded deoxyribonucleic acid (DNA) see figure 2.2 (National Institutes of Health (NIH), 2021).

Reverse transcriptase is an RNA-dependent DNA polymerase that mediates this process (Turner and Summers, 1999). HIV has three structural genes: env (envelope), which is in charge of producing the viral surface glycoproteins, and pol (polymerase), which encodes the protease, reverse transcriptase, and integrase proteins. GAG is responsible for the manufacture of the viral capsid. Additionally, HIV includes four accessory genes (vpr, vpu, nef, and vif) in addition to two regulatory genes (tat and rev) (see Figure 2.3)

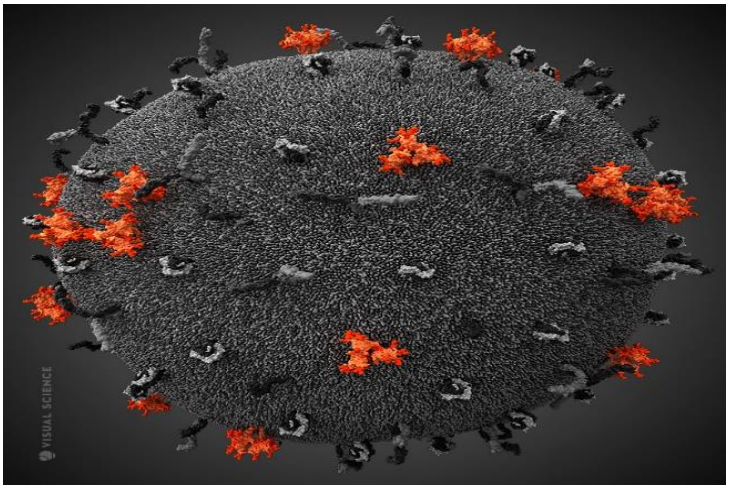

Figure 2.1: Scientific illustrations of human immunodeficiency virus (HIV)

(Source: Visual Science, 2010 - https://visual-science.com/projects/hiv/illustrations/)

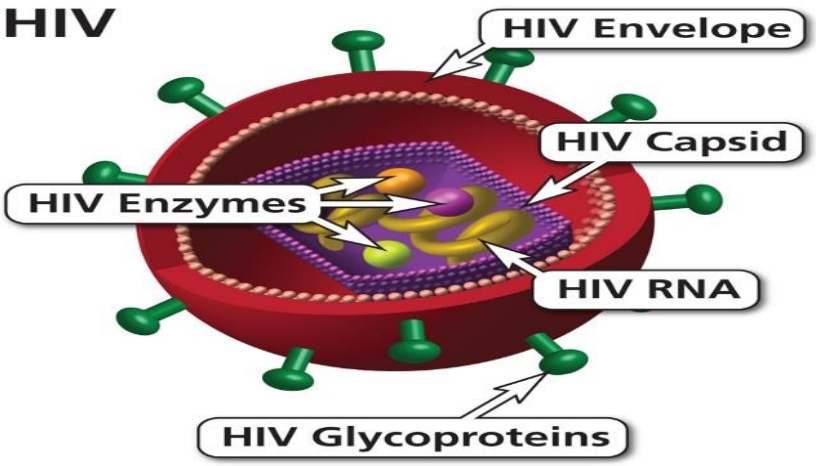

Figure 2.2: Viral Envelope for HIV.

(Source: National Institute of Health (NIH), 2021:

https://clinicalinfo.hiv.gov/en/glossary/envelope)

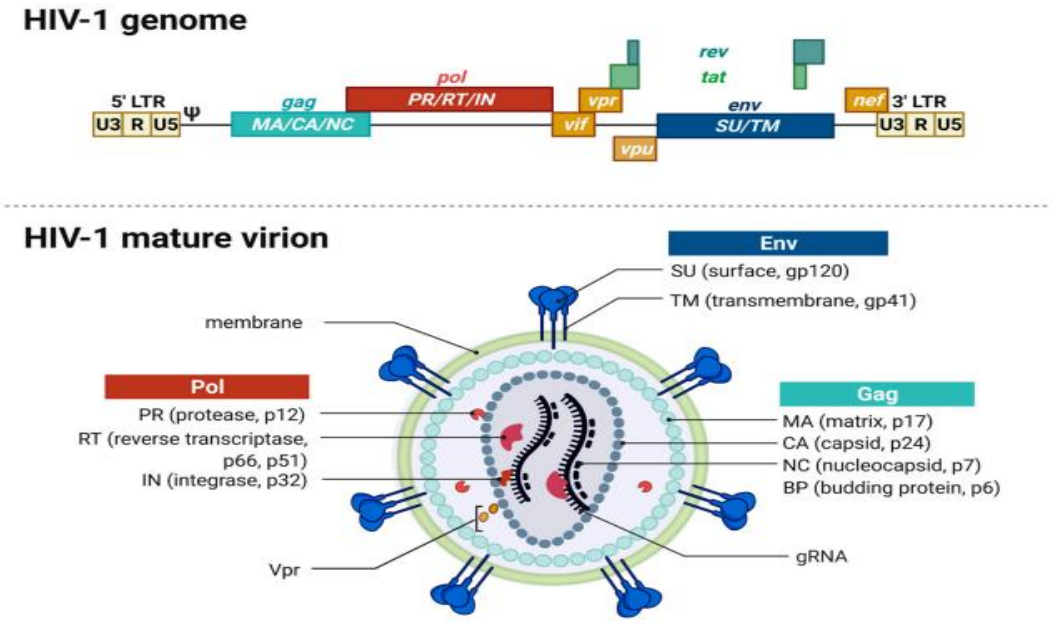

Figure 2.3: Structure of an HIV-1 genome and virion particle. (Source: Van et al., (2022).

Figure 2.3 illustrates how HIV has a lipoprotein envelope made from the target cell's membrane that exposes its surface glycoproteins (gp120), which are attached to the virus through interactions with trans-membrane glycoproteins (gp41) (Turner and Summers, 1999; Zhu, *et al*., 2006; Seitz, 2016; Burnie and Guzzo, 2019). Actin, ubiquitin, and other proteins such as the Principal Histocompatibility Complex antigens are also produced from the host cell membrane during the virus entrance process (Arthur *et al.*, 1992).

The structural matrix of HIV consists of p6 and both copies of the viral DNA, as well as matrix proteins (p17), viral capsids (p24), and nucleocapsids (p7) (Freed, 2002; Stremlau *et al.*, 2006). Inside the capsid are PR, RT, and IN. Additionally, the HIV genome is responsible for encoding the regulatory proteins Rev (transcriptional regulator of the viral gene), Tat (transcriptional transcriptivator), and accessory proteins Vpr, Vpu, Nef, and Vif. These proteins play a crucial role

in viral transcription, and as a result, host pathogenicity (Freed, 2002; Malim and Bienaiasz, 2012; Mcnatt *et al.,* 2013; Lee *et al.,* 2018; Ramdas *et al.,* 2020).

2.1.1.1 Stages of HIV Infection – (assuming no treatment)

As with all diseases, HIV also has four stages. Its progression, duration, and impact on the individual depend on a number of variables, such as the individual's overall health, lifestyle, and food, among others (Sule and Abdullah, 2019, Avert, 2020b).

Stage 1: Infection

After infection, HIV replicates swiftly in the body. Within days to weeks of infection, some people experience transient flu-like symptoms as headaches, fever, sore throat, and rashes. This is known as "sero-conversion," and it occurs when the immune system produces antibodies in response to the virus.

Stage 2: Asymptomatic

As the name implies, there are no visible signs or symptoms during this stage of HIV infection. Despite a person's appearance and apparent health, HIV nonetheless compromises their immune system. Without an HIV test, many people would not be aware that they are infected during this stage, which can extend for a number of years (on average, 8 to 10 years).

Stage 3: Symptomatic

HIV gradually weakens and damages the immune system, which causes symptoms to appear. They may start as mild, but they do get worse. Fatigue, weight loss, oral ulcers, thrush, and severe diarrhea are symptoms among others. Opportunistic infections are so-called because they profit from a person's compromised immune system. PCP, toxoplasmosis, TB, and Kaposi sarcoma are a few instances of opportunistic diseases.

Stage 4: AIDS/Progression of HIV to AIDS

No single test exists for AIDS. To diagnose AIDS, physicians will consider a number of symptoms, such as the CD4 count, viral load, and the presence of opportunistic infections.

HIV Transmission

Although heterosexual transmission accounts for the vast majority of new HIV infections worldwide, drug injection is nevertheless a substantial risk factor in some regions (WHO, 2017a). Unprotected anal or vaginal sex, sharing needles, blood transfusions, hemodialysis, during pregnancy or delivery, and via breast-feeding (i.e., mother-to-child transmission; MTCT) are all ways in which HIV can be spread to a child (vertical transmission) (Center of Disease Control and Prevention (CDC, 2019a). Both forms (HIV-1 and HIV-2) are also spread through direct contact with HIV-infected body fluids such as blood, sperm, and vaginal secretions (National Institute of health (NIH), 2021). People who have syphilis, herpes, chlamydia, gonorrhea, or bacterial vaginosis and who inject drugs and share needles, syringes, and other injecting equipment and drug solutions are at risk. Also, those who receive unsafe injections, blood transfusions, tissue transplantations, medical procedures involving unsterile cutting or piercing, and/or who sustain accidental needle sticks are at an increased risk of contracting HIV (WHO, 2018a).

It is important to remember that HIV cannot be spread through casual contact like hugging, kissing, dancing, or shaking hands (WHO, 2020a).

HIV Signs and Symptoms

HIV symptoms can range from mild to severe, depending on the progression of the disease. Despite the fact that the majority of HIV-positive patients are at their most contagious in the first few months of their disease, many are not diagnosed until a more advanced stage (WHO, 2019a). In

the weeks following infection, some people may show no symptoms at all, while others may develop flu-like symptoms such as fever, headache, rash, or sore throat (Mayo Foundation 2020a). Swollen lymph nodes, weight loss, fever, diarrhea, and cough are just some of the symptoms that can appear when the immune system gradually declines due to the illness (CDC, 2018). Illnesses as serious as tuberculosis, hepatitis, cryptococcal meningitis, severe bacterial infections, and malignancies, including lymphomas and Kaposi's sarcoma, may develop if they are not treated (UNAIDS, 2019).

Prevention and Treatment

The following may be considered as potential measures to help curb the spread of HIV. HIV prevention strategies include Treatment as Prevention (TasP), Post-Exposure Prophylaxis (PEP), Pre-Exposure Prophylaxis (PrEP), Clean Needle Policy, HIV Counseling and Testing (HCT), and male and female Condom use. To lessen the likelihood of HIV transmission, TasP incorporates antiretroviral therapy into HIV prevention initiatives.

Treatment decreases the HIV viral load in the body to undetectable levels. These people are protected from HIV transmission since their viral loads have been reduced. Additionally, PrEP entails the daily use of HIV medications by those at extremely high risk of contracting the virus. Prevention of HIV transmission by the body is the primary function of PrEP. On the other hand, PEP is only useful if it is administered in accordance with the established protocol (CDC, 2021a). Treatment with antiretroviral drugs (ART) begins shortly after HIV infection. According to a single study, there is scant evidence that PEP is effective in preventing HIV infection if started more than 72 hours after exposure. When used appropriately, PEP can reduce the risk of HIV transmission, but not entirely. This therapy is meant to limit the ability of HIV to persist and spread

within the body, thus guarding against reinfection and lowering the risk of HIV transmission (CDC, 2021a). PEPs are recommended by the WHO for both occupational and non-occupational exposures in both adults and children (WHO, 2021a).

HIV preventive strategies that include HCT are crucial. One's ability to get counseling and medical care, as well as one's ability to prevent the transmission of HIV, depends on knowing one's HIV status (CDC, 2021a). However, HCT is constrained in the present day since 40% of HIV-positive people worldwide do not know their status (WHO, 2021a).

In addition, men should seriously consider circumcision and prenatal care for pregnant women. As of January 26, 2021, the World Health Organization (WHO) suggested that the dapivirine vaginal ring (DPV-VR) be made available as an additional prevention option for women at high risk of HIV infection as part of combination prevention strategies (WHO, 2020a). Antiretroviral therapy (ART) is essential for HIV/AIDS treatment because it reduces HIV viral load to undetectable levels (50 copies mL1), which is especially helpful when treatment is started early in the course of infection. Reverse transcriptase inhibitors, protease inhibitors, fusion/entry inhibitors, integrase inhibitors, and multidrug combinations are the five main medication types used to treat HIV/AIDS. Finally, MI combines medications from several classes to circumvent the development of drug-resistant viral strains. This is what's referred to as "highly active antiretroviral therapy" (HAART) (Wahl and Nowak, 2000).

HIV Diagnoses

Blood or saliva testing can be used to diagnose HIV. Antigen/antibody testing, antibody tests, nucleic acid tests (NATs) (WHO, 2020a), and quick diagnostic tests are among the available

options (RDTs). Typically, these tests offer test findings on the same day, which is critical for same-day diagnosis and early treatment and care,

2.1.2 Hepatitis C Virus Virology, Pathogenesis, and Clinical Course

HCV is a positive-sense, single-stranded RNA virus (Kato, 2000; Lindenbach and Rice, 2005; Alter, 2007). There are 7 major genotypes and up to 100 subgroups denoted by lowercase letters (Bukh, 2016). HCV replication is error-prone, resulting in quasispecies (Gomez *et al*., 1999; Duffy et al., 2008). These virologic features and other host genetic variables can alter illness development, viral clearance, and therapy response (AASLD-IDSA, 2016). Acute HCV infection is often asymptomatic, although 25–30% may have fever, jaundice, and stomach pain (Kamal, 2008). 15%–25% of newly infected people with HCV have spontaneous resolution (Thomas and Seeff, 2005). As of the early stages of infection, "approximately 15–30% of asymptomatic patients and more than 50% of symptomatic patients with acute hepatitis C spontaneously eliminate the virus" (Reluga et al., 2009). Recent estimates say 15–45% of HCV-infected people eradicate the virus within 6 months without treatment (WHO, 2018).

The likelihood of resolution varies according to age, virology, and host genetics (Mack *et al*., 2012). Those who don't clear their infection acquire chronic HCV infection, defined as the existence of detectable HCV RNA at least six months after the acute infection (Thomas and Seeff, 2005). Over time, persons with chronic HCV infection may get liver fibrosis of various severity; approximately 15–20 percent of those with chronic infection may experience cirrhosis, the most severe form of fibrosis. Cirrhosis normally develops over a few decades, the rates of liver fibrosis advancement are controlled by host genetic variables, age of infection, co-morbid illnesses like diabetes, and some environmental factors like concurrent alcohol usage (Thein *et al*., 2008a).

Decompensation rates for those with cirrhosis range from 2–4 percent year, while hepatocellular carcinoma rates range from 1–7 percent annually (Thomas and Seeff, 2005). HCV can also cause a variety of extrahepatic illness symptoms, such as lichen planus, porphyria cutanea tarda, non-B Hodgkin's cell lymphoma, diabetes mellitus, cryoglobulinemia, and non-B Hodgkin's cell lymphoma (Lee *et al*., n.d.; 2012). People with HCV have experienced symptoms including weariness that have a negative impact on their quality of life (Kallman *et al.*, 2007).

Muhibi *et al*., (2018) conducted some investigations to ascertain the seroprevalence of hepatitis C virus infection among youths enrolled in school. The Enzyme Immunoassay Technique was used to detect the existence of antibodies against the hepatitis C virus in blood samples taken from 70 undergraduate students. The majority of participants (91.4 percent) are between the ages of 21 and 25. None of the participants tested positive for anti-HCV antibodies, according to the study. The outcome may have been positively influenced by education and awareness levels. To get rid of HCV and its effects on our society, it is very important to do regular HCV screenings and run public education campaigns all the time.

Shenge *et al*., (2019) identified the genotypes of HCV isolates circulating among HIV/HCV co-infected patients. The HIV laboratory provided 125 HIV/HCV IgM positive samples, and the University of Ibadan was the site of their investigation. The results and the discovered alterations in the NS5B gene suggested that patients who are HIV/HCV co-infected require screening and surveillance. In order to ascertain the prevalence of and risk factors for HCV and HIV infections among healthy individuals.

Oshun and Odeghe, (2019) conducted a study. Apparently healthy people who showed up for health screening at a private laboratory facility in Lagos from May 2014 to June 2016 were

included in this retrospective investigation to investigate the prevalence of hepatitis C virus antibodies and HIV.

HCV Transmission

When the blood of a person infected with Hepatitis C enters the circulation of someone who is not affected, this is called transmission or spread. Transmission can occur through the sharing of needles or other equipment used to inject drugs, through sex between a man and a woman, through unprotected anal sex between two men, when men have several sex partners, when they engage in rough sex, when they have sexually transmitted diseases, when they are infected Infections can also spread during dental, medical, or surgical procedures, through tattooing, or by the use of razors or other tools contaminated with blood (WHO, 2019b).

Hepatitis C has a 2-month to 6-month incubation period (CDC, 2021b). Hepatitis C cannot be spread by normal social interactions including kissing, hugging, holding hands, casual contact, sneezing, coughing, sharing utensils, food, or drink, or even breastfeeding (unless nipples are cracked and bleeding) (WHO, 2019b).

HCV Signs and Symptoms

Many people are unaware they have HCV infection until the disease has caused significant liver damage. This could happen years or even decades later, during otherwise regular medical examinations. Symptoms of HCV infection include, but are not limited to, excessive bleeding, bruising, weakness, lack of appetite, yellowing of the skin and eyes (jaundice), dark urine, itchy skin, fluid accumulation in the abdomen (ascites), swelling in the legs, weight loss, confusion, drowsiness, and slurred speech (hepatic encephalopathy), and spider-like blood vessels on the skin (angiomas) (Mayo Foundation, 2020b). Depression, moderate cognitive impairment, and a loss of

appetite are all possible side effects of this infection. Its effects can be short-lived (a few weeks) or long-lasting (a lifetime). About 80% of infected individuals will not develop symptoms after the initial infection (WHO, 2019b).

HCV Prevention and Treatment

There is currently no vaccination available for the prevention of Hepatitis C, in contrast to Hepatitis A and Hepatitis B. However, there are currently effective treatments for Hepatitis C, and the disease may be cured even without a vaccine (or cleared from the body). Until recently, hepatitis C therapy consisted on weekly injections and oral drugs, both of which many HCV-infected patients were unable to take due to other health issues or undesirable side effects. In other words, that's evolving. With daily dosing of oral drugs for two to six months, chronic HCV can now be cured in most patients (Mayo Foundation, 2020b).

When a blood test is performed 3 months following treatment for Hepatitis C and shows no trace of the virus, doctors declare the patient to be "cured." This is known as a "sustained virologic response" (SVR) (Mayo Foundation, 2020b; WHO, 2020b; American Liver Foundation (ALF), 2020; Hepmag, 2020).

HCV Diagnostic Procedure

HCV infection is identified in two stages:

1. People who have been infected with the virus are found by doing a serological test for anti-HCV antibodies.

2. If the anti-HCV antibody test is positive, a nucleic acid test for HCV ribonucleic acid (RNA) is required to confirm the existence of a chronic infection and the requirement for therapy. This test is crucial since roughly 30% of HCV-infected individuals spontaneously clear the infection

through a potent immune response, eradicating it without the need for therapy. They will test positive for anti-HCV antibodies despite no longer being infected. You can either perform this nucleic acid for HCV RNA in a lab or in a clinic with a straightforward point-of-care device (WHO, 2020b).

2.1.3 HIV-HCV Co-infection

There are several hypothesized routes via which active HCV infection may affect HIV infection. In HIV-untreated individuals, HCV co-infection may boost immunological activation, resulting in CD4 T-cell death and a faster development to severe immunodeficiency (Moyer, 2013). However, there is mixed evidence about how HCV infection affects CD4 cell recovery after HAART; some papers suggest that co-infected individual have a worse CD4 response than mono-infected individuals (Denniston *et al*., 2010), but others do not (McHutchison *et al*., n.d. 1998; Poynard *et al*., n.d. 1998; Moyer, 2013; Conteduca *et al.*, 2014).

Tremeau-Bravard *et al.,* (2012) conducted a retrospective analysis of HBV and HCV sero-prevalence in the Nigerian population undergoing HIV/AIDS treatment at our Abuja clinic. Between September 2010 and May 2011, medical data was collected from 443 HIV-positive patients. Standard enzyme immunoassays were used to determine the serological prevalence of hepatitis B (HBsAg) and C (anti-HCV antibody) among HIV-positive individuals (0.7 percent), 10.8% of people worldwide have hepatitis-HIV.

Hamza *et al.,* (2013) conducted a cross-sectional study among (440) consecutive HIV-positive adult patients who were seen and gave their consent to the study and were screened for markers of HBV and HCV using the Enzyme-linked Immunosorbent Assay (ELISA) technique. The most impacted age group was 40 years old and under.

In a community of pregnant women with HIV infection, the prevalence of the hepatitis C virus (HCV) was calculated by (Adesina *et al*., 2016). Women who tested positive or negative for the virus were compared, and the risk factors for HCV infection were outlined. 1433 pregnant women's data were presented. For the analysis of data from 1433 pregnant women, the significance level for the Chi-square test and the student's t-test was set at $P<0.05$. According to (Majekodunmi *et al.,* 2016), CD4+ T cell recovery in children with HIV/HCV co-infection and HIV mono-infection was compared. All 401 children's CD4+ T cell reconstitution to age-standardized CD4 counts was modeled using an asymptotic nonlinear mixed-effects approach, and factors influencing the rate and depth of recovery were examined.

Kerkerian *et al.,* (2017) highlighted the case of an HIV-infected female identified as a long-term non-progressor (LTNP) of HIV in whom many instances of spontaneous clearance of HCV were documented. It is necessary to review databases of HIV LTNPs to discover similar instances where people may have been repeatedly exposed to HCV but did not develop chronic infection. Meijide *et al.,* (2017) examined changes in HIV patient mortality rates, re-admission rates, and hospital admission rates to examine the impact of HCV co-infection. A retrospective cohort analysis was done on all HIV patients admitted to hospitals between 1993 and 2013. To compare the two study times (1993–2002 and 2003–2013), a comparative cross-sectional analysis was done.

In order to facilitate HIV/HCV testing in community settings and to give training in overdose prevention and response, (Aronson *et al.*, 2017) created the mobile Intervention Kit (MIK), a tablet computer-based intervention should address these three challenges—rising rates of opioid overdose deaths, persistent ongoing issues with undiagnosed HIV and HCV infection, and frequent occurrences of these conditions in areas with inadequate access to basic care and other standard medical services—together. Odjimogho *et al.,* (2018) examined the prevalence of hepatitis B and

C in HIV/AIDS patients undergoing treatment at Bingham University Teaching Hospital Jos Plateau State, Nigeria. According to the study, hepatitis B and C are common among HIV-positive people. As a result, HIV patients should undergo routine screening for hepatitis B and C indicators.

López-Huertas *et al.,* (2019) studied HCV co-impact infection's on HIV-1 reservoir size in resting CD4+ T-cells (CD25-CD69-HLADR). In a multicenter cross-sectional analysis of 97 cART-treated HIV-1 patients, including 36 with HIV and HCV-chronic co-infection without anti-HCV treatment, 32 with HCV spontaneous clearance, and 29 HIV mono-infected individuals, rCD4+ T-cells and total DNA were recovered.

Ghiglione *et al.,* (2020) studied the influence of HCV clearance with DAAs on immunological activation and HIV persistence in HIV/HCV co-infected people on antiretroviral therapy (ART). Elimination of HCV in HIV/HCV-co-infected individuals alters immune function and the transcriptional activity of latently infected cells, which provides insight into the effects of HCV co-infection on HIV. Omar *et al.,* (2021) did a retrospective secondary analysis of HCV mono-infected and HIV/HCV co-infected patients treated with DAAs at an HIV clinic (n=214). Binomial logistic regression was used to predict longer time to treatment (6 months).

2.1.3.1 Prevalence of Hepatitis C Infection among the HIV-Positive Population

Serological evidence of previous or present HCV infection is present in about 2.3 million people (interquartile range: 1.3 - 4.4) out of the estimated 36.7 million people living with HIV worldwide (positive for antibodies to HCV, anti-HCV positive). However, anti-HCV antibodies were found in 6.2% of HIV-positive people (Platt *et al.,*2016). People who inject drugs have the highest prevalence of anti-HCV antibodies (82.4%), followed by men who have sex with other men

(6.4%), and pregnant women (4%). This prevalence is significantly lower among HIV-infected people who do not engage in high-risk behaviors (2.4 percent) (WHO, 2017).

Even though fewer data are available, studies suggest very high rates among prisoners living with HIV. Injection drug use has led to high rates of Hepatitis C virus (HCV) infection in parts of Eastern Europe and Central Asia, where 27 percent of people living with HIV also have evidence of previous or present HCV infection. A mother's chance of passing HCV to her kid is increased by twofold when she is also HIV-positive (Floreani, 2013; Benova *et al.*, 2014). Additionally, HIV co-infection is linked to impaired HCV clearance, increased viral levels, and accelerated liver disease development (Thomas *et al.*, 2000; Greub, 2001; Shepard *et al.*, 2005; Valle *et al.*, 2007). In light of this, it is imperative that HIV-positive individuals also be tested for HCV infection (WHO, 2016).

Two out of 273 patients (0.7 percent) were discovered by (Ajayi *et al.*, 2011) to have positive serum anti HCV antibodies; this included 79 men (28.9 percent) and 194 women (71.11 percent; F:M = 2.46: 1). Cell counts of CD4+ T- Lymphocytes varied from 5 to 1050 cells/l, with a mean of 286.19 233.31 cells/l. Seventy-one percent of patients had a CD4+ T- Lymphocytes cell count of less than 350 cells/l. Out of 443 people who tested positive for HIV, (Tremeau-Bravard *et al.*, 2012) identified 35 with hepatitis B virus infection (7.9%), 10 with hepatitis C virus infection (2.3%), and 3 with both viruses (0.7%). This equates to a hepatitis-HIV prevalence of 10.8%. Among 281 people with hepatitis, (Adesegun *et al.*, 2020) observed that 6.0% also had hepatitis B, 14.6% also had hepatitis C, and 1.1% had all three types of hepatitis. Researchers (Lawal *et al.*, 2020) observed a prevalence of HCV infection of 0.5 percent (p = 1.000) among a sample of 187 HIV-infected and HIV-naive children.

2.1.3.2 The Impact of HIV on Hepatitis C

The transmission and natural history of hepatitis C are modified by the interaction between HIV and hepatitis C. (Graham, *et al.,* 2001). It is less likely that hepatitis infection will be cured in those who do not receive HIV treatment. Additionally, they experience a quicker course of hepatitis illness and have greater hepatitis viral loads than HIV-negative patients. People who are HIV-positive and are infected with HCV tend to develop HCV more rapidly, have greater virus loads, and are more effective HCV transmitters (Hernandez and Sherman, 2011).

On the other hand, persons who take antiretroviral treatment for HIV also tend to keep their hepatitis C under control, which improves treatment outcomes for HIV patients. Co-infection with HIV and another disease typically poses greater dangers and has more dire outcomes for individuals. When HIV is present alongside HCV, the advancement of HCV is hastened. Furthermore, if the CD4 count drops below 200cells/mm, the risk of serious liver disease increases. Furthermore, those who are co-infected are at a higher risk for developing cirrhosis, end-stage liver disease, hepatocellular carcinoma, and dying from a liver-related cause (Thein et al., 2008b). There is evidence that HIV treatment can decrease the natural development of HCV infection and lower HCV-related liver disease mortality (Hernandez and Sherman, 2011).

Additionally, they may identify with marginalized communities that face criminalization and stigmatization, making it difficult for them to gain access to health care (WHO, 2017c). People living with HIV had a lower response rate to previous generations of hepatitis C medicines, but this is not the case with current therapies (Avert, 2020b).

2.2 Review of Methodological Approaches

A review of the various methods used in this study is shown in this section.

2.2.1 Existence and Uniqueness of Solutions

Theorem 2.1: (Derrick and Grossman, 1976)

Let D^1 represent the region $|t - t_0| \leq a, \|x - x_0\| \leq b, x = (x_1, x_2, \ldots x_n), x_0 = (x_{10}, x_{20}, \ldots x_{n0})$ and assume that $f(t,x)$ meets the Lipschitz requirements $\|f(t,x_1) - f(t,x_2)\| \leq k\|x_1 - x_2\|$. When the pairings $(t,x_1)\ and\ (t,x_2)$ correspond to D^1 where k is a constant that is positive. Then, there exists a constant $\delta > 0$ such that a unique continuous solution $x(t)$ of the system exists in the interval $t - t_0 \leq \delta$. Importantly, the condition is satisfied if $\frac{\partial f_i}{\partial x_j}, i = 1,2 \ldots$, is continuous and bounded in D^1.

2.2.2 Next Generation Matrix

The approach of next-generation matrix formulation is one way to calculate the basic reproduction number of any model with many infected classes (Diekmann *et al.*, 1990; Van den and Watmough 2002). (Diekmann and Hesterbeck, 2002; Hefferman *et al.*, 2005) investigated the next-generation matrix method as a natural approach to the determination of the basic reproduction number in models that contain various classes of infected individuals. Consequently, the basic reproduction number has been defined as the spectrum radius (or domain eigenvalue) of the subsequent generation matrix. Define x_s as the collection of all disease-free states, or.

$$x_s = \{x \geq 0 | x_i = 0, i = 1,2, \ldots\ldots m\} \qquad (2.1)$$

In order to calculate R_0, it is necessary to differentiate between infectious and noninfectious population changes.

Let $F_i(x)$ be the rate of appearance of new infections in the compartment;

V_i^+ be the rate of transfer of individuals into compartment *i* by all other mechanisms

V_i^- represents the rate at which people leave compartment *i*.

It is assumed that each function ($F_i(x)$, V_i^+, and V_i^-) is continuously differentiable to each variable at least twice.

The transmission model consists of the non-negative initial conditions together with the following system of equations:

$$x_i = f_i(x) = F_i(x) - V_i(x), i = 1,2,\ldots\ldots,n \quad (2.2)$$

Where $V_i = V_i^- - V_i^+$ and the functions satisfying condition:

A1: if $x \geq 0$ then $F_i, V_i^-, V_i^+ \geq 0$ for $i = 1,2,n$

Note that if the compartment is empty due to death, infection, or any other cause, there can be no transfer of individuals from the compartment.

A2: if $x_i = 0$, then $V_i^- = 0$ (No one leaves the compartment). In particular if $x \in X_s$, then

$$V_i^- = 0 \text{ For } i = 1,2,\ldots\ldots m \quad (2.3)$$

A3: $F_i = 0, i > m$ (m is the number of infective classes)

A4: if $x \in X_s$, then $F_i = 0$, and $V_i = 0$ for all $i = 1,2,\ldots\ldots m$

A5: if $F(x)$is then set to zero, then all the eigenvalues of $Df(x_0)$ having negative real parts.

Lemma 2.1:

If x_0 is a disease-free equilibrium (DFE) of (2.1) and $f_i(x)$ satisfies A1-A5 then the derivatives $Df(x_0)$ and $Dv(x_0)$ are partitioned as

$$DF(x_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, V(x_0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix} \quad (2.4)$$

Where F and V are the m x n matrices defined by

$$F = \left[\frac{\partial F(x_0)}{\partial x_i}\right] \text{ and } \quad V = \left[\frac{\partial V(x_0)}{\partial x_j}\right] \quad (2.5)$$

With$1 \leq i \leq m$, F is non – negative and V is a non- singular M-matrix.

From Diekmann *et al.* (1990) $FV^{-1}$is called the model's next-generation matrix and R_0 is set to be equal to the spectral radius $p(FV^{-1})$ i.e.

$$R_0 = p(FV^{-1}) \quad (2.6)$$

where ρ is the value of the maximum absolute eigenvalues of (FV^{-1}).

2.2.3 Asymptotically Stable

2.2.3.1 Locally Asymptotically Stable

The equation point P_0 is considered locally asymptotically stable if it is stable and there is a ball surrounding it such that any trajectory that enters the circle at some point approaches P_0 as $t \to \infty$.

2.2.3.2 Globally Asymptotically Stable

Globally asymptotically stable describes the equilibrium point P_0 . If any trajectory approaches the equilibrium point P_0 $as\ t \to +\infty$ (regardless of previous behavior), then P_0 is deemed globally asymptotically stable.

2.2.4 Stability

The stability characteristics define how a system operates if its state is began near but not precisely at a specified point of equilibrium. If a system is initially equal to an equilibrium point with the state, it can never move by definition. When began nearby, the state may remain nearby or step on.

Suppose $\overline{X}$ is an equilibrium point of the time-invariant system then $\overline{X}$ is an equilibrium point of

$$X(t) = f(X(t)) \quad (2.7)$$

2.2.5 Linearization and Stability

According to definitions, the stability properties depend only on the nature of the system near the equilibrium point. Therefore, replacing the complete nonlinear definition with a simplified description that approximates the true system near the point of equilibrium to perform an analysis of stability is always technically valid and mathematically convenient. To disclose the properties of stability, a close approximation is often enough. In its definition, the linearization of the nonlinear system is based on the linearization of the nonlinear function f. The procedure approximates f close b, which is defined by a single function of a single variable for the first-order method.

$$f(\bar{x} + y) = f(\bar{x} + \frac{df(\bar{x})}{dx})y \tag{2.8}$$

An n-order system describes n functions, each of which is dependent on n variables. In this situation, each individual functions as approximated by the relations

$$f_i(\overline{x_1} + y_1, \overline{x_2} + y_2, \cdots \overline{x_n} + y_n) \approx f_i(\overline{x_1}, \overline{x_2}, \cdots \overline{x_n}) + \frac{\partial f_1(\overline{x_1}, \overline{x_2}, \cdots \overline{x_n})}{\partial x_1} y_1 + \frac{\partial f_2(\overline{x_1}, \overline{x_2}, \cdots \overline{x_n})}{\partial x_2} y_2 + \cdots +$$

$$\frac{\partial f_i(\overline{x_1}, \overline{x_2}, \cdots \overline{x_n})}{\partial x_i} y_n \tag{2.9}$$

where $i = 1,2, \ldots . n$ is in matrix form. This can be written as

$$f(\bar{x} + y) \approx f(\bar{x}) + f(y) \tag{2.10}$$

$$\text{where } f = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} \cdots & \frac{\partial f_1}{\partial x_n} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} \cdots & \frac{\partial f_2}{\partial x_n} \\ \vdots & \vdots & \vdots \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \frac{\partial f_n}{\partial x_n} \end{bmatrix} \tag{2.11}$$

The matrix f is called the Jacobian matrix of F. Now, consider the matrix equation

$$x = f(x(t)) \tag{2.12}$$

Setting$x(t) = \bar{x} + y(t)$, to obtain

$$y = f(\bar{x} + y(t)) = f(\bar{x}) + F(y(t)) \quad (2.13)$$

Since $\bar{x}$ is an equilibrium point of f, $f(\bar{x}) = 0$

therefore,

$$y(t) = F(y(t)) \quad (2.14)$$

Consequently, the stability characteristics of the original system can be deduced from the linearized system using the following results:

1. $\bar{x}$ is asymptotically stable for the nonlinear system if all of F's eigenvalues are confined to the left half-plane.

2. If at least one of F's eigenvalues has a positive real component, $\bar{x}$ is unstable for the nonlinear system.

3. $\bar{x}$ may be stable, asymptotically stable, or unstable for the nonlinear system if all of F's eigenvalues are on the left half-plane, but at least one has a zero real component (Lungu *et al*., 2007).

Theorem 2.2:

Derrick and Grossman, (1976): Consider the system

$$\left.\begin{aligned} x^1 &= a_{11}x + a_{12}y \\ y^1 &= a_{21}x + a_{22}y \end{aligned}\right\} \quad (2.15)$$

where the $a_{ij}$are constants and $a_{11}a_{22} - a_{12}a_{21} \neq 0$ so that the original (0, 0) is the only initial point

Let $\lambda_1$and λ_2 be the two roots of the auxiliary equation

$$\lambda^2 - (a_{11} + a_{22})\lambda + (a_{11}a_{22} - a_{12}a_{21}) = 0 \quad (2.16)$$

then

(a) The origin is stable if $\lambda_1$and λ_2 are pure imaginary.

(b) The origin is asymptotically stable if $Re\,\lambda_1 < 0$ and

(c) The origin is unstable in all other cases.

Moreover, the behaviour of the orbits near the origin is shown in Table 2.1

Table 2.1: Behaviour of the orbits near the origin after Derrick and Grossman, (1976)

	λ_1, λ_2	Type of critical point
1	Real, distinct, negative	Stable node
2	Real, distinct, positive	Unstable node
3	Real, distinct, opposite signs	Saddle point (unstable)
4	Real, equal, negative	Stable node
5	Real, equal, positive	Unstable node
6	Complex conjugate, not pure imaginary negative real parts	Stable forms
7	Complex conjugate, not pure imaginary positive real parts	Unstable
8	Pure imaginary	Center (stable)

2.2.6 Centre Manifold Theorem

Consider a general system of ODEs with a parameter $\boldsymbol{\phi}$

$$\dot{x} = f(x, \phi);\ f: R^n \times R \to R^n;\ f \in C^2(R^n \times R) \qquad (2.17)$$

Without loss of generality, assume that $x = 0$ is an equilibrium for the system (2.17) (Buonomo

and Lacitignola, 2011).

Theorem 2.3

i) Assume $A = D_x f(0,0)$ is the linearization matrix of the system (2.17). All other A eigenvalues have negative real portions except zero around the equilibrium.

ii) Matrix A has a nonnegative right eigenvector w and a zero-eigenvector v. Let $f_m$be the mth complements of f and

$$a = \sum_{m,j,i=1}^{n} v_m w_i w_j \frac{\partial^2 f_m(0,0)}{\partial x_i \partial x_j}; \quad (2.18)$$

$$b = \sum_{m,j,i=1}^{n} v_m w_i \frac{\partial^2 f_m(0,0)}{\partial x_i \partial \phi} \quad (2.19)$$

then $a\ and\ b$ determines the system's local dynamics (2.17) about $x = 0$.

a) When $\phi < 0\ and\ a > 0,\ b > 0$, with $|\phi| \ll 1,\ x = 0$ is locally asymptotically stable and a positive unstable equilibrium exists; when $0 < \phi \ll 1,\ x = 0$ is unstable and a negative locally asymptotically stable equilibrium exists.

b) $a < 0, b < 0,\ x = 0$ is unstable when $\phi < 0$, with $|\phi| \ll 1$; when $0 < \phi \ll 1,\ x = 0$ is locally asymptotically stable and a positive unstable equilibrium exists.

c) $a > 0,\ b < 0,$ when $\phi < 0,$ with $|\phi| \ll 1,\ x = 0$ is unstable and there is a locally asymptotically stable negative equilibrium.

d) when $\phi < 0$, with $|\phi| \ll 1,\ x = 0$ is stable and a positive unstable equilibrium $a > 0,$ $b < 0$. arises. $x = 0$ becomes unstable when ϕ becomes positive. Unstable equilibrium becomes positive and asymptotically stable. (Castillo-Chavez and Song, 2004) proves theorem 2.3.

2.2.7 Descartes' Rule of Signs

Theorem 2.4:

The number of positive zeros of a polynomial with real coefficients is either equal to or even less than the number of variations in the polynomial's sign.

Proof:

The idea of the proof is this: group together the factors belonging to negative and imaginary roots, on the other hand:

$$p(x) = [(x - r_1)(x - r_2)\dots(x - r_k].\, x[(x - r_{k+1})(x - r_{k+2})\dots(x - r_n)] \qquad (2.20)$$

(We assume that the leading coefficient of $p(x)$ is unity, since the roots are unchanged by dividing by a_n in case $a_n$is root unity). We show two things:

(a) The number of variations in sign of the factors corresponding to the negative and imaginary roots is even, i.e., if the expression

$$p(x) = (x - r_{k+1})(x - r_{k+2})\dots(x - r_n) \qquad (2.21)$$

(b) When a polynomial $g(x)$ is multiplied by $(x - r)$,with r positive, the number of variations is sign of $(x - r)\ g(x)$ is at least one more than the number of variations in sign of $g(x)$.

Once (a) and (b) have been proved, the proof of the theorem is complete by returning to (2.16) and rewriting (2.17) as

$$p(x) = [(k - n)\dots.(x - r_k)]p(x) \qquad (2.22)$$

and reworking (a), we conclude that $p(x)$ has an even number of variations in sign.

Then, by (b),

$(x - r_k)p(x)$

has at least two more variations in sign that does $p(x)$. By (b) again;

$(x - r_{k-1})[(x - r_k)p(x)]$

has at least two more variations in sign than does $p(x)$, and finally

$$p(x) = [(x - r_1)(x - r_2)\ldots(x - r_k]p(x) \quad (2.23)$$

has at least k more variations in sign than does $p(x)$. Observe, however, k is the number of positive zeros of $p(x)$,and if we let $n(p), n(p)$ denote the number of variations in sign of $p(x), p(x)$ respectively, then,

$$\left.\begin{array}{l} n(p) \geq k + n(p) \\ \text{or} \\ k \leq n(p) - n(p) \end{array}\right\} \quad (2.24)$$

But according to (a), $n(p)$is even and hence the theorem is proved.

The theorem also suggests that the number of negative roots is equal to or less than an even number of variations in the symbol.

2.2.8 Lyapunov Stability Method

Lyapunov stability method is used to determine the stability of the mode. In the Lyapunov process, stability of linear and nonlinear systems can be obtained without any prior knowledge of the solutions.

Two methods for demonstrating stability were suggested by Lyapunov (1892). In a sequence that was then shown to be convergent within limits, the first approach established the solution. The second, which is used almost exclusively nowadays, use a function of Lyapunov $v(k)$ that has an analogy to the potential function of classical dynamics.

Consider the autonomous system.

$$\left.\begin{aligned} \overset{1}{x_1} &= f_1(x_1, x_2, x_3) \\ \overset{1}{x_2} &= f_2(x_1, x_2, x_3) \\ \overset{1}{x_3} &= f_3(x_1, x_2, x_3) \end{aligned}\right\} \qquad (2.25)$$

where it is assumed that the origin is the critical point.

Let $v(x_1, x_2, x_3)$ be a continuous real-valued function on the x_1, x_2, x_3 plane with continuous partial derivatives. If D is the region containing the origin, then:

Theorem 2.5:

Derrick and Grossman, (1976) stated that:

I. if $v(0,0,0) = 0$ and $v(x_1, x_2, x_3) > 0$ for all other points in D, then $v(x_1, x_2, x_3)$ is said to be positive definite in D.

II. if $v(0,0,0) = 0$ and $v(x_1, x_2, x_3) < 0$ for all other points in D, then $v(x_1, x_2, x_3)$ is said to be negative definite.

III. if $v(x_1, x_2, x_3) \geq 0$, then $v(x_1, x_2, x_3)$ is said to be positive semi-definite in D.

IV. if $v(x_1, x_2, x_3) \leq 0$, then $v(x_1, x_2, x_3)$ is said to be negative semi-definite in D.

V. if $v(x_1, x_2, x_3)$ satisfies none of the above conditions, then v is said to be indefinite in D.

2.2.8.1 Lyapunov Functions

Let $v(x_1, x_2, x_3)$ be a continuous differentiable, positive definite function and

$$v(X_1, X_2, X_3) = \frac{\partial v}{\partial x_1} x_1 + \frac{\partial v}{\partial x_2} x_2 + \frac{\partial v}{\partial x_3} x_3$$

$$= \frac{\partial v}{\partial x_1} f_1(x_1, x_2, x_3) + \frac{\partial v}{\partial x_2} f_2(x_1, x_2, x_3) + \frac{\partial v}{\partial x_3} f_3(x_1, x_2, x_3) \quad (2.26)$$

Conditions for Lyapunov function of a system

(1) $v(X_1, X_2, X_3)$ must be continuously differentiable

(2) $v(X_1, X_2, X_3)$ must be positive definite

(3) $v(X_1, X_2, X_3)$ must have its derivative along the orbits defined by (2.26)

Theorem 2.6:

let $v(X_1, X_2, X_3)$ be a Lyapunov function for the system (2.25), then if

I. $v(X_1, X_2, X_3)$ is negative semi-definite, the origin is stable

II. $v(X_1, X_2, X_3)$ is negative definite, the origin is asymptotically stable

(Derrick and Grossman, 1976).

2.2.9 Bifurcation

Center manifold theory was used to evaluate a non-hyperbolic equilibrium's local stability (linearization matrix has at least one own value with zero real part) (Carr, 1982; Gukerhamer and Homes, 1983; Wiggins 2003). We will describe a theory that can determine the local equilibrium of the non-hyperbolic balance and solve the problem of another balance being present (bifurcated from the non-hyperbolic stability). This theory is based on the idea of the general centre-manifold. Let us consider a general system of ODEs with parameter φ:

$$\frac{dx}{dt} = f(x, \varphi), f: \Re^n \times \Re \to \Re^n, f \in C^2(\Re^n \times \Re) \quad (2.27)$$

Without loss of generality, we assume that $x = 0$ is an equilibrium for system (2.27) for all values of the parameter φ that is $f(0, \varphi) = 0$ for all φ.

Theorem 2.7:

Assume:

A1: $A = D_x f(0,0) = \left(\frac{\partial f_i}{\partial x_j}(0,0)\right)$ is the linearization matrix of the system (2.27) around equilibrium $x = 0$ with φ evaluated at 0. Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts;

A2: Matrix A has a (nonnegative) right eigenvector w and a left eigenvector v corresponding to the zero eigenvalue.

Let $f_k$denote the k^{th}component of f, and

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0) \qquad (2.28)$$

$$b = \sum_{k,j=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \varphi_j}(0,0) \qquad (2.29)$$

The local dynamics of the system (2.27) around $x = 0$ are determined by a and b.

i. $a > 0, b > 0$,when $\varphi > 0$, with $|\varphi| << 1, x = 0$ is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 > \varphi << 1, x = 0$, is unstable and there exists a negative and locally asymptotically stable equilibrium;

ii. $a < 0, b < 0$, when $\varphi < 0$, with$|\varphi| << 1, x = 0$ is unstable; when $0 > \varphi << 1, x = 0$, is locally asymptotically stable and exists a positive and unstable equilibrium.

iii. $a > 0, b > 0$, when $\varphi < 0$, with $|\varphi| << 1, x = 0$ is unstable and there exists a locally asymptotically stable negative equilibrium; when $0 > \varphi << 1, x = 0$, is stable and a positive unstable equilibrium appears;

iv. $a < 0, b < 0$, when φ changes from negative to positive, $x = 0$ changes its stability from stable to unstable. Correspondently, a negative unstable equilibrium becomes positive and locally asymptotically stable.

Proof:

Let $\xi^c$and ξ^c be the generalized eigenspaces of A for the zero eigenvalue and all other eigenvalues, respectively, it follows from the centre manifold theory that the centre manifold W^c is one-dimensional and $\Re^n = \xi^c \otimes \xi^s$. Parameterize the centre manifold by $c(t)$and decompose it into $\xi^c$and ξ^c, that is,

$$W = \{c(t)w + h(c,\varphi): v, h(c,\varphi) = 0, |c| \leq c_0, c(0) = 0\}, \quad (2.30)$$

Where $c(t) \in \xi^c$and $h(c,\varphi) \in \xi^c$. Because the centre manifold is tangent to ξ^cat the origin, $h(c,\varphi)$ is the higher-order term ($h(c,\varphi)$ has at least order 2). It also follows by the invariance of the centre manifold under the flow that;

$$\frac{d}{dt}((c(t)w + h(c,\varphi)) = f(c(t)w + h(c,\varphi),\varphi), \quad (2.31)$$

Applying Taylor expansion to the right-hand side of equation (2.30) at (0, 0) and noticing that $h(c,\varphi)$ is higher-order, we obtain that

$$f(c(t)w + h(c,\varphi),\varphi) = f(0,0) + D_x f(0,0)((c(t)w + h(c,\varphi) + D_\varphi f(0,0)\varphi + \frac{1}{2}(I_n \otimes (cw + h(c,\varphi))^1)(D^2_{xx} f(0,0))(c(t)w + h(c,\varphi)) + \varphi(D^2_{x\varphi} f(0,0))(cw + h(c,\varphi)) + \frac{1}{2}\varphi^2(D^2_{\varphi\varphi} f(0,0)) + \textit{higher order term}, \quad (2.32)$$

where $D^2_{x\varphi}$ is the Hessian matrix; I_n is the identity matrix of order n; $\otimes$ is the Kronecker product. Using

$$f(0,0) = D_x f(0,0)c(t)w = D_\varphi f(0,0) = D^2_{\varphi\varphi} f(0,0) = 0 \quad (2.33)$$

and the fact that $ch(c,\varphi)$ is of higher-order, simplifying the above expansion for f as (higher-order terms are dropped).

$$f(0,0) = (D_x f)h(c,\varphi) + \frac{c^2}{2}(I_n \otimes w')(D_{xx}^2 f)w + c\varphi(D_{x\varphi}^2)w \quad (2.34)$$

Multiplying both sides of equation (2.34) by v and using the fact that $v,h = 0$ and $vD_x f(0,0) = 0$,

following equation for $c(t)$ is obtain

$$\frac{dc}{dt} = \frac{c^2}{2} v(I_n \otimes w')D_{xx}^2 fw + c\varphi v D_{x\varphi}^2 fw \quad (2.35)$$

$$= \frac{c^2}{2}\sum_{k,i,j}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j} + \sum_{kj}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial x_\varphi} c\varphi \quad (2.36)$$

$$= \frac{q}{2}c^2 + b\varphi c \quad (2.37)$$

Namely,

$$\frac{dc}{dt} = \frac{a}{2}c^2 + b\varphi c \quad (2.38)$$

Obviously, at $\varphi = 0$ a transcritical bifurcation takes place in equation (2.38).

2.2.10 Pontryagin's Maximum Principle

In optimal control theory, Pontryagin's maximum principle is applied to determine the optimal viable control for transitioning a dynamical system from one state to another, particularly when state or input controls are constrained.

Theorem 2.8:

For $\left(x_0^*, u^*(t)\right)$ to be an optimal initial condition and optimal control for the optimal control problem, there must be a non-zero k-dimensional vector with $\lambda_1 \leq 0$ and an n-dimensional vector function $P(t)$ such that for $t \in [t_0, t_1]$:

(i) $P(t)' = -P(t)' f_x\big(t, x^*(t), u^*(t)\big)$; for $t \in (t_0, t_1)$ and $u \in U$

(ii) $P(t)'\big[f(t, x^*(t), u) - f\big(t, x^*(t), u^*(t)\big)\big] \leq 0$;

(iii) $P(t_1)' = \lambda' \phi_{x_1}(e)$;

(iv) $P(t_0)' = -\lambda' \phi_{x_0}(e)$;

(v) $P(t_1)' f\big(t_1, x^*(t_1), u^*(t_1)\big) = -\lambda' \phi_{t_1}(e)$;

(vi) $P(t_0)' f\big(t_0, x^*(t_0), u^*(t_0)\big) = \lambda' \phi_{t_0}(e)$;

If $f(t, x, u)$ has a continuous partial derivative $f_t(t, x, u)$, then the condition

(vii) $P(t)' f\big(t, x^*(t), u^*(t)\big) = \lambda' \phi_{t_0}\big(t_0, t_1, x^*(t_0), x^*(t_1)\big) +$

$\int_{t_0}^{t} P(s)'\, f_t\big(s, x^*(s), u^*(s)\big) ds$

holds for each $t \in [t_0, t_1]$.

The proof of theorem 2.8 can be found in (Fleming and Rishel, 1975)

2.2.11 Sensitivity Indices

Using the approach of (Arriola and Hyman, 2005), the sensitivity of the reproduction number R_0 to each of the parameters, which measures the initial spread of the disease, as shown by (Arriola and Hyman, 2005). When a parameter changes, sensitive indices measure how much the state variable changes in comparison. When the variable is a function of the parameter that can be changed, the sensitivity index can also be found by using partial derivatives. The formula $\hbar_\ell^k = \frac{\partial k}{\partial \ell}\frac{\ell}{k}$ gives the forward sensitivity index for each of the parameters used in the HIV/HCV models.

2.3 Gaps Identified in Literature

In the literature, many mathematical models have been used to examine the dynamics of HIV and other diseases, such as Hepatitis C virus, genital warts, TB, and STD co-infections (Fred and Carlos, 2001; Bhunu *et al.*, 2009; Roeger *et al*., 2009; Mushayabasa *et al.*, 2011; Fred and Carlos, 2012; Yovanna *et al.*, 2013; Caro-Vega *et al*., 2015; David, 2015; Pinto and Carvalho, 2015; Zerehpoush and Kheiri, 2017; Nwankwo and Okuonghae, 2018; Hassan and Hussaini , 2021; Castry *et al*., 2021) but only (Yovanna *et al*., 2013; Pinto and Carvalho, 2015; and Zerehpoush and Kheiri, 2017) used a related model to investigate the dynamics of HIV and HCV co-infections. Bhunu *et al.,* (2009) made and analyzed a deterministic model of the co-dynamics of the hepatitis C virus and HIV/AIDS to see how they affect the course of each disease when treatment is given. They presume that AIDS patients are not sexually active in their model, hence they cannot tranmit infection.

Mukandavire *et al*., (2010) modeled the HIV/AIDS epidemic with ongoing recruitment and sexually active AIDS patients. The centre manifold theory proved endemic equilibrium's local stability. Poincare-Bendixson property proved global asymptotic stability. On the idea that poor usage of antiretroviral therapy (ART) was prevalent, the treatment of HIV-positive patients who did not yet exhibit AIDS symptoms was overlooked.

Moualeu-ngangue *et al.*, (2011) introduced and analyzed a deterministic model for HCV and HIV co-infection. The HCV-only and HIV/AIDS-only endemic equilibria are demonstrated to be locally asymptotically stable when their associated reproduction numbers are bigger than unity using the Centre Manifold theory. Their findings demonstrated that higher rates of HIV to AIDS progression have a sizable impact on the level of HCV prevalence. The HCV disease-induced

death rate was neglected since it was assumed to be minimal; also, HIV testing for persons infected with HCV and vice versa was not considered.

Bhunu & Mushayabasa, (2013) constructed and studied a deterministic model of the co-dynamics of hepatitis C virus and HIV/AIDS in order to determine the impact of treatment on the dynamics of each disease. In their model, AIDS patients were considered to be sexually inactive and hence excluded from the transmission process.

Yovanna *et al*., (2013) suggested a new joint mathematical model that accounts for co-infection with the two viruses among injection drug users (IDUs). Statistical concepts and methods were employed to evaluate the model and get more information. Because HIV treatment is not widely used, it was overlooked.

Carvalho and Pinto, (2014) investigated a mathematical model of HIV and HCV co-infection. In the case of HIV, the innovation of their strategy is the inclusion of therapy for both diseases and vertical transmission from mother to kid. Extrapolated from the model's results were practical procedures that may be implemented to lower the number of affected individuals. HIV testing and condom use were not prioritized.

Birger *et al*., (2015) constructed a within-host mathematical model of HCV/HIV co-infection by adapting a previously published model of HCV mono-infection to incorporate an immune system component in infection clearance. Result showed that, increased HIV viral load and decreased CD4+ count are associated with decreased spontaneous clearance and SVR probabilities. They are unable to include dynamically, the process of immunological recovery following ART for HIV in their model because of the static nature of how HIV is incorporated.

Aggarwala, (2015) provided a mathematical model that describes the evolution of HCV and HIV co-infection. It was believed that whereas HIV and/or HCV infection happens through physical contact (sexual, sharing needles, etc.), co-infection occurs simply because infected individuals live in close proximity. Consequently, it was also hypothesized that a certain proportion of individuals infected with HCV in a densely populated area are also infected with HIV, and vice versa.

Pinto and Carvalho, (2015) created a new co-infection model for the hepatitis C virus (HCV) and human immunodeficiency virus (HIV) (HIV). Examining treatment for both diseases, screening, ignorance and awareness of HIV infection, and condom use. The results indicated that particular HIV infection prevention methods should be addressed. Vertical transmission and homogeneous random mixing populations was overlooked in favor of horizontal transmission and a consistent recruitment rate.

Sánchez-González, (2016) proposed a mathematical model for HIV co-infection with TB and HCV. The model was developed to add control parameters for care coverage, making it useful for analyzing the cost-effectiveness of public policy. They made the assumption that there is no infection transfer between classes, which limits the model's application to high-risk groups like injecting drug users.

Durfee, (2016) presented and developed a mathematical model of the biological component. The study's biological component is the Hepatitis C virus. Based on the simulation results, it is obvious that the enhanced treatment has significantly decreased the proportion of the population with known chronic Hepatitis C.

Zahnd *et al*., (2016) developed an individual-based model of liver disease progression in HIV/HCV co-infected MSM. They presupposed that the percentage of the population who engages

in hazardous sex is a constant proportion of those exhibiting high-risk behavior. They also decided it was fair to exclude HIV-negative MSM from their demographic model.

Birger et al., (2017) developed a deterministic compartmental ODE model that includes HIV illness progression, HCV disease progression, and PWID demography layers. It was assumed that MMT lengthens life expectancy by reducing the extra risk of death from drug-related problems and by increasing enrollment in ART programs.

Zerehpoush and Kheiri, (2017) presented a deterministic model for HCV and HIV infection transmission and evaluated the possible impact of antiviral therapy using this model. If the control reproduction number is more than one, there is a locally unstable infection-free equilibrium and a single, globally asymptotically stable endemic equilibrium, according to the results and vice versa.

Nwankwo and Okuonghae, (2018) studied the synergistic interaction between HIV and syphilis using a mathematical model that examines the influence of syphilis therapy on syphilis and HIV co-infection in a human community where HIV treatment is not widely available.

Carvalho and Pinto, (2018) examined the impact of HIV viral load and cell-to-cell transfer on HIV/HCV co-infection. The model includes treatment for HIV/HCV fractional model dynamics. Specific strategies are said to be needed to minimize HIV viral load and cell-to-cell dissemination in HCV infection.

Carvalho *et al.*, (2018) explored the burden of HIV viremia and treatment efficacy in HIV/HCV co-infection severity. For this, a simple non-integer-order (fractional-order) model for co-infection dynamics was created. Conclusively, treatment efficacy was found to impact the natural progression of HCV on the HIV/HCV co-infection and it's replicated for all values of the order of the fractional derivative.

Ndako *et al*., (2019) studied HCV infection in diabetics. A slightly increased prevalence of hepatitis C infection in type 2 diabetics warrants for frequent screening. To prevent problems among diabetic patients, public education on the link between HCV and T2DM was also highlighted.

Heffernan *et al.,* (2019) developed a dynamic transmission model of the global HCV epidemic, calibrated to 190 countries, which incorporates data on demography, PWID. They evaluated the impact of public health interventions on the global HCV epidemic and whether WHO's elimination targets could be met. They hypothesized that ignoring mortality unrelated to the liver would likely to underestimate the effect of therapies.

Altawalah *et al*., (2019) tested PWID in Kuwait for hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV. An April-September 2017 cross-sectional study was done. Their data suggested that injecting drug users have higher rates of HBV, HCV, and HIV than the general population and emphasize the necessity of interventions and harm reduction measures to reduce needle sharing. Injection drug user was considered as the route of transmission.

Mayanja *et al.,* (2020) developed and tested a mathematical model to investigate the dynamics of HIV and HCV co - infection in the absence of medication. They claimed that because they are too weak to engage in sexual activity or find new partners, full-blown AIDS patients are thought to not transmit HIV or advanced HCV patients. Constant hiring rate was taken into consideration

Cepeda *et al*., (2020) evaluated stimulant injection's role in HIV/HCV transmission in PWID. HIV and HCV transmission models included extra injecting and sexual risk among stimulant-injecting PWID. They concluded that stimulant injection causes HIV and HCV in PWID. Scaling up NSPs

and developing new interventions for PWID who inject stimulants was suggested to be needed, ignoring other risk factors.

Castry *et al*., (2021) created a dynamic compartmental model to simulate the impact of test-and-treat and risk-reduction strategies on the HCV epidemic among MSM living with HIV in France. The study found that combining test-and-treat and risk-reduction methods could have a major influence on the HCV epidemic, opening the door for HCV elimination among MSM living with HIV. Transmission between heterosexual and was neglected.

Goyal *et al.,* (2021) analyzed HCV RNA in liver biopsies from mono-infected (n = 4) and HCV/HIV co-infected (n = 5) subjects. Their data reveal that HIV co-infection affects intracellular HCV RNA accumulation, the clustering of HCV-infected cells, and the proportion of HCV-infected cells.

Hassan and Hussaini (2021) constructed and dynamically analyzed a mathematical delay model for HIV and hepatitis C infection. Model's basic features are proven. When the length of time delay exceeds a crucial value, it was seen that the number of cumulatively infectious individuals decreases. However, treatment of HIV infected individual was neglected.

CHAPTER THREE

3.0 METHODOLOGY

The non-linear differential equations are solved by first linearizing the system around its equilibrium point to establish the disease-free and endemic equilibrium.

The models' local and global stabilities are verified using the Routh-Hurwitz theorem and Lyapunov function respectively. This is a mathematical test that establishes necessary and sufficient conditions for the stability of the control system. The next-generation matrix is used to derive the basic reproduction number to determine the nature of the outbreak. The center manifold theorem is employed to investigate bifurcation analysis for each of the models, and each model undergoes a sensitivity analysis to identify any parameters that would have a favorable impact on the models.

In order to demonstrate how the parameters affect each model, the numerical computations are performed on the Windows 10 operating system core i5 using the MAPLE 21 program pseudocode, with computation times of 5.0s when there are no optimal controls imposed on the model. Optimal control assessments were also conducted to demonstrate the significance of control on the activities of the models using Pontryagin's maximum. With the aid of MATLAB, Runge-Kutta's forward-backwards sweep method is used to analyse the behaviour of the control functions and co-states after imposing optimal control on the model.

3.1 Mathematical Model Formulation

The mathematical model that is considered and investigated is divided into (15) different groups, namely, the susceptible populace for both HIV and HCV $S(t)$, the HIV-infected unaware $H_U(t)$,

the HIV-infected aware, $H_A(t)$, HIV on treatment $H_T(t)$, the AIDS populace on treatment $A_A(t)$, acutely infected $I_c(t)$ and chronically infected $C_c(t)$ infected HCV, HIV-unaware co-infected with acute and chronic HCV ($H_{uI}(t)\ and\ H_{uC}(t)$), HIV-aware co-infected with acute and chronic HCV ($H_{AI}(t)\ and\ H_{AC}(t)$), HIV-positive individuals receiving treatment for HIV who are co-infected with acute and chronic HCV ($H_{TI}(t)\ and\ H_{TC}(t)$), HIV-positive individuals in stage-IV co-infected with acute and chronic HCV ($A_{AI}(t)\ and\ A_{AC}(t)$) respectively.

The epidemiology of HIV and HCV co-infection is depicted schematically in Figure 3.1. The various disease phases are represented by the different compartments (circles), and the arrows show how individuals advance from one stage to the next. At time t, susceptible individuals; S are assumed to enter the population at a constant rate, $(1-\varphi H_u)\Lambda$. A portion of infants are infected with HIV during birth and are thus directly recruited into the infectious class, H_u where φ, is the rate of newborns and Λ is the rate of HIV recruitment through immigration or emigration.

Individuals in all classes die at a consistent natural mortality rate, μ. Individuals with AIDS (A_a, A_{aI}, A_{aC}) have an extra death rate owing to AIDS, d_a. Disease co-dynamics are complex processes, but for the sake of simplicity, we assume that both mono and co-infected individuals can transmit HIV or HCV but not both at the same time. Individual S, who is susceptible to HIV infection, is at risk of acquiring HIV infection at a rate of λ_H, (force of infection associated with HIV) when in contact with the $H_U, H_A, and\ A_a$ individuals, where

$$\lambda_H = c_h(1-\psi\xi)b_h\frac{H_U(t)+A_A(t)+\kappa_1\left(H_{uI}(t)+H_{uC}(t)\right)}{N} \tag{3.1}$$

The parameter b_h is the chance that a person will get HIV from a contact, and the parameter, c_h is the average number of sexual partners a person who could get HIV has each year or per unit of

time. To represent condom use as a key preventative method, we assume that the level of protection from a condom is given by $\psi\xi \in [0,1]$. If $\xi = 0$, condom use offers no protection, $\xi = 1$ denotes perfect protection, where ψ is the use of a condom.

When compared to individuals who are only infected with HIV, the relative infectiousness of individuals who are acutely infected with HCV and unaware of their HIV infection (H_{UI}) and individuals who are chronically infected with HCV and HIV (H_{Uc}), is accounted for by the parameters $\kappa_1 > 1$. HIV unaware class, H_U, H_{UI}, H_{UC} singly and dually infected with HCV advances to HIV diagnosed class H_A, H_{AI}, H_{AC} after testing at a rate, $\alpha_1, \alpha_2, \alpha_3$ and those aware of HIV were enrolled on therapy at the rate $\theta_1, \theta_3, \theta_5$ in class H_T, H_{TI}, H_{TC}. Nevertheless, some individuals who were placed on HIV treatment default from or drop out of the HAART treatment after which they develop AIDS due to drug resistance and progress to class A_A, A_{AI}, A_{AC} at a rate $\upsilon_1, \upsilon_2, \upsilon_3$.

People with HIV and HCV who don't know their HIV status, H_U, H_{UI}, H_{UC} and didn't get tested and moved to the AIDS class A_A, A_{AI}, A_{AC}. at a rate ρ_1, ρ_2, ρ_3, People with AIDS symptoms singly and dually infected with HCV are given treatment at a rate of $\theta_2, \theta_4, \theta_6$ respectively. AIDS infected can respond well to treatment and return to H_T, H_{TI}, H_{TC} (Carvalho and Pinto, 2014; Moualeu-ngangue *et al*., 2011) and die because of AIDS at an incidence da.

Susceptible people get HCV infection from people in the I_c, C_c, H_{UI}, H_{UC}at a rate of λ_C where λ_C is the force of infection linked with HCV, given by

$$\lambda_C = c(1 - \psi\xi)b_c \frac{I_c(t) + C_c(t) + \kappa_2\big(H_{uI}(t) + H_{uC}(t)\big)}{N} \tag{3.2}$$

To simulate the reality that individuals who are dually infected are more infectious than the mono-

infected, we use the notation $\kappa_2 > 1$, where b_c the likelihood that contact will result in HCV. People who are only infected with HIV $(H_U, H_A, H_T, and\ A_a)$ acquired HCV at a rate $(\delta_1\lambda_c, \delta_2\lambda_c, \delta_3\lambda_c)$ and moved to classes $(H_{UI}, H_{AI}, H_{TI}, A_{AI})$, an increased risk of HCV acquisition is accounted for by the modification parameter $\delta_1, \delta_2, \delta_3 > 1$. People who are only infected with HCV (Ic, C_c) are more likely to get HIV (H_{uI}, H_{uC}) than people who are only infected with HCV at a rate $\gamma\lambda_H, \tau\lambda_H$ where $\gamma, \tau > 1$ means that the risk of getting HIV is higher for people whose immune systems are weakened by HCV.

HIV and AIDS patients, dually infected with the acute HCV H_{UI}, H_{TI}, A_{AI}; at a rate η, becomes chronically infected and are treated for chronic HCV epidemic at $(r_i, i = 1,2, \dots)$ while the remaining populace $(\omega_i, i = 1,2, \dots)$ spontaneously clear the virus to return to susceptible class S.

Data suggest that, after 12 weeks of complete HCV treatment, if individuals experience sustained virological response (SVR) he/she will stay virus-free indefinitely. We then assume that an individual whose immune system helps in clearing the virus can become re-infected at a rate λ_C if expose or engage in risk behaviors such as injection drug use (ALF, 2020), drinking alcohol (Mayo Foundation, 2020b), multiple sex partners and sex between two men (hepmag, 2020) since the clearance does not confer permanent immunity (hepmag, 2020).

An HCV-positive person stays acutely infected for an average of $1/\sigma_c$ days. Since newer combinations of direct-acting antivirals (DAAs) have shown high cure rates of 90%-95% in phase II and III clinical trials, we did not take treatment failure for chronic HCV carriers into account. However, researchers are beginning to report sporadic incidences of treatment failure in HCV (Catie, 2017; WHO, 2020b; ALF, 2020).

Little is known about the correlation between spontaneous HCV clearance and long-term control

of HIV infection in HIV-HCV co-infected individuals. As a result of co-infection, the likelihood of acute HCV virus clearing itself naturally decreases (ALF). Because HIV speeds up the development of HCV, a high viral load for this virus may also indicate a rapid progression of liver disease (Hepmag, 2020; ALF, 2020). To take into account the additional viral load resulting from co-infection, we use the term ε_1 to impact spontaneous clearance and the term ε_2 to accelerate the disease progression, due to co-infection. Because HCV and HIV-1 are transmitted in the same ways, about 10-15% of acute HCV infections resolve on their own, but less than 10% of HIV-1 infections do (López-Huertas *et al.*, 2019).

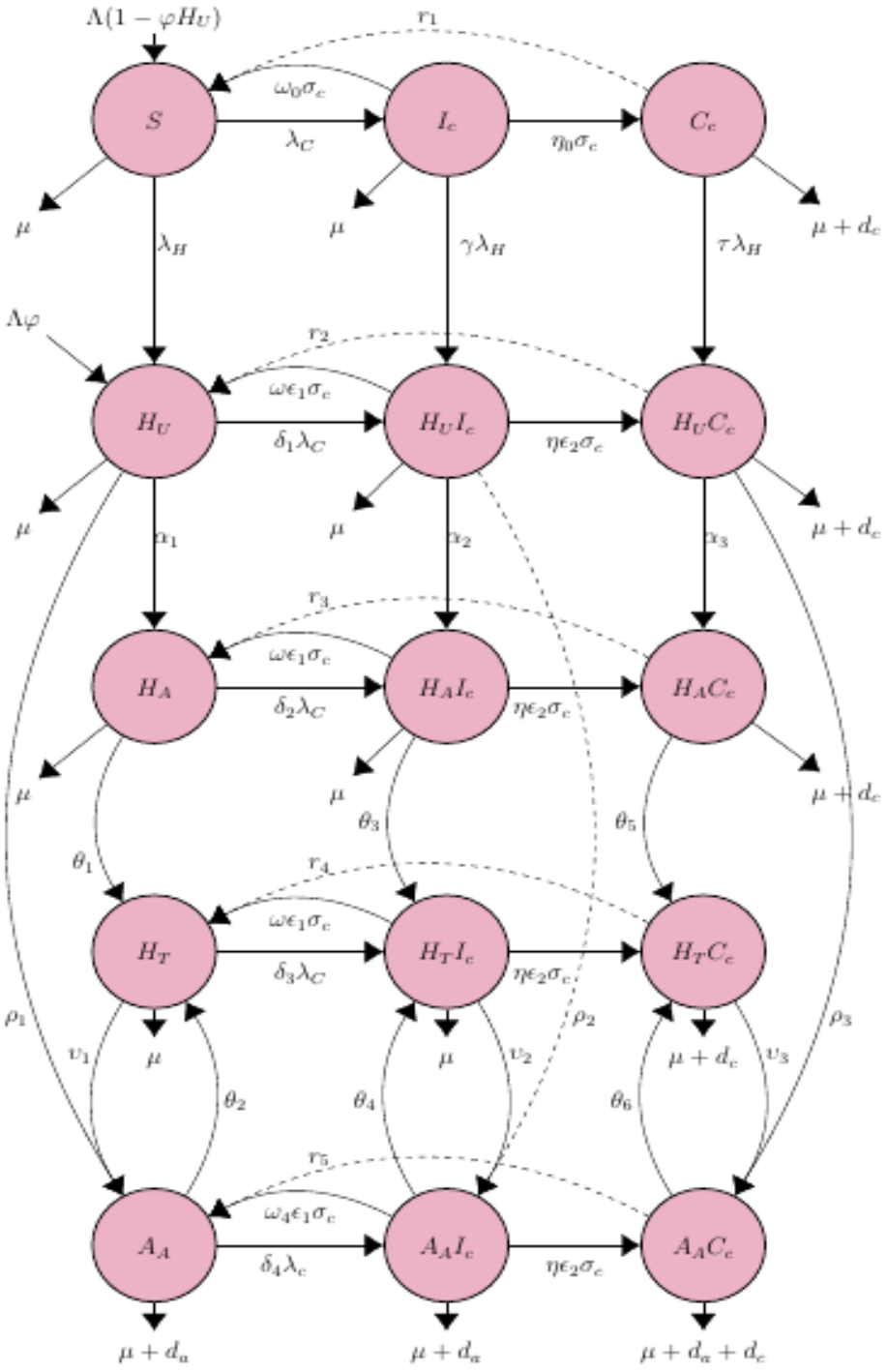

Figure 3.1: The Compartmental Flow Diagram of the HIV-HCV Co-Infection

The above flow chart leads to the 15 systems of ordinary differential equations listed below.

$$
\begin{aligned}
\frac{dS}{dt} &= (1-\varphi H_u)\Lambda + \omega_0\sigma_c I_c + r_1 C_c - (\lambda_H + \lambda_C + \mu)S \\
\frac{dH_U}{dt} &= \lambda_H S + \varphi\Lambda H_U + \omega\epsilon_1\sigma_c H_{UI} + r_2 H_{UC} - (\delta_1\lambda_C + \alpha_1 + \rho_1 + \mu)H_U \\
\frac{dH_A}{dt} &= \alpha_1 H_U + \omega\epsilon_1\sigma_c H_{AI} + r_3 H_{AC} - (\delta_2\lambda_C + \theta_1 + \mu)H_A \\
\frac{dH_T}{dt} &= \theta_1 H_A + \omega\epsilon_1\sigma_c H_{TI} + r_4 H_{TC} + \theta_2 A_A - (\delta_3\lambda_C + \mu + \upsilon_1)H_T \\
\frac{dA_A}{dt} &= \rho_1 H_U + \upsilon_1 H_T + \omega\epsilon_1\sigma_c A_{AI} + r_5 A_{Ac} - (\delta_4\lambda_C + \mu + d_a + \theta_2)A_A \\
\frac{dI_C}{dt} &= \lambda_C S - (\omega_0 + \eta_0)\sigma_c I_C - (\gamma\,\lambda_H + \mu)I_C \\
\frac{dC_c}{dt} &= \eta_0\,\sigma_c I_c - (\tau\,\lambda_H + \mu + d_c + r_1)C_c \\
\frac{dH_{UI}}{dt} &= \delta_1\lambda_C H_U + \gamma\,\lambda_H I_c - (\eta\,\epsilon_2\sigma_c + \alpha_2 + \omega\epsilon_1\sigma_c + \rho_2 + \mu)H_{UI} \\
\frac{dH_{AI}}{dt} &= \alpha_2 H_{AI} + \delta_2\lambda_C H_A - (\eta\,\epsilon_2\sigma_c + \theta_3 + \omega\epsilon_1\sigma_c + \mu)H_{AI} \\
\frac{dH_{TI}}{dt} &= \theta_3 H_{AI} + \delta_3\lambda_C H_T + \theta_4 A_{AI} - (\eta\,\epsilon_2\sigma_c + \upsilon_3 + \omega\epsilon_1\sigma_c + \mu)H_{TI} \\
\frac{dH_{UC}}{dt} &= \tau\,\lambda_H C_c + \eta\,\epsilon_2\sigma_c H_{UI} - (r_2 + \alpha_3 + \rho_3 + \mu + d_c)H_{UC} \\
\frac{dH_{AC}}{dt} &= \alpha_3 H_{UC} + \eta\,\epsilon_2\sigma_c H_{AI} - (r_3 + \theta_5 + \mu + d_c)H_{AC} \\
\frac{dH_{TC}}{dt} &= \theta_5 H_{AC} + \eta\,\epsilon_2\sigma_c H_{TI} + \theta_6 A_{AC} - (r_4 + \upsilon_3 + \mu + d_c)H_{TC} \\
\frac{dA_{AI}}{\mathrm{d}t} &= \delta_4\lambda_C A_A + \rho_2 H_{UI} + \upsilon_2 H_{TI} - (\eta\,\epsilon_2\sigma_c + \theta_4 + \omega\epsilon_1\sigma_c + \mu + d_a)A_{AC} \\
\frac{dA_{AC}}{dt} &= \eta\,\epsilon_2\sigma_c A_{AI} + \rho_3 H_{UC} + \upsilon_3 H_{TC} - (r_5 + \theta_6 + \mu + d_a + d_c)A_{AC}
\end{aligned}
\qquad (3.3)
$$

The overall population at time t, represented by $N(t)$, is classified into the 15 classes/subgroups listed in Tables 3.1.

Where

$$N(t) = S(t) + H_u(t) + H_A(t) + H_T(t) + A_a(t) + I_c(t) + C_c(t) + H_{uI}(t) + H_{AI}(t) +$$

$$H_{TI}(t) + A_{AI}(t) + H_{UC}(t) + H_{AC}(t) + H_{TC}(t) + A_{aC}(t) \quad (3.4)$$

Table 3.1: State Variables

STATE VARIABLES	DESCRIPTION
S	Susceptible Individuals
H_U	Unaware HIV individuals
H_A	Aware HIV individuals
H_T	HIV on Treatment Individuals
A_A	AIDS individual
I_c	Acute HCV Individual
C_c	Chronic HCV Individuals
H_{uI}	Unaware HIV individual co-infected with Acute HCV
H_{AI}	Aware HIV individual co-infected with Acute HCV
H_{TI}	HIV individual on treatment co-infected with Acute HCV
A_{AI}	HIV individuals showing symptoms of AIDS co-infected with Acute HCV
H_{uC}	Unaware HIV individual co-infected with Chronic HCV
H_{AC}	Aware HIV individuals co-infected with Chronic HCV
H_{TC}	HIV individual on treatment co-infected with Chronic HCV
A_{AC}	HIV individuals showing symptoms of AIDS co-infected with Chronic HCV

Table 3.2: Parameters Description

PARAMETERS	**DESCRIPTIONS**
Λ	Recruitment rate
ω	Spontaneous clearance for Acute HCV
η	Progression rate from Acute to Chronic HCV / Non-spontaneous clearance rate
$r_i, i = 1,2, \ldots$	HCV treatment rate for HCV
λ_H	Force of infection associated with HIV infection
λ_C	Force of infection associated with HCV infection
γ	Modification parameter for Acute HCV
τ	Modification parameter for Chronic HCV
$\alpha_1, i = 1,2,3$	HIV testing rate
$\delta_{i,} i = 1,2,, \ldots$	Modification parameter
$\varepsilon_{1,}$	Factor to modify spontaneous clearance of HCV in presence of co-infection
$\varepsilon_{2,}$	Acceleration factor for disease progression of HCV in presence of co-infection
φ	Rate of newborns infected with HIV
$\rho_i, i = 1,2,3$	Progression rate from unaware HIV to AIDS
$\theta_{i,} i = 1,2,3, \ldots$	HIV/ AIDS treatment rate
$v_{i,} i = 1,2,3$	HIV defaulters from treatment rate (progression rate from aware HIV to AIDs)
μ	Natural Mortality
d_a	Mortality due to AIDS
d_c	Mortality due to HCV

$\frac{1}{\sigma_c}$	Average time an individual infected with HCV remains in a state of acute infection
c	Contact rate
b_h	Transmission Coefficient for HIV
b_c	Transmission Coefficient for HCV
t	Time

Model Assumptions

- Proportional (random) mixing between all groups where all individuals have an equal likelihood of contracting the infection if they come into effective contact with infectious individuals.
- People who are being treated for HIV don't spread the virus due to a low viral load.
- Co-infected people are approximately three times more contagious than mono-infected people (CDC, 2019).
- People co-infected with HIV who were not getting ART were presumed to spread HIV more easily due to higher viral loads.
- It is assumed that an individual could be re-infected with HCV even after successful treatment if exposed to or engaged in high-risk behaviors such as injecting drugs (ALF, 2020), drinking alcohol (Mayo Foundation, 2020b), having multiple sex partners, or sex between two men (hepmag, 2020) since the clearance and treatment does not confer permanent immunity.
- Treatment failure for people who have had HCV for a long time isn't taken into account because recent research has shown that newer combinations of direct-acting antivirals

(DAAs) have shown cure rates of 90% to 95% in phase II and III clinical trials (Catie, 2017; WHO, 2020; ALF, 2020).

- Individuals acutely infected with HCV are assumed to spontaneously clear the virus (WHO, 2018).

Mono-infected and co-infected individuals can transmit either HIV or HCV, but not both simultaneously.

3.2 Data Collection

The following default parameter values are obtained from existing theoretical works of literature based on various reports on theoretical studies of related HIV-HCV models. Due to a lack of data on HIV-HCV co-infection, we are unable to scale our analytical results. However, for illustration purposes, other parameter values are assumed to vary within realistic means, as shown in Tables 3.3, 3.4, and 3.5:

Table 3.3: Values of Parameters for the HIV model case 1

PARAMETERS	PARAMETERS VALUE	SOURCE
Λ	$29yr^{-}1$	Mukandavire *et al*., 2010
φ	0.02	[Assumed]
c	$8patners/yr$	Mukandavire *et al*., 2010
b_h	0.030	Assumed
μ	0.2	[Assumed]

α	0.7	[Assumed]
ρ	0.322	[Assumed]
υ	0.0169	Su et al., 2016
$\theta_1, i = 1,2$	1.6949	Lu et al., 2020
d_a	0.0333	[Assumed]
ψ	[0,1]	[Assumed]
ξ	[0,1]	[Assumed]

Table 3.4: Values of Parameters for the HCV model case 2

PARAMETERS	**PARAMETERS VALUE**	**SOURCE**
Λ	$4yr^{-}1$	Pinto *et al*., 2015
κ	1.0002	
c	$3patners/yr$	
b_c	0.08	
μ	0.02	
ψ, ξ	0.20	
d_c	0.05	
ω	0.25	
σ_c	5.8	Yovanna *et al*., 2013

η	0.43	Yovanna *et al*., 2013
r	3.3	Elbasha, 2013

Table 3.5: Values of Parameters for the HIV-HCV Co-infection

PARAMETERS	**PARAMETERS VALUE**	**SOURCE**
Λ	$29yr^{-}1$	[Assumed]
φ	0.02	[Assumed]
c_h	$3patners/yr$	Mukandavire *et al*., 2010
c_c	$2patners/yr$	Assumed
b_h	0.036	Pinto and Carvalho, 2015
b_c	0.05	
μ	0.020	
$\alpha_1, i = 1,2,3..$	0.65	[Assumed]
$\rho_i, i = 1,2,3$	0.322	[Assumed]
$\upsilon_{i,} i = 1,2,3$	0.0169	Su *et al*., 2016
θ_1	1.6949	Assumed
$\theta_1, i = 2,3..$	1.6949	Lu *et al*., 2020

d_a	0.333yr−1	Mukandavire *et al.*, 2010
d_c	0.005	WHO, 2019
$\psi\ \xi$	0.02	Abu-Raddad et al., 2010
$1/\sigma_c$	5.8months	Yovanna *et al*., 2013
η	0.43	
$r_i, i = 1,2, \ldots$	3.3	Elbasha, 2013
ω	0.25	Ingiliz *et al*., 2017
ε_1	2.23	Yovanna *et al*., 2013
ε_2	1.15	
$\kappa_i, i = 1,2$	1.0002	[Assumed]

3.3 Model Analysis

In this section, HIV and HCV are analyzed independently. Thereafter, the co-infection analyses is been carried out.

Three (3) cases shall be considered in this section:

Case 1: HIV analysis

Case 2: HCV analysis

Case 3: HIV and HCV co-infection.

3.4 Case 1: HIV Model Analysis

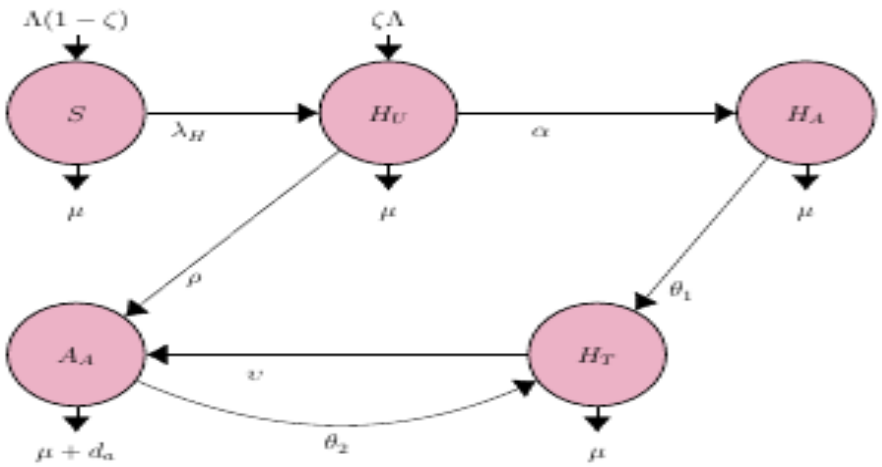

Figure 3.2: The Compartmental Flow Diagram of the HIV model

HIV only model occur by setting $[I_C = C_C = H_{UI} = H_{UC} = H_{AI} = H_{AC} = H_{TI} = H_{TC} = A_{AI} = A_{AC} = 0]$ in the system (3.3), and this gives

$$\begin{aligned}
\frac{dS}{dt} &= (1-\varphi H_U)\Lambda - (\lambda_H + \mu)S \\
\frac{dH_U}{dt} &= \lambda_H S + \varphi\Lambda H_U - (\alpha + \rho + \mu)H_U \\
\frac{dH_A}{dt} &= \alpha H_U - (\theta_1 + \mu)H_A \\
\frac{dH_T}{dt} &= \theta_1 \mathrm{H_A} + \theta_2 A_A - (\upsilon + \mu)H_T \\
\frac{dA_A}{dt} &= \upsilon \mathrm{H_T} + \rho H_U - (\theta_2 + \mu + d_a)A_A
\end{aligned} \qquad (3.5)$$

Where $\lambda_H = c(1-\psi\xi)b_h \frac{H_U+H_A+A_A}{N_h}$, with total population given as

$$N_h(t) = S(t) + H_U(t) + H_A(t) + H_T(t) + A_A(t) \qquad (3.6)$$

3.4.1 Basic Properties of the Model Case 1

Here, considering equation (3.5), there is a need to show that the state variables are always positive and that the solution is always positive as long as $t \geq 0$. In this case, it is assumed that all parameters in the model are positive. The possible solutions are shown to be bounded in the region:

$\Omega = \{\big(S(t), H_U(t), H_A(t), H_T(t), A_A(t)\big) \in \mathbb{R}_+^5 : N(t) \leq 0.$

3.4.1.1 Positivity and Boundedness of Solution

The following theorems are considered:

Theorem 3.1: Let $\Omega = \{\big(S(t), H_U(t), H_A(t), H_T(t), A_A(t)\big) \in \mathbb{R}_+^5 : N(t) \leq 0.\}$ by the set of possible solution of equation (3.5), then the solution set $\{\big(S(t), H_U(t), H_A(t), H_T(t), A_A(t)\big)\}$ is positive for all $t \geq 0$ if the initial values of the parameters are $\{(S(t) \geq 0, H_U(t) \geq 0, H_A(t) \geq 0, H_T(t) \geq 0, A_A(t) \geq 0 \; and \; N(0) \geq 0)\} \in \Omega$,

Proof:

The first equation from model (3.5) is

$$\frac{dS}{dt} = (1 - \varphi H_U)\Lambda - \left(c(1 - \psi\xi)b_h \frac{H_U + H_A + A_A}{N_h} + \mu\right)S$$

We have

$$\frac{dS}{dt} \geq -\left(c(1 - \psi\xi)b_h \frac{H_U + H_A + A_A}{N_h} + \mu\right)S$$

$$\int \frac{1}{S} dS \geq \int -\left(c(1 - \psi\xi)b_h \frac{H_U + H_A + A_A}{N_h} + \mu\right)dt$$

$$S \geq S_0 e^{-\left(c(1-\psi\xi)b_h \frac{H_U+H_A+A_A}{N_h}+\mu\right)t} \geq 0$$

Thus, $S \geq 0$.

Considering the second equation in model (3.5)

$$\frac{dH_U}{dt} = \lambda_H S + \varphi \Lambda H_U - (\alpha\ + \rho + \mu)H_U$$

$$\frac{dH_U}{dt} \geq -(\alpha\ + \rho + \mu)H_U$$

$$\int \frac{1}{H_U} dH_U \geq \int -(\alpha\ + \rho + \mu)\, dt$$

$H_U \geq H_{U0} e^{-(\alpha\ +\rho+\mu)t} \geq 0$.

So, $H_U \geq 0$

The third equation in (3.5),

$$\frac{dH_A}{dt} = \alpha H_U - (\theta_1 + \mu)H_A$$

$$\frac{dH_A}{dt} \geq -(\theta_1 + \mu)H_A$$

$$\int \frac{1}{H_A} dH_A \geq \int -(\theta_1 + \mu)\, dt$$

$H_A \geq H_{A0} e^{-(\theta_1+\mu)t} \geq 0$.

Hence, $H_A \geq 0$.

The fourth equation in (3.5),

$$\frac{dH_T}{dt} = \theta_1 \mathrm{H_A} + \theta_2 A_A - (\upsilon + \mu) H_T$$

We have

$$\frac{dH_T}{dt} \geq -(\upsilon + \mu) H_T$$

$$\int \frac{1}{H_T} dH_T \geq \int -(\upsilon + \mu)\, dt$$

$H_T \geq H_{T0} e^{-(\upsilon+\mu)t} \geq 0$.

Hence, $H_T \geq 0$

The fifth equation five in (3.5),

$$\frac{dA_A}{dt} = \upsilon \mathrm{H_T} + \rho H_U - (\theta_2 + \mu + d_a) A_A$$

We have

$$\frac{dA_A}{dt} \geq -(\theta_2 + \mu + d_a) A_A$$

$$\int \frac{1}{A_A} dA_A \geq \int -(\theta_2 + \mu + d_a)\, dt$$

$$A_A \geq A_{A0} e^{-(\theta_2+\mu+d_a)t} \geq 0$$

Hence, $A_A \geq 0$.

The proof above establishes that the state variables are positive on the $\mathbb{R}^5_+$ boundary.

Theorem 3.2:

For any time $t \geq 0$, the solution for the system (3.5) is confined and stays within the region Ω.

Proof:

Recall, the entire population size in equation (3.6). Differentiating (3.6) we have

$$N_h{}'(t) = S' + H_U' + H_A' + H_T' + A_A' \quad (3.7)$$

By substituting the derivatives of (3.7) with respect to t into the systems of the equation in (3.5), we obtain

$$N_h{}' = (1-\varphi H_U)\Lambda - (\lambda_H + \mu)S + \lambda_H S + \varphi\Lambda H_U - (\alpha + \rho + \mu)H_U + \alpha H_U - (\theta_1 + \mu)H_A +$$

$$\theta_1 \mathrm{H_A} + \theta_2 A_A - (\upsilon + \mu)H_T + \upsilon \mathrm{H_T} + \rho H_U - (\theta_2 + \mu + d_a)A_A \quad (3.8)$$

Simplifying (3.8) gives:

$$N_h{}' = \Lambda - \mu(S + H_U(t) + H_A(t) + H_T(t) + A_A(t)) + d_a A_A \quad (3.9)$$

$$N_h{}' = \Lambda - \mu \mathrm{N} + d_a A_A \quad (3.10)$$

$$N_h{}' \leq \Lambda - \mu \mathrm{N} \quad (3.11)$$

Integrating (3.11) gives:

$$N_h{}' \leq \frac{\Lambda}{\mu} + ke^{-\mu t}$$

$$\max_{\lim_{n\to\infty}} N_h \leq \lim_{n\to\infty}\left(\frac{\Lambda}{\mu} + ke^{-\mu t}\right) \leq \frac{\Lambda}{\mu}$$

The solutions (3.5) of the model system are positive and have limits in the region

$$\Omega = \{(S + H_U + H_A + H_T + A_A)\} \in \mathbb{R}_+^5 : S + H_U + H_A + H_T + A_A \leq \frac{\Lambda}{\mu}$$

A well-posed model can be defined as one containing the system dynamics (3.5), based on Theorems 3.1 and 3.2.

3.4.1.2 The Existence and Uniqueness of Solution for the Model

The validity and usability of any mathematical model depend on whether the given equation has a

solution. If it has, is the solution unique? This subsection is concerned with showing if the system of the equation has a solution and if the solution to the system is unique. Using the Lipschitz condition to verify the existence and uniqueness of the system of equations from theorem 2.1 in the review of methodologies, the interest is in the region $0 \leq \propto \leq \mathbb{R}$.

Let

$$\left.\begin{aligned}
&\frac{dS}{dt} = (1-\varphi H_U)\Lambda - (\lambda_H + \mu)S, && S(t_0) = S_0 \\
&\frac{dH_U}{dt} = \lambda_H S + \varphi\Lambda H_U - (\alpha\ + \rho + \mu)H_U, && H_U(t_0) = H_{U0} \\
&\frac{dH_A}{dt} = \alpha H_U - (\theta_1 + \mu)H_A, && H_A(t_0) = H_{A0} \\
&\frac{dH_T}{dt} = \theta_1 \mathrm{H_A} + \theta_2 A_A - (\upsilon + \mu)H_T, && H_T(t_0) = H_{T0} \\
&\frac{dA_A}{dt} = \upsilon \mathrm{H_T} + \rho H_U - (\theta_2 + \mu + d_a)A_A, && A_A(t_0) = A_{A0}
\end{aligned}\right\} \qquad (3.12)$$

Where $f_i = (S, H_U, H_A, H_T, A_A)$

Theorem 3.3:

Let D' represent the area $0 \leq \alpha\ \leq R$. Then equation (3.5) has a distinct solution in D', we then prove that $\frac{\partial f_i}{\partial x_j}, i, j = 1,2,3,4,5$ are continuous and bounded.

Proof:

Let $D = \{\big|(S, H_U, H_A, H_T, A_A)t)\ ||S - S_0| \leq a, |H_u - H_{u0}| \leq b, |H_A - H_{A0}| \leq c, |H_T - H_{T0}| \leq d, |A_A - A_{A0}| \leq e\big|\}$

Now,

$$\frac{dS}{dt} = f_1(S, H_U, H_A, H_T, A_A) = (1-\varphi H_U)\Lambda - (\lambda_H + \mu)S, \qquad S(t_0) = S_0 \qquad (3.13)$$

$$\frac{dH_U}{dt} = f_2(S, H_U, H_A, H_T, A_A) = \lambda_H S + \varphi\Lambda H_U - (\alpha\ + \rho + \mu)H_U, \quad H_U(t_0) = H_{U0} \qquad (3.14)$$

$$\frac{dH_A}{dt} = f_3(S, H_U, H_A, H_T, A_A) = \alpha H_U - (\theta_1 + \mu)H_A, \qquad H_A(t_0) = H_{A0} \qquad (3.15)$$

$$\frac{dH_T}{dt} = f_4(S, H_U, H_A, H_T, A_A) = \theta_1 \mathrm{H_A} + \theta_2 A_A - (\upsilon + \mu)H_T, \qquad H_T(t_0) = H_{T0} \qquad (3.16)$$

$$\frac{dA_A}{dt} = f_5(S, H_U, H_A, H_T, A_A) = \upsilon \mathrm{H_T} + \rho H_U - (\theta_2 + \mu + d_a)A_A, \qquad A_A(t_0) = A_{A0} \qquad (3.17)$$

From (3.13), the partial derivatives below are derived

$$\left|\frac{\partial f_1}{\partial S}\right| = \left|-(\frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)}{N_h} - \frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2} + \mu)\right| < \infty;\ \left|\frac{\partial f_1}{\partial H_U}\right| =$$

$$\left|-(\varphi\Lambda + \frac{cb_h(1-\psi\xi)\,S}{N_h} - \frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2})\right| < \infty;\ \left|\frac{\partial f_1}{\partial H_A}\right| =$$

$$\left|\frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2} - \frac{cb_h(1-\psi\xi)\,S}{N_h}\right| < \infty; \left|\frac{\partial f_1}{\partial H_T}\right| = \left|\frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2}\right| <$$

$$\infty; \left|\frac{\partial f_1}{\partial A_A}\right| = \left|\frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2} - \frac{cb_h(1-\psi\xi)\,S}{N_h}\right| < \infty$$

These partial derivatives exist, continuous and bounded. Similarly, from equations (3.14) - (3.17),

$$\left|\frac{\partial f_2}{\partial S}\right| = \left|-\frac{cb_h(1-\psi\xi)\,(H_U+H_A+A_A)S}{N_h^2} + \frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)}{N_h}\right| < \infty;\ \left|\frac{\partial f_2}{\partial H_U}\right| = \left|\varphi\Lambda + \frac{cb_h(1-\psi\xi)\,S}{N_h} -\right.$$

$$\left.(\frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2} + \alpha\ + \rho + \mu)\right| < \infty;\ \left|\frac{\partial f_2}{\partial H_A}\right| = \left|\frac{cb_h(1-\psi\xi)\,S}{N_h} - \frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2}\right| <$$

$$\infty; \left|\frac{\partial f_2}{\partial H_T}\right| = \left|-\frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2}\right| < \infty; \left|\frac{\partial f_2}{\partial A_A}\right| = \left|\frac{cb_h(1-\psi\xi)\,S}{N_h} - (\frac{cb_h(1-\psi\xi)(H_U+H_A+A_A)\,S}{N_h^2}\right| <$$

$$\infty$$

$$\left|\frac{\partial f_3}{\partial S}\right| = 0 < \infty;\ \left|\frac{\partial f_2}{\partial H_U}\right| = |\alpha| < \infty;\ \left|\frac{\partial f_3}{\partial H_A}\right| = |-(\theta_1 + \mu)| < \infty; \left|\frac{\partial f_3}{\partial H_T}\right| = 0 < \infty; \left|\frac{\partial f_3}{\partial A_A}\right| = 0 < \infty$$

$$\left|\frac{\partial f_4}{\partial S}\right| = 0 < \infty;\ \left|\frac{\partial f_4}{\partial H_U}\right| = 0 < \infty;\ \left|\frac{\partial f_4}{\partial H_A}\right| = |\theta_1| < \infty; \left|\frac{\partial f_4}{\partial H_T}\right| = |-(\upsilon + \mu)| < \infty; \left|\frac{\partial f_4}{\partial A_A}\right| = |\theta_2| < \infty$$

$$\left|\frac{\partial f_5}{\partial S}\right| = 0 < \infty;\ \left|\frac{\partial f_5}{\partial H_U}\right| = |\rho| < \infty;\ \left|\frac{\partial f_5}{\partial H_A}\right| = 0 < \infty; \left|\frac{\partial f_5}{\partial H_T}\right| = |\upsilon| < \infty; \left|\frac{\partial f_5}{\partial A_A}\right| = |-(\theta_2 + \mu +$$

$$d_a)| < \infty$$

There are finite and bounded partial derivatives of the whole system of equations, as illustrated above. Therefore, based on Theorem 3.3, a unique solution exists for the model system (3.13) - (3.17).

3.4.2 Points of Equilibrium and the Reproduction Numbers

When there is no infection $H_U = H_A = H_T = A_A = 0$, the system of equations in (3.5) possesses equilibrium that is disease-free, as follows:

$$E_o = (S, H_U, H_A, H_T, A_A) = \left[\frac{\Lambda}{\mu}, 0,0,0,0\right] \tag{3.18}$$

The total population changes proportionately to the recruitment and death rates in the absence of infection.

For the endemic equilibrium, there is an existence of infection hence $H_U \neq H_A \neq H_T \neq A_A \neq 0$. The total population dynamics can be altered when an individual with a disease is introduced into a population. By setting the equation system in (3.5) to zero and setting $S = S^*, H_U = H_U^*, H_A = H_A^*, H_T = H_T^*, and\ A_A = A_A^*$, which is present when $R_0 > 1$ exists, and the endemic steady states can be computed. So that,

$$\left.\begin{aligned} 0 &= (1 - \varphi H_U)\Lambda - (\lambda_H + \mu)S \\ 0 &= \lambda_H S + \varphi \Lambda H_U - (\alpha + \rho + \mu)H_U \\ 0 &= \alpha H_U - (\theta_1 + \mu)H_A \\ 0 &= \theta_1 \mathrm{H_A} + \theta_2 A_A - (\upsilon + \mu)H_T \\ 0 &= \upsilon \mathrm{H_T} + \rho H_U - (\theta_2 + \mu + d_a)A_A \end{aligned}\right\} \tag{3.19}$$

Solving equations (3.19) simultaneously give rise to:

$$\left.\begin{aligned} S^* &= \frac{\Lambda(\Lambda\varphi - k_1)}{\Lambda\mu\varphi - \lambda k_1 - \mu k_1} \\ H_U^* &= \frac{\Lambda\lambda}{\Lambda\mu\varphi - \lambda k_1 - \mu k_1} \\ H_A^* &= \frac{\Lambda\alpha\lambda}{(\Lambda\mu\varphi - \lambda k_1 - \mu k_1)k_2} \\ H_T^* &= \frac{(\alpha\theta_1 k_4 + \rho\theta_2 k_2)\Lambda\lambda}{(k_2(\Lambda\mu\upsilon\varphi\theta_2 - \Lambda\mu\varphi k_3 k_4 - \lambda\upsilon k_1\theta_2 + \lambda k_1 k_3 k_4 - \mu\upsilon k_1\theta_2 + \mu k_1 k_3 k_4))} \\ A_A^* &= \frac{\Lambda\lambda(\alpha\upsilon\theta_1 + \rho k_2 k_3)}{(k_2(\Lambda\mu\upsilon\varphi\theta_2 - \Lambda\mu\varphi k_3 k_4 - \lambda\upsilon k_1\theta_2 + \lambda k_1 k_3 k_4 - \mu\upsilon k_1\theta_2 + \mu k_1 k_3 k_4))} \end{aligned}\right\} \quad (3.20)$$

Where

$$\lambda = c(1-\psi\xi)b_h\frac{H_U + H_A + A_A}{N_h}, k_1 = \alpha + \rho + \mu, k_2 = \theta_1 + \mu, k_3 = \upsilon + \mu,$$

$$k_4 = \theta_2 + d_a + \mu$$

A next-generation matrix approach was used to compute the basic reproduction number. To determine the next-generation matrix for the model considered in HIV only sub-model case 1, R_{eH} the following are considered:

1. The number of ways that new infections can arise or be created

2. The number of ways that infections can be transferred between compartments

Rearranging equations (3.5) such that we start with the infective classes.

There are four infected classes in this model, the $H_U, H_A, H_T, and\ A_A$, hence our $m = 4$

F_i and V_i are then calculated as follows:

$$F = \begin{pmatrix} c(1-\psi\xi)b_h \dfrac{H_U + H_A + A_A}{N_h} S \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$$V_i^+ = \begin{pmatrix} \varphi\Lambda H_U \\ \alpha H_U \\ \theta_1 \mathrm{H_A} + \theta_2 A_A \\ \upsilon \mathrm{H_T} + \rho H_U \end{pmatrix}, V_i^- = \begin{pmatrix} (\alpha\ + \rho + \mu)H_U \\ (\theta_1 + \mu)H_A \\ (\upsilon + \mu)H_T \\ (\theta_2 + \mu + d_a)A_A \end{pmatrix}$$

$$V = V_i^- + V_i^+ = \begin{pmatrix} (\alpha\ + \rho + \mu - \varphi\Lambda)H_U \\ (\theta_1 + \mu)H_A - \alpha H_U \\ (\upsilon + \mu)H_T - \theta_1 \mathrm{H_A} - \theta_2 A_A \\ (\theta_2 + \mu + d_a)A_A - \upsilon \mathrm{H_T} - \rho H_U \end{pmatrix}$$

Disease-free equilibrium (DFE) evaluation of the F and V variational matrices

$E_{oH} = \left[\frac{\Lambda}{\mu}, 0,0,0,0\right]$ is given by

$$F = \begin{pmatrix} \dfrac{\partial f_1}{\partial H_U} & \dfrac{\partial f_1}{\partial H_A} & \dfrac{\partial f_1}{\partial H_T} & \dfrac{\partial f_1}{\partial A_A} \\ \dfrac{\partial f_2}{\partial H_U} & \dfrac{\partial f_2}{\partial H_A} & \dfrac{\partial f_2}{\partial H_T} & \dfrac{\partial f_2}{\partial A_A} \\ \dfrac{\partial f_3}{\partial H_U} & \dfrac{\partial f_3}{\partial H_A} & \dfrac{\partial f_3}{\partial H_T} & \dfrac{\partial f_3}{\partial A_A} \\ \dfrac{\partial f_4}{\partial H_U} & \dfrac{\partial f_4}{\partial H_A} & \dfrac{\partial f_4}{\partial H_T} & \dfrac{\partial f_4}{\partial A_A} \end{pmatrix} = \begin{pmatrix} c(1-\psi\xi)b_h & c(1-\psi\xi)b_h & 0 & c(1-\psi\xi)b_h \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \dfrac{\partial v_1}{\partial H_U} & \dfrac{\partial v_1}{\partial H_A} & \dfrac{\partial v_1}{\partial H_T} & \dfrac{\partial v_1}{\partial A_A} \\ \dfrac{\partial v_2}{\partial H_U} & \dfrac{\partial v_2}{\partial H_A} & \dfrac{\partial v_2}{\partial H_T} & \dfrac{\partial v_2}{\partial A_A} \\ \dfrac{\partial v_3}{\partial H_U} & \dfrac{\partial v_3}{\partial H_A} & \dfrac{\partial v_3}{\partial H_T} & \dfrac{\partial v_3}{\partial A_A} \\ \dfrac{\partial v_4}{\partial H_U} & \dfrac{\partial v_4}{\partial H_A} & \dfrac{\partial v_4}{\partial H_T} & \dfrac{\partial v_4}{\partial A_A} \end{pmatrix} = \begin{pmatrix} k_1 - \varphi\Lambda & 0 & 0 & 0 \\ -\alpha & k_2 & 0 & 0 \\ 0 & -\theta_1 & k_3 & -\theta_2 \\ -\rho & 0 & -\upsilon & k_4 \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{\varphi\Lambda - k_1} & 0 & 0 & 0 \\ \frac{\alpha}{k_2(\varphi\Lambda - k_1)} & \frac{1}{-k_2} & 0 & 0 \\ -\frac{\alpha k_4\theta_1 + \rho k_2\theta_2}{k_2(\varphi\Lambda - k_1)(\upsilon\theta_2 - k_3k_4)} & \frac{k_4\theta_1}{(\upsilon\theta_2 - k_3k_4)k_2} & \frac{k_4}{\upsilon\theta_2 - k_3k_4} & \frac{\theta_2}{\upsilon\theta_2 - k_3k_4} \\ -\frac{\alpha\upsilon\theta_1 + \rho k_2k_3}{k_2(\varphi\Lambda - k_1)(\upsilon\theta_2 - k_3k_4)} & \frac{\upsilon\theta_1}{k_2(\upsilon\theta_2 - k_3k_4)} & \frac{\upsilon}{\upsilon\theta_2 - k_3k_4} & \frac{k_3}{\upsilon\theta_2 - k_3k_4} \end{pmatrix}$$

FV^{-1}

$$= \begin{pmatrix} c(1-\psi\xi)b_h & c(1-\psi\xi)b_h & 0 & c(1-\psi\xi)b_h \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\varphi\Lambda - k_1} & 0 & 0 & 0 \\ \frac{\alpha}{k_2(\varphi\Lambda - k_1)} & \frac{1}{-k_2} & 0 & 0 \\ -\frac{\alpha k_4\theta_1 + \rho k_2\theta_2}{k_2(\varphi\Lambda - k_1)(\upsilon\theta_2 - k_3k_4)} & \frac{k_4\theta_1}{(\upsilon\theta_2 - k_3k_4)k_2} & \frac{k_4}{\upsilon\theta_2 - k_3k_4} & \frac{\theta_2}{\upsilon\theta_2 - k_3k_4} \\ -\frac{\alpha\upsilon\theta_1 + \rho k_2k_3}{k_2(\varphi\Lambda - k_1)(\upsilon\theta_2 - k_3k_4)} & \frac{\upsilon\theta_1}{k_2(\upsilon\theta_2 - k_3k_4)} & \frac{\upsilon}{\upsilon\theta_2 - k_3k_4} & \frac{k_3}{\upsilon\theta_2 - k_3k_4} \end{pmatrix}$$

The largest eigenvalue of the given matrix, denoted by $R_{\mathrm{eH}} = b_{\mathrm{U}} + b_{\mathrm{A}} + b_{\mathrm{Aa}}$, is its spectral radius, which is provided by $R_{eH} = \rho(FV^{-1}) = max(\lambda_1, \lambda_2, \lambda_3, \lambda_4)$.

Thus, R_{eH} is the dominant eigenvalue for the HIV-only model (the number of HIV infections produced by one HIV case). Hence

$$\left.\begin{aligned} b_{\mathrm{U}} &= \frac{c(1-\psi\xi)b_{\mathrm{h}}}{\Lambda\varphi - k_1} \\ b_{\mathrm{A}} &= \frac{c(1-\psi\xi)b_{\mathrm{h}}\alpha}{k_2(\Lambda\varphi - k_1)} \\ b_{\mathrm{Aa}} &= \frac{c(1-\psi\xi)b_{\mathrm{h}}(\alpha\upsilon\theta_1 + \rho k_2k_3)}{(\varphi\Lambda - k_1)k_2(\upsilon\theta_2 - k_3k_4)} \end{aligned}\right\} \qquad (3.21)$$

Therefore, the basic reproduction number denoted by R_{eH} after simplifying is

$$R_{\mathrm{eH}} = \frac{c(1-\psi\xi)b_{\mathrm{h}}((\alpha(\theta_1 - \theta_2) - k_2\theta_2)\upsilon + \big((k_4 + \rho)k_2 + k_4\alpha\big)k_3)}{k_2(k_3k_4 - \upsilon\theta_2)(k_1 - \Lambda\varphi)} \qquad (3.22)$$

3.4.3 Stability Analysis of the Model

3.4.3.1 An analysis of the stability of the HIV-free equilibrium in a local state, H_o

At the HIV disease-free equilibrium, H_0 the local stability of the equilibrium was investigated. Theorem 3.4 establishes the local stability of H_0, the HIV disease-free equilibrium.

Theorem 3.4:

If $R_{eH} < 1$, the disease-free equilibrium H_o is asymptotically stable locally, otherwise, it is unstable.

Proof:

In the linearized model, $\frac{dX}{dt} = AX$ is the resulting matrix.

$X = (x_1, x_2, x_3, x_4, x_5)^T, (x_1, x_2, x_3, x_4, x_5) \in R_+^5$, and

$$A = \begin{bmatrix} G_1 - \mu & -(\Lambda\varphi + G_2) & -G_2 & \frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)x_1}{x_1+x_2+x_3+x_4+x_5} & -G2 \\ -G_3 & \Lambda\varphi + G_4 - k_1 & G_4 & -\frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)x_1}{x_1+x_2+x_3+x_4+x_5} & G_4 \\ 0 & \alpha & -k_2 & 0 & 0 \\ 0 & 0 & \theta_1 & k_3 & \theta_2 \\ 0 & \rho & 0 & \upsilon & -k_4 \end{bmatrix} \quad (3.23)$$

Where

$$G_1 = \frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)x_1}{(x_1+x_2+x_3+x_4+x_5)^2} - \frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)}{x_1+x_2+x_3+x_4+x_5},$$

$$G_2 = \frac{c(1-\psi\xi)b_h x_1}{x_1+x_2+x_3+x_4+x_5} + \frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)x_1}{(x_1+x_2+x_3+x_4+x_5)^2},$$

$$G_3 = \frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)x_1}{(x_1+x_2+x_3+x_4+x_5)^2} + \frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)}{x_1+x_2+x_3+x_4+x_5},$$

$$G_4 = \frac{c(1-\psi\xi)b_h x_1}{x_1+x_2+x_3+x_4+x_5} - \frac{c(1-\psi\xi)b_h(x_2+x_3+x_5)x_1}{(x_1+x_2+x_3+x_4+x_5)^2}$$

The resulting Jacobian matrix of (3.23) at $H_o: S = \frac{\Lambda}{\mu}, H_U = 0,\ H_A = 0,\ H_T = 0,\ A_A = 0$ is

$|\ A(H_0) - \lambda I| =$

$$\begin{bmatrix} -\mu-\lambda & \Lambda\varphi - c(1-\psi\xi)b_h & -c(1-\psi\xi)b_h & 0 & -c(1-\psi\xi)b_h \\ 0 & \Lambda\varphi + c(1-\psi\xi)b_h - k_1 - \lambda & c(1-\psi\xi)b_h & 0 & c(1-\psi\xi)b_h \\ 0 & \alpha & -k_2-\lambda & 0 & 0 \\ 0 & 0 & \theta_1 & -k_3-\lambda & \theta_2 \\ 0 & \rho & 0 & \upsilon & -k_4-\lambda \end{bmatrix} = 0 \qquad (3.24)$$

Clearly from (3.24), two eigenvalues are $\lambda_1 = -\mu$, and 2nd is $\lambda_2 = -k_4$ (evaluate along the first column)), so that the remaining eigenvalues are obtained from the remaining $3X3$ matrix

$$H_0 = \begin{vmatrix} \Lambda\varphi + c(1-\psi\xi)b_h - k_1 - \lambda & c(1-\psi\xi)b_h & 0 \\ \alpha & -k_2-\lambda & 0 \\ 0 & \theta_1 & -k_3-\lambda \end{vmatrix} = 0 \qquad (3.25)$$

`The remaining 3 eigenvalues are determined by analyzing the 3x3 matrix in (3.25) using the Routh-Hurwitz condition`

` The condition is:`

` (1) $Trace\ (H_0) < 0$ (2) $Determinant(H_0) > 0$ `

Trace $(H_0) = \Lambda\varphi + c(1-\psi\xi)b_h - k_1 - k_2 - k_3 < 0$ and

$$\text{Determinant}(H_0) = k_3(\Lambda\varphi k_2 + \alpha c b_h + c b_h k_2 - \alpha c b_h \psi\xi - c b_h \psi\xi k_2 - k_1 k_2) > 0 \; if \; R_{eH} < 1$$

Then, since the values are assumed to be positive if, $\lambda_3, \lambda_4, \lambda_5 < 0$, if $R_{eH} < 1$, H_o is stable and unstable as long as $R_{eH} > 1$.

3.4.3.2 Global HIV Free Equilibrium Stability for the HIV Only Model

The global stability of the HIV-free equilibrium H_0 was investigated using the comparison method at the HIV disease-free equilibrium. The global stability of the HIV disease-free equilibrium H_0 is demonstrated by Theorem 3.5.

Theorem 3.5:

The HIV-free equilibrium H_0 of the system (3.5) is globally asymptotically stable if $R_{eH} < 1$ and unstable otherwise.

Proof:

Here, the Comparison theorem as described by (Lakshmikantham *et al*., 1989) and (Mushayabasa *et al*., 2011) is applied. The rate of change of the system's exposed and infected components (3.5) can be expressed as:

$$\begin{pmatrix} \frac{dH_U}{dt} \\ \frac{dH_A}{dt} \\ \frac{dH_T}{dt} \\ \frac{dA_A}{dt} \end{pmatrix} = (F - V)\begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \end{pmatrix} - \left(1 - \frac{S_h}{N_h}\right) F \begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \end{pmatrix}$$

Since the disease-free $H_U = H_A = H_T = A_A = 0 \rightarrow (0,0,0,0)$ and $S_h \leq N_h$, as $t \rightarrow \infty$ in Γ_{hv}, F and V are defined as described for system (3.5) in section 3.4.2. Thus,

$$\begin{pmatrix} \frac{dH_U}{dt} \\ \frac{dH_A}{dt} \\ \frac{dH_T}{dt} \\ \frac{dA_A}{dt} \end{pmatrix} \leq \left(\begin{pmatrix} (c(1-\psi\xi)b_h + \Lambda\varphi - k_1) & c(1-\psi\xi)b_h & 0 & c(1-\psi\xi)b_h \\ \alpha & -k_2 & 0 & 0 \\ 0 & \theta_1 & -k_3 & \theta_2 \\ \rho & 0 & \upsilon & -k_4 \end{pmatrix} \right) \begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \end{pmatrix}$$

$$\begin{pmatrix} \frac{dH_U}{dt} \\ \frac{dH_A}{dt} \\ \frac{dH_T}{dt} \\ \frac{dA_A}{dt} \end{pmatrix} \leq (F - V) \begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \end{pmatrix}$$

Since all matrix $(F - V)$ eigenvalues have negative real components, we can say that

$$\begin{vmatrix} (c(1-\psi\xi)b_h + \Lambda\varphi - k_1 - \lambda) & c(1-\psi\xi)b_h & 0 & c(1-\psi\xi)b_h \\ \alpha & -k_2 - \lambda & 0 & 0 \\ 0 & \theta_1 & -k_3 - \lambda & \theta_2 \\ \rho & 0 & \upsilon & -k_4 - \lambda \end{vmatrix} = 0 \qquad (3.26)$$

Evaluating (3.26) along the first column gives the characteristic equation

$$(c(1-\psi\xi)b_h + \Lambda\varphi - k_1 - \lambda)(-k_2 - \lambda)(-k_3 - \lambda)(-k_4 - \lambda) - c(1-\psi\xi)b_h\theta_1\alpha\upsilon = 0$$

$$\lambda^4 + (cb_h\psi\xi - \Lambda\varphi - cb_h + k_2 + k_3 + k_4 + k_1)\lambda^3 + (\alpha cb_h\psi\xi + cb_h\rho\psi\xi + cb_hk_2\psi\xi +$$

$$cb_hk_3\psi\xi + cb_hk_4\psi\xi - \Lambda\varphi k_2 - \Lambda\varphi k_3 - \alpha cb_h - \rho cb_h - ck_2b_h - ck_3b_h - ck_4b_h - \upsilon\theta_2 +$$

$$k_2k_3 + k_2k_4 + k_2k_1 + k_4k_3 + k_3k_1 + k_4k_1)\lambda^2 + (\alpha cb_h\psi\xi k_3 + \alpha cb_h\psi\xi k_4 + cb_h\rho\psi\xi k_2 +$$

$$cb_h\rho\psi\xi k_3 - cb_h\psi\xi\upsilon\theta_2 + cb_h\psi\xi k_2k_3 + cb_h\psi\xi k_2k_4 + cb_h\psi\xi k_3k_4 + \Lambda\upsilon\varphi\theta_2 - \Lambda\varphi k_2k_3 -$$

$\Lambda\varphi k_2k_4 - \Lambda\varphi k_3k_4 - \alpha cb_hk_3 - \alpha cb_hk_4 - cb_h\rho k_2 - cb_h\rho k_3 + cb_h\upsilon\theta_2 - cb_hk_2k_3 -$
$cb_hk_2k_4 - cb_hk_3k_4 - \upsilon k_2\theta_2 - \upsilon k_1\theta_2 + k_2k_3k_4 + k_1k_2k_3 + k_1k_2k_4 + k_1k_3k_4)\lambda +$
$\alpha cb_h\upsilon\psi\xi\theta_1 - \alpha cb_h\upsilon\psi\xi\theta_2 + \alpha cb_h\psi\xi k_3k_4 + cb_h\rho\psi\xi k_2k_3 - cb_h\upsilon\psi\xi k_2\theta_2 + cb_h\psi\xi k_2k_3k_4 +$
$\Lambda\upsilon\varphi k_2\theta_2 - \Lambda\varphi k_2k_3k_4 - \alpha cb_h\upsilon\theta_1 + \alpha cb_h\upsilon\theta_2 - \alpha cb_hk_3k_4 - cb_h\rho k_2k_3 + cb_h\upsilon k_2\theta_2 -$
$cb_hk_2k_3k_4 - \upsilon k_1k_2\theta_2 + k_1k_2k_3k_4 = 0$ (3.27)

By Descartes' rule of signs, (3.27) has four negative roots if

$(\alpha cb_h\upsilon\psi\xi\theta_1 - \alpha cb_h\upsilon\psi\xi\theta_2 + \alpha cb_h\psi\xi k_3k_4 + cb_h\rho\psi\xi k_2k_3 - cb_h\upsilon\psi\xi k_2\theta_2 + cb_h\psi\xi k_2k_3k_4 +$
$\Lambda\upsilon\varphi k_2\theta_2 - \Lambda\varphi k_2k_3k_4 - \alpha cb_h\upsilon\theta_1 + \alpha cb_h\upsilon\theta_2 - \alpha cb_hk_3k_4 - cb_h\rho k_2k_3 + cb_h\upsilon k_2\theta_2 -$
$cb_hk_2k_3k_4 - \upsilon k_1k_2\theta_2 + k_1k_2k_3k_4) < \langle(cb_h\psi\xi - \Lambda\varphi - cb_h + k_2 + k_3 + k_4 + k_1) +$
$(\alpha cb_h\psi\xi + cb_h\rho\psi\xi + cb_hk_2\psi\xi + cb_hk_3\psi\xi + cb_hk_4\psi\xi - \Lambda\varphi k_2 - \Lambda\varphi k_3 - \alpha cb_h - \rho cb_h -$
$ck_2b_h - ck_3b_h - ck_4b_h - \upsilon\theta_2 + k_2k_3 + k_2k_4 + k_2k_1 + k_4k_3 + k_3k_1 + k_4k_1)(\alpha cb_h\psi\xi k_3 +$
$\alpha cb_h\psi\xi k_4 + cb_h\rho\psi\xi k_2 + cb_h\rho\psi\xi k_3 - cb_h\psi\xi\upsilon\theta_2 + cb_h\psi\xi k_2k_3 + cb_h\psi\xi k_2k_4 +$
$cb_h\psi\xi k_3k_4 + \Lambda\upsilon\varphi\theta_2 - \Lambda\varphi k_2k_3 - \Lambda\varphi k_2k_4 - \Lambda\varphi k_3k_4 - \alpha cb_hk_3 - \alpha cb_hk_4 - cb_h\rho k_2 -$
$cb_h\rho k_3 + cb_h\upsilon\theta_2 - cb_hk_2k_3 - cb_hk_2k_4 - cb_hk_3k_4 - \upsilon k_2\theta_2 - \upsilon k_1\theta_2 + k_2k_3k_4 + k_1k_2k_3 +$
$k_1k_2k_4 + k_1k_3k_4)\rangle$

J is a positive matrix because $S(t) \leq \frac{\Lambda}{\mu}$ in the invariant set. Consequently, it follows that $\frac{dx}{dt} \leq$
$(F - V)X$

When $R_{\mathrm{eH}} < 1$, the eigenvalues of the matrix $F - V$ are negative. The linearized differential inequality (3.27) is therefore stable whenever $R_{eH} < 1$. The result is that $(H_U, H_A, H_T, A_A) \rightarrow$ (0,0,0,0) as $t \rightarrow \infty$. System (3.5) evaluation at $H_U = H_A = H_T = A_A = 0$ yields $S_h \rightarrow 1$ for $R_{eH} <$ 1. Therefore, if $R_{eH} < 1$, the HIV-free equilibrium H_0 of the system (3.5) is globally

asymptotically stable. If $R_{eH} > 1$, it immediately follows that the HIV disease-free equilibrium H_0 of the system (3.5) is unstable.

3.4.3.3 HIV Endemic Equilibrium's Local Asymptotic Stability

Theorem 3.6:

If $R_{eH} > 1$, the endemic equilibrium is asymptotically stable locally.

Proof:

The system's endemic equilibria (3.5), which are shown by $(S^*, H_U^*, H_A^*, H_T^*, A_A^*)$, can also be written as:

Let $S = x + S^*, H_U = y + H_U^*, H_A = z + H_A^*, H_T = j + H_T^*, A_A = p + A_A^*$

From (3.23)

$E^*|A - \lambda I| =$

$$\begin{pmatrix} G_1 - \mu - \lambda & -(\Lambda\varphi + G_2) & -G_2 & \frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)S^*}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} & -G2 \\ -G_3 & \Lambda\varphi+G_4 - k_1 - \lambda & G_4 & -\frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)S^*}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} & G_4 \\ 0 & \alpha & -k_2 - \lambda & 0 & 0 \\ 0 & 0 & \theta_1 & k_3 - \lambda & \theta_2 \\ 0 & \rho & 0 & \upsilon & -k_4 - \lambda \end{pmatrix} = 0$$

Considering the upper triangular matrix

$$E^* = \begin{pmatrix} G_1 - \mu - \lambda & -(\Lambda\varphi + G_2) & -G_2 & \frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)S^*}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} & -G2 \\ 0 & \Lambda\varphi+G_4-k_1-\lambda & G_4 & -\frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)S^*}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} & G_4 \\ 0 & 0 & -k_2-\lambda & 0 & 0 \\ 0 & 0 & 0 & k_3-\lambda & \theta_2 \\ 0 & 0 & 0 & 0 & -k_4-\lambda \end{pmatrix} = 0 \quad (3.28)$$

From (3.28)

1. $\text{Trace} = -\frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)S^*}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} + \frac{c(1-\psi\xi)b_hS^*}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} - \mu + \Lambda\varphi - k_1 - k_2 - k_3 - k_4$
2. $\text{Determinant} = (\frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)S^*}{(S^*+H_U^*+H_A^*+H_T^*+A_A^*)^2} - \frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} - \mu)(\Lambda\varphi +$

   $\frac{c(1-\psi\xi)b_hS^*}{S^*+H_U^*+H_A^*+H_T^*+A_A^*} - \frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)S^*}{(S^*+H_U^*+H_A^*+H_T^*+A_A^*)^2} - k_1)k_2k_3k_4$

` (1) $\text{Trace}\,(H_0) < 0$ (2) $\text{Determinant}(H_0) > 0$

The itemize 1 and 2 are satisfied by equation (3.28).

As a result, endemic equilibrium is asymptotically stable locally.

3.4.3.4 Stability of Global Endemic Equilibrium

Theorem 3.7:

The model equation (3.5) have a globally asymptotically stable positive distinctive endemic equilibrium whenever $R_{eH} > 1$, which is denoted by the term asymptotically stable.

Proof:

Taking into account the Lyapunov function defined as:

$$L(S^*, H_U^*, H_A*, H_T^*, A_A^*) = \left(S - S^* ln\left(\frac{S}{S^*}\right)\right) + \left(H_U - H_U^* ln\left(\frac{H_U}{H_U^*}\right)\right) + \left(H_A - H_A^* ln\left(\frac{H_A}{H_A^*}\right)\right) +$$

$$\left(H_T - H_T^* ln\left(\frac{H_T}{H_T^*}\right)\right) + \left(A_A - A_A^* ln\left(\frac{A_A}{A_A^*}\right)\right) \quad (3.29)$$

where L's derivative is taken directly along the system as:

$$\frac{dL}{dt} = (1 - \frac{S^*}{S})\frac{dS}{dt} + (1 - \frac{H_U^*}{H_U})\frac{dH_U}{dt} + (1 - \frac{H_A^*}{H_A})\frac{dH_A}{dt} + (1 - \frac{H_T^*}{H_T})\frac{dH_T}{dt} + (1 - \frac{A_A^*}{A_A})\frac{dA_A}{dt} \quad (3.30)$$

$$\begin{aligned}\frac{dL}{dt} = (1 - \frac{S^*}{S})\langle \Lambda(1 - \varphi H_U) - ((\frac{cb_h(1 - \psi\xi)b_{\mathrm{h}}(H_U + H_A + A_A)}{N}) + \mu)S\rangle + (1 \\ - \frac{H_U^*}{H_U})\langle(\frac{cb_h(1 - \psi\xi)b_{\mathrm{h}}(H_U + H_A + A_A)}{N})S - (\alpha + \rho + \mu)H_U \\ + \Lambda\varphi H_U\rangle + (1 - \frac{H_A^*}{H_A})\langle\alpha H_U - (\theta_1 + \mu)H_A\rangle + (1 - \frac{H_T^*}{H_T})\langle\theta_1 H_A + \theta_2 A_A \\ - (\upsilon + \mu)H_T\rangle + (1 - \frac{A_A^*}{A_A})\langle\rho H_U + \upsilon H_T - (\theta_2 + d_a + \mu)A_A\rangle\end{aligned} \quad (3.31)$$

At equilibrium

$$\begin{aligned}\Lambda(1 - \varphi H_U) &= (\frac{cb_h(1-\psi\xi)b_{\mathrm{h}}(H_U+H_A+A_A)}{N})S^* + \mu S^* \\ (\alpha + \rho + \mu + \Lambda\varphi) &= (\frac{cb_h(1-\psi\xi)b_{\mathrm{h}}(H_U+H_A+A_A)}{N})S^* \\ (\theta_1 + \mu) &= \frac{\alpha H_U^*}{H_A^*} \\ (\upsilon + \mu) &= \frac{\theta_1 H_A^* + \theta_2 A_A^*}{H_T^*} \\ (\theta_2 + d_a + \mu) &= \frac{\rho H_U^*}{A_A^*} + \frac{\upsilon H_T^*}{A_A^*}\end{aligned} \quad (3.32)$$

Substituting (3.32) in (3.31)

$$\frac{dL}{dt} = (1-\frac{S^*}{S})\langle(\frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)}{N^*})S^* + \mu S^* - \langle(\frac{c(1-\psi\xi)b_h(H_U+H_A+A_A)}{N}) + \mu)S\rangle + (1-$$

$$\frac{H_U^*}{H_U})\langle(\frac{c(1-\psi\xi)b_h(H_U+H_A+A_A)}{N})S - (\frac{c(1-\psi\xi)b_h(H_U^*+H_A^*+A_A^*)}{H_U^*N^*})S^*H_U + (1-\frac{H_A^*}{H_A})\langle\alpha H_U - (\frac{\alpha H_U^*}{H_A^*})H_A\rangle +$$

$$(1-\frac{H_T^*}{H_T})\langle(\theta_1 H_A + \theta_2 A_A) - (\frac{\theta_1 H_A^* + \theta_2 A_A^*}{H_T})H_T + (1-\frac{A_A^*}{A_A})\langle\rho H_U + \upsilon H_T - (\frac{\rho H_U^*}{A_A^*} + \frac{\upsilon H_T^*}{A_A^*})A_A\rangle \qquad (3.33)$$

Expanding (3.33)

$$= (1-\frac{S^*}{S})\langle\frac{cb_h(1-\psi\xi)H_U^*}{N^*}S^* + \frac{cb_h(1-\psi\xi)H_A^*}{N^*}S^* + \frac{cb_H(1-\psi\xi)A_A^*}{N^*}S^* + \mu S^* - \frac{cb_h(1-\psi\xi)H_U}{N}S -$$

$$\frac{cb_h(1-\psi\xi)H_A}{N}S - \frac{cb_h(1-\psi\xi)A_A}{N}S - \mu S\rangle + (1-\frac{H_U^*}{H_U})\langle\frac{cb_h(1-\psi\xi)H_U}{N}S + \frac{cb_h(1-\psi\xi)H_A}{N}S +$$

$$\frac{cb_h(1-\psi\xi)A_A}{N}S - \frac{cb_h(1-\psi\xi)H_U^*S^*H_U}{H_U^*N^*} - \frac{cb_h(1-\psi\xi)H_A^*S^*H_U}{H_U^*N^*} - \frac{cb_h(1-\psi\xi)A_A^*S^*H_U}{H_U^*N^*}S\rangle + (1-\frac{H_A^*}{H_A})\langle\alpha H_U -$$

$$\frac{\alpha H_U^* H_A}{H_A^*}\rangle + (1-\frac{H_T^*}{H_T})(\theta_1 H_A + \theta_2 A_A - \frac{\theta_1 H_A^* H_T}{H_T} - \frac{\theta_2 A_A^* H_T}{H_T}) + (1-\frac{A_A^*}{A_A})\langle\rho H_U + \upsilon H_T - \frac{\rho H_U^* A_A}{A_A^*} - \frac{\upsilon H_T^* A_A}{A_A^*}\rangle$$

Expanding

$$= (1-\frac{S^*}{S})\langle\frac{cb_h(1-\psi\xi)H_U^*S}{N}(1-\frac{H_U^*S^*N}{H_USN^*}) - cb_h(1-\psi\xi)H_AS(1-\frac{H_A^*S^*N}{H_ASN^*}) - cb_h(1-\psi\xi)A_AS(1-$$

$$\frac{H_A^*S^*N}{A_ASN^*}) - \mu S(1-\frac{S^*}{S}) + (1-\frac{H_U^*}{H_U})\langle\frac{cb_h(1-\psi\xi)H_US}{N}(1-\frac{H_U^*S^*N}{H_U^*SN^*}) + \frac{cb_h(1-\psi\xi)H_AS}{N}(1-\frac{H_A^*S^*H_U}{H_ASH_U^*N^*}) +$$

$$\frac{cb_h(1-\psi\xi)A_AS}{N}(1-\frac{A_A^*S^*H_U}{A_ASH_U^*N^*})\rangle + (1-\frac{H_A^*}{H_A})\langle\alpha H_U(1-\frac{H_U^*}{H_U})(1-\frac{H_A^*}{H_A})(1-\frac{H_A^*}{H_A})\rangle + (1-\frac{H_T^*}{H_T})\langle(\theta_1 H_A(1-$$

$$\frac{H_A^*}{H_A})(1-\frac{H_T^*}{H_T})\rangle + (1-\frac{A_A^*}{A_A})\langle\rho H_U(1-\frac{H_U^*}{H_U})(1-\frac{A_A^*}{A_A}) + \upsilon H_T(1-\frac{A_T^*}{A_T}(1-\frac{A_A^*}{A_A})\rangle \qquad (3.34)$$

Simplifying (3.34)

$$= -\mu S(1-\frac{S^*}{S})^2 + P_1(S, H_U, H_A, H_T, A_A) + P_2(S, H_U, H_A, H_T, A_A)$$

where

$$P_1(S, H_U, H_A, H_T, A_A) = -\frac{cb_h(1-\psi\xi)H_U S}{N}(1-\frac{S^*}{S})(1-\frac{H_U^* S^* N}{H_U S N^*}) - \frac{cb_h(1-\psi\xi)H_A^* S^* N}{H_A S N^*}(1-\frac{S^*}{S})(1-$$

$$\frac{H_A^* S^* N}{H_A S N^*}) - \frac{cb_h(1-\psi\xi)A_A S}{N}(1-\frac{S^*}{S})(1-\frac{A_A^* S^* N}{A_A S N^*})$$

$$P_2(S, H_U, H_A, H_T, A_A,) = All \quad others$$

$$P_1 \leq 0 \quad whenever \quad H_U S N^* \geq H_U^* S^* N, \quad H_A S N^* \geq H_A^* S^* N, A_A S N^* \geq A_A^* S^* N \qquad (3.35)$$

$$P_2 \leq 0 \quad whenever \quad H_U * S N^* \geq H_U^* S^* N, \quad H_A S H_U^* N^* \geq H_A^* S^* H_U, A_A S H_U^* N^* \geq$$

$$A_A^* S^* H_U, H_U H_A^* \geq H_U^* H_A, H_T^* H_A, H_U A_A^* \geq H_U^* A_A, A_A \qquad (3.36)$$

Thus

$\frac{dL}{dt} \leq 0$ If (3.35) and (3.35) hold.

As a result, the equilibrium is globally asymptotically stable in the positive region R_+^5 according to the Lasalle theorem.

3.4.4 Bifurcation Analysis

Many traditional epidemic models contain thresholds, which are established by the basic reproductive process. In the feasible region, the HIV-free equilibrium of the equivalent model is globally stable if $R_{eH} \leq 1$, and if $R_{eH} > 1$, the model has a globally stable endemic equilibrium in addition to the unstable HIV-free equilibrium. This means that HIV is eradicated if $R_{eH} < 1$, and it persists in the population if $R_{eH} > 1$. Nonetheless, mounting evidence suggests that the basic reproductive number of HIV; R_{eH} alone is not enough to fully understand how HIV spreads

around the world. In fact, backward bifurcation with multiple endemic equilibria and Hopf bifurcation with a periodic solution can happen with some simple epidemiologic models (Hadler and Castillo-Chavez, 1995; Alexander and Moghades, 2004; 2005).

When R_{eH} is less than but close to one in a system with backward bifurcation, the model has two endemic equilibria, one of which is a saddle and the other of which is locally asymptotically stable.; however, When R_{eH} is greater than but close to one in a model with only forward bifurcation, the level (number of the fraction) of infective individuals is low. Even though the forward bifurcation model has a distinct endemic equilibrium, the level (or fraction) of infected individuals is higher when R_{eH} is greater than but close to one. For systems with backward bifurcation, there are typically two thresholds: $R_{eH} = R_c (0 < R_c < 1)$. At $R_{eH} = R_c$, a saddle-node bifurcation occurs, and at $R_{eH} = 1$, a backward bifurcation.

The center manifold theory is used in this study to perform bifurcation analysis at the disease-free equilibrium as presented in (Buonomo and Lacitignola, 2011).

The focus is now on the HIV disease-free equilibrium H_0, with the transcritical bifurcation at $R_{eH} = 1$ being investigated.

At the HIV-free equilibrium H_0, the Jacobian matrix of equation (3.24) is given as:

$$J(H_0) = \begin{bmatrix} -\mu & \Lambda\varphi - c(1-\psi\xi)b_h & -c(1-\psi\xi)b_h & 0 & -c(1-\psi\xi)b_h \\ 0 & \Lambda\varphi + c(1-\psi\xi)b_h - k_1 & c(1-\psi\xi)b_h & 0 & c(1-\psi\xi)b_h \\ 0 & \alpha & -k_2 & 0 & 0 \\ 0 & 0 & \theta_1 & -k_3 & \theta_2 \\ 0 & \rho & 0 & \upsilon & -k_4 \end{bmatrix} \quad (3.37)$$

Using the Centre Manifold Theorem 2.2.6, we can check if the system (3.5) undergoes a backward or forward bifurcation at $R_{eH} = 1$ as follows:

Recall that

$$R_{eH} = \frac{k_3((k_4+\rho)k_2 + k_4\alpha))((-k_2\theta_2 + \alpha(\theta_1 - \theta_2))\upsilon(1-\psi\xi)cb_h}{k_2(k_3k_4 - \upsilon\theta_2)(k_1 - \Lambda\varphi)}$$

Consider b_h =$b_h{}^*$ to be a bifurcation parameter if the case$R_{eH} = 1$ is considered.

By solving for $b_h = b_h{}^*$, then

$$\frac{k_3((k_4+\rho)k_2 + k_4\alpha))((\alpha(\theta_1 - \theta_2) - k_2\theta_2)\upsilon(1-\psi\xi)cb_h}{k_2(k_3k_4 - \upsilon\theta_2)(k_1 - \Lambda\varphi)} = 1$$

$$b_h = b_h{}^* = \frac{k_2(k_3k_4 - \upsilon\theta_2)(k_1 - \Lambda\varphi)}{k_3((k_4+\rho)k_2 + k_4\alpha))((\alpha(\theta_1 - \theta_2) - k_2\theta_2)\upsilon(1-\psi\xi)c} \qquad (3.38)$$

If $b_h < b_h{}^*$, then H_0, the HIV-free equilibrium, is locally stable, but if $b_h < b_h{}^*$, then H_0 is no longer stable. Therefore, $b_h = b_h{}^*$ is a bifurcation value, which is why it is a critical value. At $b_{h_H} = b_h{}^*$ (or equivalently at $R_{eH} = 1$), the HIV-free equilibrium H_0 undergoes a bifurcation, the nature of which is explored here.

To start, we calculate the Jacobian matrix of the system (3.5) at the origin $(H_0, b_h{}^*)$, as shown in the following equation.

$|J(H_0, b_h{}^*) - \lambda \mathrm{I}| =$

$$\begin{bmatrix} -\mu-\lambda & \Lambda\varphi - c(1-\psi\xi)b_h{}^* & -c(1-\psi\xi)b_h{}^* & 0 & -c(1-\psi\xi)b_h{}^* \\ 0 & \Lambda\varphi + c(1-\psi\xi)b_h{}^* - k_1 - \lambda & c(1-\psi\xi)b_h{}^* & 0 & c(1-\psi\xi)b_h{}^* \\ 0 & \alpha & -k_2-\lambda & 0 & 0 \\ 0 & 0 & \theta_1 & -k_3-\lambda & \theta_2 \\ 0 & \rho & 0 & \upsilon & -k_4-\lambda \end{bmatrix} = 0 \qquad (3.39)$$

has a zero eigenvalue, thus.

$|J(H_0, b_h{}^*) - \lambda \mathrm{I}| = 0$

$\lambda_1 = -\mu, \lambda_2 = -k_4,\ \lambda_3 = -k_2$ and the resulting quadratic equation is written as:

$$f(\lambda) = \lambda^2 + (b_h c\psi\xi - \Lambda\varphi - cb_h + k_1 + k_3)\lambda \tag{3.40}$$

By Descartes' rule of signs, the roots of (3.40), there are two negative eigenvalues. The assumptions of Theorem 2.2.6 (the Centre Manifold theorem) are thus confirmed, as $\lambda_4 = 0$ is a simple zero eigenvalue and the remaining eigenvalues are real and negative. The zero eigenvalue $\lambda_3 = 0$ is also connected with the right eigenvector, which can be found using the expression $w = (w_1, w_2, w_3, w_4, w_5)^T$.

$$\begin{bmatrix} -\mu & \Lambda\varphi - c(1-\psi\xi){b_h}^* & -c(1-\psi\xi){b_h}^* & 0 & -c(1-\psi\xi){b_h}^* \\ 0 & \Lambda\varphi + c(1-\psi\xi){b_h}^* - k_1 & c(1-\psi\xi){b_h}^* & 0 & c(1-\psi\xi){b_h}^* \\ 0 & \alpha & -k_2 & 0 & 0 \\ 0 & 0 & \theta_1 & -k_3 & \theta_2 \\ 0 & \rho & 0 & \upsilon & -k_4 \end{bmatrix} \begin{bmatrix} w_1 \\ w_2 \\ w_3 \\ w_4 \\ w_5 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \tag{3.41}$$

$$-\mu w_1 + (\Lambda\varphi - c(1-\psi\xi){b_h}^*)w_2 + (-c(1-\psi\xi){b_h}^*)w_3 + (-c(1-\psi\xi){b_h}^*)w_5 = 0 \tag{3.42}$$

$$(\Lambda\varphi + c(1-\psi\xi){b_h}^* - k_1)w_2 + (c(1-\psi\xi){b_h}^*)w_3 + (c(1-\psi\xi){b_h}^*)w_5 = 0 \tag{3.43}$$

$$\alpha w_2 + (-k_2)w_3 = 0 \tag{3.44}$$

$$\theta_1 w_3 + (-k_3)w_4 + \theta_2 w_5 = 0 \tag{3.45}$$

$$\rho w_2 + \upsilon w_4 + (-k_4)w_5 = 0 \tag{3.46}$$

Solving equations (3.42) - (3.46) simultaneously gives:

$$w_1 = \frac{w_5(\upsilon\theta_2 - k_3k_4)k_1k_2}{(\alpha\upsilon\theta_1 + \rho k_2k_3)\mu}$$

$$w_2 = -\frac{k_2 w_5(\upsilon\theta_2 - k_3 k_4)}{\alpha\upsilon\theta_1 + \rho k_2 k_3}$$

$$w_3 = -\frac{w_5\alpha(\upsilon\theta_2 - k_3 k_4)}{\alpha\upsilon\theta_1 + \rho k_2 k_3}$$

$$w_4 = \frac{(\alpha k_4\theta_1 + \rho k_2\theta_2)w_5}{\alpha\upsilon\theta_1 + \rho k_2 k_3}$$

Therefore

$$w = \left(\frac{w_5(\upsilon\theta_2 - k_3 k_4)k_1 k_2}{(\alpha\upsilon\theta_1 + \rho k_2 k_3)\mu}, -\frac{k_2 w_5(\upsilon\theta_2 - k_3 k_4)}{\alpha\upsilon\theta_1 + \rho k_2 k_3}, -\frac{w_5\alpha(\upsilon\theta_2 - k_3 k_4)}{\alpha\upsilon\theta_1 + \rho k_2 k_3}, \frac{(\alpha k_4\theta_1 + \rho k_2\theta_2)w_5}{\alpha\upsilon\theta_1 + \rho k_2 k_3}\right)^T$$

$w_5 > 0$ denotes a free right eigenvector.

Similarly, the left eigenvector corresponding to the zero eigenvalue $\lambda_1 = 0$ provided by

$\bar{v} = (\bar{v}_1, \bar{v}_2, \bar{v}_3, \bar{v}_4, \bar{v}_5)$ is

$$(\bar{v}_1, \bar{v}_2, \bar{v}_3, \bar{v}_4, \bar{v}_5)\begin{bmatrix} -\mu & \Lambda\varphi - c(1-\psi\xi){b_h}^* & -c(1-\psi\xi){b_h}^* & 0 & -c(1-\psi\xi){b_h}^* \\ 0 & \Lambda\varphi + c(1-\psi\xi){b_h}^* - k_1 & c(1-\psi\xi){b_h}^* & 0 & c(1-\psi\xi){b_h}^* \\ 0 & \alpha & -k_2 & 0 & 0 \\ 0 & 0 & \theta_1 & -k_3 & \theta_2 \\ 0 & \rho & 0 & \upsilon & -k_4 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad (3.47)$$

$$\bar{v}_1(-\mu) = 0 \quad (3.48)$$

$$\bar{v}_1(\Lambda\varphi - c(1-\psi\xi){b_h}^*) + \bar{v}_2(\Lambda\varphi + c(1-\psi\xi){b_h}^* - k_1) + \bar{v}_3\alpha + \bar{v}_5\rho = 0 \quad (3.49)$$

$$\bar{v}_1(-c(1-\psi\xi){b_h}^*) + \bar{v}_2(c(1-\psi\xi){b_h}^*) + \bar{v}_3(-k_2) + \bar{v}_4\theta_1 = 0 \quad (3.50)$$

$$\bar{v}_4(-k_3) + \bar{v}_5(\upsilon) = 0 \quad (3.51)$$

$$\bar{v}_1(-c(1-\psi\xi){b_h}^*) + \bar{v}_2(c(1-\psi\xi){b_h}^*) + \bar{v}_4\theta_2 + \bar{v}_5(-k_4) = 0 \qquad (3.52)$$

The simultaneous solution of equations (3.48) - (3.52) yields:

$$\bar{v}_1 = 0, \bar{v}_2 = -\frac{(\alpha\upsilon\theta_1 - \alpha\upsilon\theta_2 + \alpha k_3 k_4 + \rho k_2 k_3 - \upsilon k_2\theta_2 + k_2 k_3 k_4)l_4}{\upsilon k_2(\Lambda\varphi - k_1)}, \frac{(\upsilon\theta_1 - \upsilon\theta_2 + k_3 k_4)l_4}{\upsilon k_2}, \bar{v}_3 =$$

$$\frac{(\upsilon\theta_1 - \upsilon\theta_2 + k_3 k_4)l_4}{\upsilon k_2}, \bar{v}_5 = \frac{k_3 l_4}{\upsilon}$$

Therefore;

$$\bar{v} = \left(0, -\frac{(\alpha\upsilon\theta_1 - \alpha\upsilon\theta_2 + \alpha k_3 k_4 + \rho k_2 k_3 - \upsilon k_2\theta_2 + k_2 k_3 k_4)l_4}{\upsilon k_2(\Lambda\varphi - k_1)}, \frac{(\upsilon\theta_1 - \upsilon\theta_2 + k_3 k_4)l_4}{\upsilon k_2}, \frac{k_3 l_4}{\upsilon}\right)^T$$

where $\bar{v}_4 > 0$ is a free left eigenvector.

3.4.4.1 The Coefficients a and b Computation for HIV Model

The coefficients (as defined in theorem 2.2.6) are as follows:

$$a = \sum_{m,i,j=1}^{5} \bar{v}_m w_i w_j \frac{\partial^2 f_m(E_{0H}, {b_h}^*)}{\partial x_i \partial x_j}, b = \sum_{m,i,j=1}^{5} \bar{v}_m w_i \frac{\partial^2 f_m(E_{0h}, {b_h}^*)}{\partial x_i \partial \varphi}$$

can now be explicitly computed while considering the system (3.5) and considering only the non-zero components of the left eigenvector v, as follows:

$$S = x_1, H_U = x_2, H_A = x_3, H_T = x_4, A_A = x_5$$

Furthermore, introducing the vector $X = (x_1, x_2, x_3, x_4, x_5)^T$, then the model in the system (3.5) can now be written in the form

$\frac{dX}{dt} = f(x)$, where $f = (f_1, f_2, f_3, f_4, f_5)^T$

It means that you can write system (3.5) in terms of the new variables as:

$$\left.\begin{aligned}
\frac{dX_1}{dt} &= f_1 = (1-\varphi H_U)\Lambda - \left(\frac{c(1-\psi\xi)b_h(H_U+H_A+A_A)}{N} + \mu\right)S \\
\frac{dX_2}{dt} &= f_2 = \frac{c(1-\psi\xi)b_h(H_U+H_A+A_A)}{N}S + \varphi\Lambda H_U - (\alpha + \rho + \mu)H_U \\
\frac{dX_3}{dt} &= f_3 = \alpha H_U - (\theta_1 + \mu)H_A \\
\frac{dX_4}{dt} &= f_4 = \theta_1 \mathrm{H_A} + \theta_2 A_A - (\upsilon + \mu)H_T \\
\frac{dX_5}{dt} &= f_5 = \upsilon \mathrm{H_T} + \rho H_U - (\theta_2 + \mu + d_a)A_A
\end{aligned}\right\} \quad (3.53)$$

$$a = \frac{2l_2c(1-\psi\xi)b_h(Q_1-\frac{w_5\Lambda}{\mu})(Q_1-\frac{(\alpha k_4\theta_1+\rho k_2\theta_2)w_5\Lambda}{(\alpha\upsilon\theta_1+\rho k_2k_3)\mu}-\frac{w_5\Lambda}{\mu})\mu^3}{\Lambda^3}$$

$$b = \frac{(Q_2)l_4w_5(\upsilon\theta_2-k_3k_4)c(1-\psi\xi)}{\upsilon(\Lambda\varphi-k_1)(\alpha\upsilon\theta_1+\rho k_2k_3)} + \frac{(Q_2)l_4w_5\alpha(\upsilon\theta_2-k_3k_4)c(1-\psi\xi)}{\upsilon k_2(\Lambda\varphi-k_1)(\alpha\upsilon\theta_1+\rho k_2k_3)} - \frac{(Q_2)l_4w_5c(1-\psi\xi)}{\upsilon k_2(\Lambda\varphi-k_1)}$$

where

$$Q_1 = \frac{k_2w_5(\upsilon\theta_2-k_3k_4)\Lambda}{(\alpha\upsilon\theta_1+\rho k_2k_3)\mu} + \frac{w_5\alpha(\upsilon\theta_2-k_3k_4)\Lambda}{(\alpha\upsilon\theta_1+\rho k_2k_3)\mu}, Q_2$$

$$= \alpha\upsilon\theta_1 - \alpha\upsilon\theta_2 + \alpha k_3k_4 + \rho k_2k_3 - \upsilon k_2\theta_2 + k_2k_3k_4$$

Since the coefficient b is always positive, the theorem 2.2.6 says that the local dynamics around the HIV-free equilibrium for $b_h = b_h{}^*$ depend on the sign of the coefficient a. Thus, the following result is established.

1. A backward bifurcation occurs when $a > 0$.
2. If $a < 0$, there is a forward bifurcation.

The following outcomes from theorem 2.2.6 items (a) and (d) summarize the preceding discussion:

Lemma 3.1:

If $R_{eH} < 1$ otherwise stable, the HIV-only model of (3.5) has an unstable positive endemic equilibrium.

Lemma 3.2:

The HIV-only model of Equation (3.5) has a unique positive endemic equilibrium that is locally asymptotically stable (LAS) if $R_{eH} > 1$ and unstable otherwise.

Since $a < 0$, the local stability of H^* entails its global stability.

3.4.5 Sensitivity Indices of HIV Only Model Case 1

Knowing the relative relevance of the different factors involved in HIV transmission and prevalence is vital for determining how effectively to minimize HIV-related death and illness. In this subsection, a sensitivity analysis is conducted to evaluate the robustness of factors that have a significant impact on the fundamental reproduction (3.54) number, R_{eH}, so that suitable intervention strategies may be implemented. Using the elasticity of R_{eH} with respect to $\alpha \; and \; \theta_1$, the effect of HIV testing and treatment on HIV/AIDS dynamics was investigated. The elasticity (Caswell, 2001) of R_{eH} with respect to $\alpha \; and \; \theta_1$ can be calculated using Equation (3.22) and the method described in (Fred and Carlos, 2001; Nakul *et al.,* 2008; Fred and Carlos, 2012) as:

$$\frac{\theta_1 \alpha}{R_{eH}} \frac{\partial R_{eH}}{\partial \theta_1 \alpha} = \frac{c(1-\psi\xi) b_h (\alpha \upsilon + \upsilon\theta_1 - \upsilon\theta_2 + k_3 k_4)}{k_2 (k_3 k_4 - \upsilon\theta_2)(k_1 - \Lambda\varphi)}$$

3.5 Case 2: HCV Disease Transmission Model

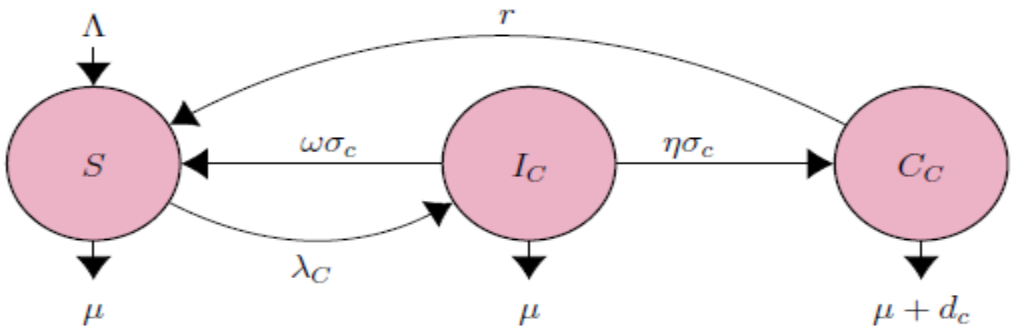

Figure 3.3: The Compartmental Flow diagram of the HCV model

HCV only model is getting by setting $H_U = H_A = H_T = A_A = H_{UI} = H_{UC} = H_{AI} = H_{AC} = H_{TI} = H_{TC} = A_{AI} = A_{AC} = 0$ in the system (3.3), and this gives

$$\left.\begin{aligned} \frac{dS}{dt} &= \Lambda + \omega\sigma_c I_c + rC_c - (\lambda_C + \mu)S \\ \frac{dI_C}{dt} &= \lambda_C S - (\omega + \eta)\sigma_c I_C - \mu I_C \\ \frac{dC_c}{dt} &= \eta\,\sigma_c I_c - (r + \mu + d_c)C_c \end{aligned}\right\} \qquad (3.55)$$

Where $\lambda_C = c(1 - \psi\xi)b_c \frac{I_C + C_C}{N_c}$, where N_c is the total number of people given as

$$N_c(t) = S(t) + I_C(t) + C_C(t) \qquad (3.56)$$

3.5.1 Basic Properties of the Case 2 Model

Here, based on the model (3.55), we demonstrate that the state variables are nonnegative and the solution is always positive for all times $t \geq 0$. Here, it is assumed that the model's parameters are positive. We demonstrate that possible solutions are restricted to a certain region:

$$\Omega = \{\big(S(t), I_C(t), C_C(t)\big) \in \mathbb{R}_+^3 : N_c(t) \leq 0.$$

The following theorems are considered:

3.5.1.1 Positivity and Boundedness of Solution for Case 2 Model

It is crucial to demonstrate that all solutions with non-negative initial conditions will continue to be non-negative for the system of equations (3.55) to have epidemiological significance. This Lemma 3.3 shows that the system of equations in the system (3.55) is positive and has a limit:

Lemma 3.3:

The parameters' initial values are

$\{S(0) \geq 0, I_C(0) \geq 0, C_c(0) \geq 0 \; and \; N(0) \geq 0\} \in \Phi$

The model's solution, $\{S(t), I_C(t), C_c(t), and \; N(t)\}$, is then positive for any $t \geq 0$.

Proof:

Taken into account is the first equation in (3.55);

$$\frac{dS}{dt} = \Lambda + \omega\sigma_c I_c + rC_c - (\lambda_C + \mu)S$$

$$\frac{dS}{dt} \geq -(\lambda_C + \mu)S$$

$$\int \frac{1}{S} dS \geq \int -(\lambda_C + \mu)\, dt$$

$$S \geq S_0 e^{-(\lambda_C + \mu)t} \geq 0$$

As a result, $S \geq 0$

relative to equation 2 in (3.55);

$$\frac{dI_C}{dt} = \lambda_C S - (\omega + \eta)\sigma_c I_C - \mu I_C$$

$$\frac{dI_C}{dt} \geq -((\omega + \eta)\sigma_c + \mu)I_C$$

$$\int \frac{1}{I_C} dI_C \geq \int -((\omega + \eta)\sigma_c + \mu)\, dt$$

$$I_C \geq I_{C_0} e^{-((\omega+\eta)\sigma_c+\mu)t} \geq 0$$

So, $I_C \geq 0$

in (3.55)'s third equation;

$$\frac{dC_c}{dt} = \eta\, \sigma_c I_c - (r + \mu + d_c)C_c$$

Suppose $I_c \to 0$

$$\frac{dC_c}{dt} \geq -(r + \mu + d_c)C_c$$

Integrating

$$\int \frac{1}{C_c} dC_c \geq \int -(r + \mu + d_c)\, dt$$

$$C_c \geq C_{c_0} e^{-(r+\mu+d_c)t} \geq 0$$

Hence, $C_c \geq 0$

The above state variables are positive on the bounding plane $\mathbb{R}^3_+$.

Therefore, we have shown from the above that the state variables are positive on the bounding plane $\mathbb{R}^3_+$.

For the boundedness of solutions theorem 3.8 holds:

Theorem 3.8:

The solution to the system (3.55), which is contained and stays within the region Ω for all time $t \geq 0$, is c Ω for all time $t \geq 0$

Proof:

The overall population size,

$N_c(t) = S(t) + I_c(t) + C_c(t)$

By substituting the derivatives of $N_c(t)$, with respect to time(t), into the systems of equations in (3.55),

$$N_c{}' = S' + I_c{}' + C_c{}'$$

$N_c{}' = \Lambda + \omega\sigma_c I_c + rC_c - (c(1-\psi\xi)\beta_1 I_C(t) + \beta_2 C_C(t))S - \mu S + (c(1-\psi\xi)\beta_1 I_C(t) +$

$\beta_2 C_C(t))S - (\omega+\eta)\sigma_c I_C - \mu I_C + \eta\sigma_c I_c - (r+\mu+d_c)C_c$ (3.57)

Simplifying (3.57) gives:

$N_c{}' = \Lambda - \mu[S + I_c + C_c] + d_c C_c$ (3.58)

$N_c{}' + \mu N = \Lambda + d_c C_c$ (3.59)

$N_c{}' + \mu N \leq \Lambda$ (3.60)

Integrating (3.60) gives:

$N_c{}' \leq \frac{\Lambda}{\mu} + ke^{-\mu t}$

$\underset{\substack{lim \\ n\to\infty}}{max}\, N_c \leq \underset{n\to\infty}{lim}\left(\frac{\Lambda}{\mu} + ke^{-\mu t}\right) \leq \frac{\Lambda}{\mu}$

Therefore, the model system's solutions (3.55) are positive and constrained in the region

$\mathcal{T} = \{(S + I_c + C_c)\} \in \mathbb{R}^3_+ : S + I_c + C_c \leq \frac{\Lambda}{\mu}$ (3.61)

Given the system dynamics (3.55), the model is said to be epidemiologically well-posed, as shown by Lemma 3.3.

3.5.1.2 The HCV Model's Existence and Uniqueness of Solution

The validity and usability of any mathematical model depend on whether the given equation has a

solution, if it has, is the solution unique? This subsection is concerned with finding if the system of the equation has a solution and if the solution to the system is unique. We will employ the Lipschitz theorem criterion to confirm the existence and uniqueness of the equation system. From theorem 2.1, in the review of methodologies, we are interested in the region $0 \leq \propto \leq \mathbb{R}$.

Let

$$\left.\begin{aligned} \frac{dS}{dt} &= \Lambda + \omega\sigma_c I_c + rC_c - (\lambda_C + \mu)S, \qquad S(t_0) = S_0 \\ \frac{dI_C}{dt} &= \lambda_C S - (\omega + \eta)\sigma_c I_C - \mu I_C, \qquad I_C(t_0) = I_{C0} \\ \frac{dC_c}{dt} &= \eta\, \sigma_c I_c - (r + \mu + d_c)C_c, \qquad C_C(t_0) = C_{C0} \end{aligned}\right\} \tag{3.62}$$

Theorem 3.9:

Let D' represent the area $0 \leq \alpha \leq R$. Then equation (3.55) has a distinct solution.in D', we then prove that $\frac{\partial f_i}{\partial x_j}, i, j = 1,2,3$ are continuous and bounded.

Proof:

Let $D = \{\big|(S, I_C, C_C)t) \,||S - S_0| \leq a, |I_C - I_{C0}| \leq b, |C_C - C_{C0}| \leq c\big|\}$

now,

$$\frac{dS}{dt} = f_1(S, I_C, C_C) = \Lambda + \omega\sigma_c I_c + rC_c - (\lambda_C + \mu)S, \qquad S(t_0) = S_0 \tag{3.63}$$

$$\frac{dI_C}{dt} = f_2(S, I_C, C_C) = \lambda_C S - (\omega + \eta)\sigma_c I_C - \mu I_C, \qquad I_C(t_0) = I_{C0} \tag{3.64}$$

$$\frac{dC_c}{dt} = f_3(S, I_C, C_C) = \eta\, \sigma_c I_c - (r + \mu + d_c)C_c, \qquad C_C(t_0) = C_{C0} \tag{3.65}$$

From (3.63) the partial derivatives below are obtained

$$\left|\frac{\partial f_1}{\partial S}\right| = \left|-(\frac{cb_c(1-\psi\xi)(I_C+C_C)}{N_c} - \frac{cb_c(1-\psi\xi)(I_C+C_C)S}{N_c^2} + \mu)\right| < \infty;\ \left|\frac{\partial f_1}{\partial I_C}\right|$$

$$= \left|\omega\sigma_c - (\frac{cb_c(1-\psi\xi)}{N_c} - \frac{cb_c(1-\psi\xi)(I_C+C_C)}{N_c^2})S\right| < \infty;\ \left|\frac{\partial f_1}{\partial C_C}\right|$$

$$= \left|r - (\frac{cb_c(1-\psi\xi)}{N_c} - \frac{cb_c(1-\psi\xi)(I_C+C_C)}{N_c^2})S\right| < \infty$$

These partial derivatives exist, continuous and bounded. Similarly, from equations (3.63) - (3.65),

$$\left|\frac{\partial f_2}{\partial S}\right| = \left|-\frac{cb_c(1-\psi\xi)(I_C+C_C)S}{N_c^2} + \frac{cb_c(1-\psi\xi)(I_C+C_C)}{N_c}\right| < \infty;\ \left|\frac{\partial f_2}{\partial I_C}\right|$$

$$= \left|\left(\frac{cb_c(1-\psi\xi)}{N_c} - \frac{cb_c(1-\psi\xi)(I_C+C_C)}{N_c^2}\right)S - (\omega+\eta)\sigma_c - \mu\right| < \infty;\ \left|\frac{\partial f_2}{\partial C_C}\right|$$

$$= \left|\left(\frac{cb_c(1-\psi\xi)}{N_c} - \frac{cb_c(1-\psi\xi)(I_C+C_C)}{N_c^2}\right)S\right| < \infty$$

$$\left|\frac{\partial f_3}{\partial S}\right| = 0 < \infty;\ \left|\frac{\partial f_3}{\partial I_C}\right| = |\eta\ \sigma_c| < \infty;\ \left|\frac{\partial f_3}{\partial C_C}\right| = |-(r+\mu+d_c)| < \infty$$

The partial derivatives of the entire system of equations exist, finite, and bounded, as was demonstrated earlier. This means that the model system (3.55) has a unique solution according to Theorem 3.3.

3.5.2 Points of Equilibrium and Reproduction for Model case 2

$I_C = C_C = 0$ in the absence of infections. A state of HCV-free equilibrium for the system of equations in (3.55) is obtained by:

$$C_o = (S, I_C, C_C,) = \left[\frac{\Lambda}{\mu}, 0,0,0,0\right] \quad (3.66)$$

When there is no infection, the overall population changes proportionally to the ratio of recruitment rates to mortality rate.

To determine the endemic stable states, the system of equations in (3.54) is set to zero and $S = S^*, I_c = I_c^*, C_c = C_c^*$ such that;

$$\begin{aligned} 0 &= \Lambda + \omega\sigma_c I_c + rC_c - (\lambda_C + \mu)S \\ 0 &= \lambda_C S - (\omega + \eta)\sigma_c I_C - \mu I_C \\ 0 &= \eta\,\sigma_c I_c - (r + \mu + d_c)C_c \end{aligned} \tag{3.67}$$

$$\begin{aligned} S^* &= \frac{(\eta\sigma_c + \omega\sigma_c + \mu)(\mu + d_c + r)\Lambda}{g_1} \\ I_C^* &= \frac{(r + \mu + d_c)\Lambda\lambda_c}{g_1} \\ C_C^* &= \frac{\Lambda\eta\lambda_c\sigma_c}{g_1} \end{aligned} \tag{3.68}$$

where,

$$g_1 = \eta\mu^2\sigma_c + \eta\mu r\sigma_c + \eta\mu d_c\sigma_c + \eta\mu\lambda_c\sigma_c + \eta d_c\lambda_c\sigma_c + \omega\sigma_c + \mu^2\omega\sigma_c + \mu\omega r\sigma_c + \mu\omega d_c\sigma_c +$$

$$\mu^3 + \mu^2 r + \mu^2 d_c + \mu^2\lambda_c + \mu r\lambda_c + \mu\lambda_c d_c\,,\ \lambda_c = c(1 - \psi\xi)b_c\frac{I_C + C_C}{N_c}$$

The next-generation matrix method was used to calculate the basic reproduction number. To determine the next generation matrix for the model considered in HCV only sub-model case 2, R_{eC} the following are considered:

1. The number of ways that new infections can arise or be created

2. The number of ways that infections can be transferred between compartments

Rearranging equations (3.54) such that we start with the infective classes

There are two infected classes in this model, the $I_C, and\ C_C$, hence our $m = 2$

Then F_i and V_i are computed as follows:

$$\left.\begin{aligned} F &= \begin{pmatrix} c(1-\psi\xi)b_c \dfrac{I_C + C_C}{N_c} S \\ 0 \end{pmatrix} \\ V_i^+ = \begin{pmatrix} 0 \\ \eta\ \sigma_c I_c \end{pmatrix}, V_i^- &= \begin{pmatrix} (\omega+\eta)\sigma_c I_C + \mu I_C \\ (r+\mu+d_c)C_c \end{pmatrix} \\ V = V_i^- + V_i^+ &= \begin{pmatrix} (\omega+\eta)\sigma_c I_C + \mu I_C \\ \eta\ \sigma_c I_c - (r+\mu+d_c)C_c \end{pmatrix} \end{aligned}\right\} \quad (3.69)$$

At the HCV-free equilibrium point, the variational matrix of F and V is evaluated, and DFE

$E_{oC} = \left[\frac{\Lambda}{\mu}, 0,0,0,0\right]$ is define as

$$\left.\begin{aligned} F &= \begin{bmatrix} c(1-\psi\xi)b_c & c(1-\psi\xi)b_c \\ 0 & 0 \end{bmatrix} \\ V &= \begin{bmatrix} (\omega+\eta)\sigma_c + \mu & 0 \\ -\eta\sigma_c & (r+\mu+d_c) \end{bmatrix} \end{aligned}\right\} \quad (3.70)$$

$$V^{-1} = \begin{bmatrix} \dfrac{1}{\omega\sigma_c + \eta\sigma_c + \mu} & 0 \\ \dfrac{\eta\sigma_c}{(\omega\sigma_c + \eta\sigma_c + \mu)(r+\mu+d_c)} & \dfrac{1}{(r+\mu+d_c)} \end{bmatrix} \quad (3.71)$$

$$FV^{-1} = \begin{bmatrix} \dfrac{c(1-\psi\xi)b_c}{\omega\sigma_c + \eta\sigma_c + \mu} + \dfrac{c(1-\psi\xi)b_c\eta\sigma_c}{(\omega\sigma_c + \eta\sigma_c + \mu)(r+\mu+d_c)} & \dfrac{c(1-\psi\xi)b_c}{r+\mu+d_c} \\ 0 & 0 \end{bmatrix} \quad (3.72)$$

$R_{eC} = \rho(FV^{-1}) = max(\lambda_1, \lambda_2)$, R_{eC} denotes the spectral radius of the given matrix, which is its biggest eigenvalue.

Therefore, the dominant eigenvalue is the basic reproduction number for HCV only model (the number of HCV infections produced by one HCV case) denoted by R_{eC}.

$$R_{eC} = \frac{c(1-\psi\xi)b_c(\eta\sigma_c + \mu + r + d_c)}{(r+\mu+d_c)(\mu + (\omega+\eta)\sigma_c)} \quad (3.73)$$

3.5.3 Stability Analysis of the Model

3.5.3.1 Analysis of Local Stability for the HCV Free Equilibrium E_o

At the HCV-free equilibrium E_0, the local stability of the HCV-free equilibrium was explored. Theorem 3.10 shows that the HCV-free equilibrium E_0 is locally stable.

Theorem 3.10:

Infection-free stability when $R_{eC}< 1$, E_0 is locally asymptotically stable, otherwise it is unstable.

Proof:

The linearized model yields the following matrix: $\frac{dX}{dt} = AX$

$X = (x_1, x_2, x_3)^T, (x_1, x_2, x_3) \in R_+^3$, and

$$A = \begin{bmatrix} D_1 - \mu & \omega\sigma_c - D_3 & r - D_3 \\ D_2 & D_4 - (\eta + \omega)\sigma_c - \mu & D_4 \\ 0 & \eta\sigma_c & -r - \mu - d_c \end{bmatrix} \qquad (3.74)$$

where

$D_1 = \frac{c(1-\psi\xi)b_c(x_2+x_3)x_1}{(x_1+x_2+x_3)^2} - \frac{c(1-\psi\xi)b_c(x_2+x_3)}{x_1+x_2+x_3}$, $D_2 = \frac{c(1-\psi\xi)b_c(x_2+x_3)}{x_1+x_2+x_3} - \frac{c(1-\psi\xi)b_c(x_2+x_3)x_1}{(x_1+x_2+x_3)^2}, D_3 = \frac{c(1-\psi\xi)b_cx_1}{x_1+x_2+x_3} + \frac{c(1-\psi\xi)b_c(x_2+x_3)x_1}{(x_1+x_2+x_3)^2}, D_4 = \frac{c(1-\psi\xi)b_cx_1}{x_1+x_2+x_3} - \frac{c(1-\psi\xi)b_c(x_2+x_3)x_1}{(x_1+x_2+x_3)^2}$

The resulting Jacobian matrix of (3.74) at E_o is

$$|J(E_0) - \lambda I| = \begin{bmatrix} -\mu - \lambda & \omega\sigma_c - cb_c(1-\psi\xi) & r - cb_c(1-\psi\xi) \\ 0 & cb_c(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu - \lambda & cb_c(1-\psi\xi) \\ 0 & \eta\sigma_c & -r - \mu - d_c - \lambda \end{bmatrix} = 0 \quad (3.75)$$

From equation (3.75) $\lambda_1 = -\mu$, so that the remaining eigenvalues are obtained from the remaining 2 x 2 matrix

$$J(E_0) = \begin{bmatrix} cb_c(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu - \lambda & cb_c(1-\psi\xi) \\ \eta\sigma_c & -r - \mu - d_c - \lambda \end{bmatrix} = 0 \quad (3.76)$$

To obtain the remaining eigen value from (3.76), the Routh-Hurwitz condition states that :

(1) Trace $J(E_0) < 0$ (2) Determinant $J(E_0) > 0$`

Trace $J(E_0) = cb_c(1-\psi\xi) - (\omega+\eta)\sigma_c - 2\mu - r - d_c < 0$

Determinant $J(E_0) = (c\eta(1-\psi\xi)b_c + (\omega+\eta)(r+\mu+d_c))\sigma_c + (r+\mu+d_c)(c(1-\psi\xi)b_c + \mu) > 0$ *since* $R_{eC} < 1$

Given that the prerequisites are met, the disease-free equilibrium is stable.

Now, λ_2,λ_3, < 0 because the values are assumed to be positive. E_o is stable If R_{eC}< 1, and unstable if $R_{eC} > 1$.

3.5.3.2 Model Case 2: Globally Stable Free Equilibrium for HCV-Only

At the HCV-free equilibrium E_0, the comparison approach was used to examine the global stability of the HCV-free equilibrium. The global stability of the HCV disease-free equilibrium, E_0 is demonstrated by Theorem (3.11).

Theorem 3.11:

The HCV disease-free equilibrium E_0 of the system (3.54), is globally asymptotically stable if $R_{eC} < 1$, and unstable if $R_{eC} > 1$.

Proof:

Here, the Comparison approach as described by Lashmkantham *et al*. (1989) and Mushayabasa *et al.* (2011) is applied. The rate of change of the system's exposed and infected components (3.54), written as:

$$\begin{pmatrix} \frac{dI_C}{dt} \\ \frac{dC_C}{dt} \end{pmatrix} = (F - V)\begin{pmatrix} I_C \\ C_C \end{pmatrix} - \left(1 - \frac{S_c}{N_c}\right) F \begin{pmatrix} I_C \\ C_C \end{pmatrix}$$

where F and V are described in sections 3.5.2 and $I_C = C_C = 0 \rightarrow (0,0)$ and $S_c \leq N_c$, as $t \rightarrow \infty$ in Γ_{cv}. Thus,

$$\begin{pmatrix} \frac{dI_C}{dt} \\ \frac{dC_C}{dt} \end{pmatrix} \leq \begin{pmatrix} c(1-\psi\xi)b_c & c(1-\psi\xi)b_c \\ 0 & 0 \end{pmatrix} - \begin{pmatrix} (\omega+\eta)\sigma_c + \mu & 0 \\ \eta\sigma_c & -(r+\mu+d_c) \end{pmatrix} \begin{pmatrix} I_C \\ C_C \end{pmatrix}$$

$$\begin{pmatrix} \frac{dI_C}{dt} \\ \frac{dC_C}{dt} \end{pmatrix} \leq (F - V)\begin{pmatrix} I_C \\ C_C \end{pmatrix} \tag{3.77}$$

Then, all of the matrix's eigenvalues (F-V) have negative real parts, i.e

$$\begin{vmatrix} c(1-\psi\xi)b_c - (\omega+\eta)\sigma_c - \mu - \lambda & c(1-\psi\xi)b_c \\ -\eta\sigma_c & r+\mu+d_c-\lambda \end{vmatrix} = 0 \tag{3.78}$$

evaluating along the first column gives the characteristic equation.

$((c(1-\psi\xi)b_c-(\omega+\eta)\sigma_c-\mu-\lambda)\,(r+\mu+d_c-\lambda))\;-((\,c(1-\psi\xi)b_c)(-\eta\sigma_c))=0$

$\lambda^2+(\psi\xi cb_c-cb_c+\sigma_c\eta+\omega\sigma_c-r-d_c)\lambda+cb_c\eta\sigma_c+c\mu b_c+crb_c+cb_cd_c-c\eta\psi\xi b_c\sigma_c-c\mu\psi\xi b_c-c\psi r\xi b_c-c\psi\xi b_cd_c-\eta\mu\sigma_c-\eta r\sigma_c-\eta d_c\sigma_c-\mu\omega\sigma_c-\omega r\sigma_c-\omega d_c\sigma_c-\mu^2-\mu r-\mu d_c=0$ (3.79)

The equation (3.79), according to Descartes' rule of signs, has two negative roots if

$(cb_c\eta\sigma_c+c\mu b_c+crb_c+cb_cd_c-c\eta\psi\xi b_c\sigma_c-c\mu\psi\xi b_c-c\psi r\xi b_c-c\psi\xi b_cd_c-\eta\mu\sigma_c-\eta r\sigma_c-\eta d_c\sigma_c-\mu\omega\sigma_c-\omega r\sigma_c-\omega d_c\sigma_c-\mu^2-\mu r-\mu d_c)\;<(\psi\xi cb_c-cb_c+\sigma_c\eta+\omega\sigma_c-r-d_c)$

J is a positive matrix because $S(t)\leq\frac{\Lambda}{\mu}$ in the invariant set. Consequently, it follows $\frac{dx}{dt}\leq(F-V)X$

When $R_{\mathrm{eC}}<1$, the eigenvalues of the matrix $F-V$ are negative. The linearized differential inequality (3.77), therefore, is stable whenever $R_{eC}<1$. As a result, $(I_C,C_C)\to(0,0)$ as $t\to\infty$. System (3.54) evaluation at $I_C=C_C=0$ yields $S_c\to1$ for $R_{eC}<1$. Therefore, the HIV-free equilibrium E_0 of the system (3.54), if $R_{eC}<1$, is globally asymptotically stable. If $R_{eC}>1$, it instantly follows that the HCV disease-free equilibrium E_0 of the system (3.55) is unstable.

3.5.3.3 HCV Endemic Equilibrium's Local Asymptotic Stability

At the HCV disease-endemic equilibrium $E_0{}^*$, the local stability of the HCV endemic equilibrium was explored. Theorem 3.12 demonstrates the local stability of HCV infection - endemic equilibrium $E_0{}^*$.

Theorem 3.12:

The endemic equilibrium is locally asymptotically stable if $R_{eC} > 1$.

Proof:

The system's endemic equilibrium, indicated by (S^*, I_C^*, C_C^*), can be expressed as follows:

Let $S = x + S^*, I_C = y + I_C^*, C_C = z + C_C^*$

At $E_0{}^*$, the resultant Jacobian matrix is

$$\mathrm{J} = \begin{bmatrix} P_1 - \mu & \omega\sigma_c - P_3 & r - P_3 \\ P_2 & P_4 - (\eta + \omega)\sigma_c - \mu & P_4 \\ 0 & \eta\sigma_c & -r - \mu - d_c \end{bmatrix} \tag{3.80}$$

where

$P_1 = \frac{c(1-\psi\xi)b_c(y+z)x}{(x+\mathrm{y}+\mathrm{z})^2} - \frac{c(1-\psi\xi)b_c(\mathrm{y}+\mathrm{z})}{x+\mathrm{y}+\mathrm{z}}, P_2 = \frac{c(1-\psi\xi)b_c(\mathrm{y}+\mathrm{z})}{x+\mathrm{y}+\mathrm{z}} - \frac{c(1-\psi\xi)b_c(\mathrm{y}+\mathrm{z})\mathrm{x}}{(x+\mathrm{y}+\mathrm{z})^2}, P_3 = \frac{c(1-\psi\xi)b_c x}{x+\mathrm{y}+\mathrm{z}} + \frac{c(1-\psi\xi)b_c(\mathrm{y}+\mathrm{z})x}{(x+\mathrm{y}+\mathrm{z})^2}, P_4 = \frac{c(1-\psi\xi)b_c x}{x+\mathrm{y}+\mathrm{z}} - \frac{c(1-\psi\xi)b_c(\mathrm{y}+\mathrm{z})x}{(x+\mathrm{y}+\mathrm{z})^2},$

Considering the upper triangular matrix of the (3.80) matrix, then

$|JC_0{}^* - \lambda I| = 0$

$$\mathrm{J} = \begin{bmatrix} P_1 - \mu - \lambda & \omega\sigma_c - P_3 & r - P_3 \\ P_2 & P_4 - (\eta + \omega)\sigma_c - \mu - \lambda & P_4 \\ 0 & \eta\sigma_c & -r - \mu - d_c - \lambda \end{bmatrix} \tag{3.81}$$

$$Trace = -\frac{c(1-\psi\xi)b_c(\mathrm{y}+\mathrm{z})}{x+\mathrm{y}+\mathrm{z}} + \frac{c(1-\psi\xi)b_c x}{x+\mathrm{y}+\mathrm{z}} - 3\mu - (\eta+\omega)\sigma_c + r - d_c \tag{3.82}$$

$$Determinant = \frac{1}{(x+y+z)^4}(c\psi\xi b_c x_3^2 + c\psi\xi b_c x_2 x_3 + c\psi\xi b_c x_2^2 + c\psi\xi b_c x_2 x_3 - cb_c x_2^2 - cb_c x_2 x_3 - cb_c x_2 x_3 - \mu x_1^2 - 2\mu x_1 x_2 - 2\mu x_1 x_3 - \mu x_2^2 - 2\mu x_2 x_3 - \mu x_3^2)(c\psi\xi b_c x_1 x_3 - c\psi\xi b_c x_1^2 - c\psi\xi b_c x_1 x_3 - cb_c x_1 x_3 + cb_c x_1^2 + cb_c x_1 x_3 - \eta\sigma_c x_1^2 - 2\eta\sigma_c x_1 x_2 - 2\eta\sigma_c x_1 x_3 - \eta\sigma_c x_2^2 - 2\eta\sigma_c x_2 x_3 - \eta\sigma_c x_3^2 - \omega\sigma_c x_1^2 - 2\omega\sigma_c x_1 x_2 - 2\omega\sigma_c x_1 x_3 - \omega\sigma_c x_2^2 - 2\omega\sigma_c x_2 x_3 - \omega\sigma_c x_3^2 - \mu x_1^2 - 2\mu x_1 x_2 - 2\mu x_1 x_3 - \mu x_2^2 - 2\mu x_2 x_3 - \mu x_3^2)((r + \mu + d_c)) \quad (3.83)$$

` (1) $Trace\ (E_0) < 0$ (2) $Determinant(E_0) > 0$

Equation (3.82) and (3.83) shows that 1 and 2 are true.

As a result of $trace[J]$ being negative and the $determinat[J]$ being positive, so, the steady of the endemic equilibrium is asymptotically stable at the local level.

3.5.3.4 Global Endemic Equilibrium Stability for HCV Model Case 2

Theorem 3.13:

The model's equations exhibit a globally asymptotically stable positive distinctive endemic equilibrium whenever $R_{eC} > 1$.

Proof:

Taking into account the Lyapunov function, which is defined as:

$$L(S^*, I_C*, C_c*) = \left(S - S^* ln\left(\frac{S}{S^*}\right)\right) + \left(I_C - I_C * ln\left(\frac{I_C}{I_C*}\right)\right) + \left(C_c - C_c * ln\left(\frac{C_c}{C_c*}\right)\right)$$

where L's derivative is taken directly along the system as:

$$\frac{dL}{dt} = (1 - \frac{S^*}{S})\frac{dS}{dt} + (1 - \frac{I_C*}{I_C})\frac{dI_C*}{dt} + (1 - \frac{C_c*}{C_c})\frac{dC_c*}{dt}$$

$$\frac{dL}{dt} = (1 - \frac{S^*}{S})[\Lambda + \omega\sigma_c I_c + rC_c - ((\frac{c(1-\psi\xi)b_c(I_C+C_c\ )}{N}) + \mu)S] + (1 - \frac{I_C*}{I_C})[((\frac{c(1-\psi\xi)b_c(I_C+C_c\ )}{N}))S - (\omega +$$

$$\eta)\sigma_c I_C - \mu I_C\ ] + (1 - \frac{C_c*}{C_c})[\eta\ \sigma_c I_c - (r + \mu + d_c)C_c\ ] \qquad (3.84)$$

At equilibrium,

$$\left.\begin{aligned} \Lambda &= (\frac{c(1-\psi\xi)b_c(I_c*+C_c*\ )}{N*})S^* + \mu S^* - \ \omega\sigma_c I_C * + rC_c * \\ (\omega + \eta)\sigma_c - \mu) &= (\frac{c(1-\psi\xi)b_c(I_C+C_c\ )}{N*I_C*})S^* \\ (r + \mu + d_c) &= \frac{\eta\ \sigma_c I_C*}{C_c*} \end{aligned}\right\} \qquad (3.85)$$

Substituting equation (3.85) in (3.84)

$$\frac{dL}{dt} = (1 - \frac{S^*}{S})[(\frac{c(1-\psi\xi)b_c(I_c*+C_c*\ )}{N})S^* + \mu S^* - \ \omega\sigma_c I_C * + rC_c * + \omega\sigma_c I_c + rC_c -$$

$$((\frac{c(1-\psi\xi)b_c(I_C+C_c\ )}{N}) + \mu)S] + (1 - \frac{I_C*}{I_C})[((\frac{c(1-\psi\xi)b_c(I_C+C_c\ )}{N}))S - (\frac{c(1-\psi\xi)b_c(I_C*+C_{c*}\ )}{NI_C*})S^* I_C\ ] +$$

$$(1 - \frac{C_c*}{C_c})[\eta\ \sigma_c I_c - \left(\frac{\eta\ \sigma_c I_C*}{C_c*}\right) C_c\ ] \qquad (3.86)$$

Expanding (3.86)

$$\frac{dL}{dt} = (1 - \frac{S^*}{S})[\frac{c(1-\psi\xi)b_c(I_c*\ S^*)}{N*} + \frac{c(1-\psi\xi)b_c(C_c*\ S^*\ )}{N*}) + \mu S^* - \ \omega\sigma_c I_C * + rC_c * + \omega\sigma_c I_c + rC_c -$$

$$\frac{c(1-\psi\xi)b_c I_c S}{N} - \frac{c(1-\psi\xi)b_c C_c S}{N} - \mu S] + (1 - \frac{I_C*}{I_C})[\frac{c(1-\psi\xi)b_c S}{N} + \frac{c(1-\psi\xi)b_c C_c S}{N} - \frac{c(1-\psi\xi)b_c(I_c*\ S^* I_C\ )}{N*I_C*} -$$

$$\frac{c(1-\psi\xi)b_c(C_c*\ S^*\ I_C\ )}{N*I_C*}\ ] + (1 - \frac{C_c*}{C_c})[\eta\ \sigma_c I_c - \frac{\eta\ \sigma_c I_C*C_c}{C_c*}\ ]$$

$$= (1 - \frac{S^*}{S})[\frac{c(1-\psi\xi)b_c(I_c * S^*)}{N*} + \frac{c(1-\psi\xi)b_c(C_c * S^*)}{N*}) + \mu S^* - \omega\sigma_c I_C * + rC_c * + \omega\sigma_c I_c$$

$$+ rC_c - \frac{c(1-\psi\xi)b_c I_c S}{N} - \frac{c(1-\psi\xi)b_c C_c S}{N} - \mu S] + (1 - \frac{I_C *}{I_C})[\frac{c(1-\psi\xi)b_c S}{N}$$

$$+ \frac{c(1-\psi\xi)b_c C_c S}{N} - \frac{c(1-\psi\xi)b_c(I_c * S^* I_C)}{N * I_C *} - \frac{c(1-\psi\xi)b_c(C_c * S^* I_C)}{N * I_C *}]$$

$$+ (1 - \frac{C_c *}{C_c})[\eta\, \sigma_c I_c - \frac{\eta\, \sigma_c I_C * C_c}{C_c *}]$$

$$= (1 - \tfrac{S^*}{S})\langle \tfrac{c(1-\psi\xi)b_c(I_c S)}{N}(1 - \tfrac{I_c * S^* N}{I_c S N^*}) - \tfrac{c(1-\psi\xi)b_c(C_c S)}{N}(1 - \tfrac{C_c * S^* N}{C_c S N^*}) - \mu S(1 - \tfrac{S^*}{S}) - \omega\sigma_c I_C(1 -$$

$$\tfrac{I_C *}{I_C}) + rC_c(1 - \tfrac{C_C *}{C_C}) +] + (1 - \tfrac{I_C *}{I_C})[\tfrac{c(1-\psi\xi)b_c(I_c S)}{N}(1 - \tfrac{I_c * S^* N}{I_c S N^*}) - \tfrac{c(1-\psi\xi)b_c(C_c S)}{N}(1 - \tfrac{C_c * S^* N}{C_c S N^*}) +$$

$$(1 - \tfrac{C_c *}{C_c})[\eta\, \sigma_c I_c(1 - \tfrac{\eta\, \sigma_c I_C * C_c}{C_c * I_c})\,] \rangle \qquad (3.87)$$

Simplifying (3.87)

$$\frac{dL}{dt} = -\mu S(1 - \frac{S^*}{S})^2 + P_1(S, I_C, C_c) + P_2(S, I_C, C_c)$$

where

$$P_1(S, I_C, C_c) = \frac{c(1-\psi\xi)b_c(I_c S)}{N}(1 - \frac{I_c * S^* N}{I_c S N^*}) - \frac{c(1-\psi\xi)b_c(I_c S)}{N}(1 - \frac{I_c * S^* N}{I_c S N^*}) -) + (1$$

$$- \frac{C_c *}{C_c})[\eta\, \sigma_c I_c(1 - \frac{\eta\, \sigma_c I_C * C_c}{C_c * I_c})\,]$$

$$P_2(S, I_C, C_c) = All \quad others$$

$$P_1 \leq 0 \quad whenever \quad I_C S N^* \geq I_C * S^* N, \quad C_c S N^* \geq C_c * S^* N \qquad (3.88)$$

$$P_2 \leq 0 \quad whenever \quad I_C * S N^* \geq I_C S^* N, \quad C_c S N^* \geq C_c * S^* N \qquad (3.89)$$

Thus

$\frac{dL}{dt} \leq 0$ if (3.88) and (3.89) hold.

Hence, by the Lasalle theorem, the equilibrium in the positive region $R_+^3$is globally asymptotically stable.

3.5.4 Bifurcation Analysis for Case 2 Model

In this study, bifurcation analysis is done at the disease-free equilibrium by using the center manifold theory, as presented in (Buonomo and Lacitignola, 2011). The focus is now on the HCV disease-free equilibrium E_0, with the transcritical bifurcation at $R_{eC} = 1$ being investigated.

At the HCV-free equilibrium E_0, the Jacobian matrix of equation (3.55) is given as:

$$J(E_0) = \begin{bmatrix} -\mu - \lambda & \omega\sigma_c - cb_c(1-\psi\xi) & r - cb_c(1-\psi\xi) \\ 0 & cb_c(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu - \lambda & cb_c(1-\psi\xi) \\ 0 & \eta\sigma_c & -r - \mu - d_c - \lambda \end{bmatrix} = 0$$

The Centre Manifold Theorem as stated in Theorem 2.2.6 is now used to ascertain whether the system (3.55) exhibits a backward or forward bifurcation at $R_{eC} = 1$ as follows:

Bear in mind that

$$R_{eC} = \frac{c(1-\psi\xi)b_c(\eta\sigma_c + \mu + r + d_c)}{(r+\mu+d_c)(\mu + (\omega+\eta)\sigma_c)}$$

Assuming that $R_{eC} = 1$ is taken into account in the scenario where $b_C = b_C^*$ is a bifurcation parameter.

By solving for $b_c = b_c^*$, then

$$\frac{c(1-\psi\xi)b_c(\eta\sigma_c + \mu + r + d_c)}{(r+\mu+d_c)(\mu + (\omega+\eta)\sigma_c)} = 1$$

$$b_c = b_c^* = \frac{(r+\mu+d_c)(\mu+(\omega+\eta)\sigma_c)}{(1-\psi\xi)(\eta\sigma_c+\mu+r+d_c)}$$

The HCV disease-free equilibrium E_0 is hence locally stable when $b_c < b_c^*$, but loses stability when $b_c > b_c^*$. Consequently, the bifurcation value is the crucial number $b_c = b_c^*$.

The following steps are taken to study the nature of the bifurcation involving the HCV disease-free equilibrium E_0 at $R_{eC} = 1$ or, equivalently, at $b_{c_C} = b_c^*$.

First, it is established that the Jacobian matrix of system (3.50) at point (E_0, b_C^*) is.

$$J(E_0, b_c^*) = \begin{bmatrix} -\mu-\lambda & \omega\sigma_c - cb_c^*(1-\psi\xi) & r - cb_c^*(1-\psi\xi) \\ 0 & cb_c^*(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu - \lambda & cb_c^*(1-\psi\xi) \\ 0 & \eta\sigma_c & -r-\mu-d_c-\lambda \end{bmatrix} = 0 \qquad (3.90)$$

The zero eigenvalue of (3.90)'s characteristic equation is

$|J(E_0, b_c^*) - \lambda \mathrm{I}\ | = 0$

The quadratic equation that results from $\lambda_1 = -\mu$ is:

$$f(\lambda) = \lambda^2 + (b_c c\psi\xi - b_c + \eta\sigma_c + \omega\sigma_c + 2\mu + r + d_c)\lambda \qquad (3.91)$$

Equation (3.91), according to Descartes' rule of signs, has as its roots two negative eigenvalues. Consequently, since $\lambda_2 = 0$ is a simple zero eigenvalue and the other eigenvalues are real and negative, the assumptions of theorem 2.2.6 (Centre Manifold theorem) are then verified.

In addition, the right eigenvector associated with the zero eigenvalue $\lambda_3 = 0$ given by

$w = (w_1, w_2, w_3, w_4, w_5)^T$ are obtained as follows:

$$\begin{bmatrix} -\mu & \omega\sigma_c - cb_c{}^*(1-\psi\xi) & r - cb_c{}^*(1-\psi\xi) \\ 0 & cb_c{}^*(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu & cb_c{}^*(1-\psi\xi) \\ 0 & \eta\sigma_c & -r-\mu-d_c \end{bmatrix} \begin{bmatrix} w_1 \\ w_2 \\ w_3 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \quad (3.92)$$

$$-\mu w_1 + \big(\omega\sigma_c - cb_c{}^*(1-\psi\xi)\big)w_2 + \big(r - cb_c{}^*(1-\psi\xi)\big)w_3 = 0 \quad (3.93)$$

$$(cb_c{}^*(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu)w_2 + \big(cb_c{}^*(1-\psi\xi)\big)w_3 = 0 \quad (3.94)$$

$$\eta\sigma_c w_2 + (-r-\mu-d_c)w_3 = 0 \quad (3.95)$$

Solving equations (3.93) -(3.95) simultaneously gives:

$$w_1 = -\frac{w_3(\eta\mu\sigma_c + \eta\sigma_c d_c + \mu^2 + \mu r + \mu d_c)}{\eta\mu\sigma_c}$$

$$w_2 = \frac{w_3(r+\mu+d_c)}{\eta\sigma_c}$$

Therefore

$$w = \left(-\frac{w_3(\eta\mu\sigma_c + \eta\sigma_c d_c + \mu^2 + \mu r + \mu d_c)}{\eta\mu\sigma_c}, \frac{w_3(r+\mu+d_c)}{\eta\sigma_c}\right)^T$$

where $w_3 > 0$ denotes a free right eigenvector.

In the same way, the left eigenvector corresponding to the zero eigenvalue $\lambda_1 = 0$ given by

$\bar{v} = (\bar{v}_1, \bar{v}_2, \bar{v}_3)$ is

$$(\bar{v}_1, \bar{v}_2, \bar{v}_3)\begin{bmatrix} -\mu & \omega\sigma_c - cb_c{}^*(1-\psi\xi) & r - cb_c{}^*(1-\psi\xi) \\ 0 & cb_c{}^*(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu & cb_c{}^*(1-\psi\xi) \\ 0 & \eta\sigma_c & -r-\mu-d_c \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \quad (3.96)$$

$$\bar{v}_1(-\mu) = 0 \tag{3.97}$$

$$\bar{v}_1\left(\omega\sigma_c - cb_c{}^*(1-\psi\xi)\right) + \bar{v}_2(cb_c{}^*(1-\psi\xi) - (\omega+\eta)\sigma_c - \mu) + \bar{v}_3\eta\sigma_c = 0 \tag{3.98}$$

$$\bar{v}_1\left(r - cb_c{}^*(1-\psi\xi)\right) + \bar{v}_2(cb_c{}^*(1-\psi\xi)\kappa) + \bar{v}_3(-r-\mu-d_c) = 0 \tag{3.99}$$

The simultaneous solution of equations (3.97) - (3.99) yields:

$$\bar{v}_1 = 0, \bar{v}_2 = \frac{(\eta\sigma_c + \mu + r + d_c)l_3}{(\eta\sigma_c + \omega\sigma_c + \mu)}$$

Therefore;

$$\bar{v} = \left(0, \frac{(\eta\sigma_c + \mu + r + d_c)l_3}{(\eta\sigma_c + \omega\sigma_c + \mu)}\right)^T$$

where $\bar{v}_3 > 0$ is a free left eigenvector.

3.5.4.1 Coefficients a and b computation for the HCV model

According to theorem 2.2.6, the coefficients are:

$$a = \sum_{m,i,j=1}^{3} \bar{v}_m w_i w_j \frac{\partial^2 f_m(E_{0C}, b_C{}^*)}{\partial x_i \partial x_j}, b = \sum_{m,i,j=1}^{3} \bar{v}_m w_i \frac{\partial^2 f_m(E_{0C}, b_C{}^*)}{\partial x_i \partial \varphi}$$

may now be explicitly computed when the system (3.55) is taken into consideration and just the non-zero components of the left eigenvector $\bar{v}$ are considered, it follows that:

$S = x_1$, $I_C = x_2$,$C_C = x_3$

The model in the system (3.55) can now be written in the form

$\frac{dX}{dt} = f(x)$, where $f = (f_1, f_2, f_3)^T$

. This is accomplished by introducing the vector $X = (x_1, x_2, x_3)^T$.

It suggests that system (3.55) can be expressed using the new variables as follows:

$$\left.\begin{aligned} \frac{dX_1}{dt} &= f_1 = \Lambda + \omega\sigma_c I_c + rC_c - (\frac{c(1-\psi\xi)b_C(I_C+C_C)}{N_C} + \mu)S \\ \frac{dX_2}{dt} &= f_2 = \frac{c(1-\psi\xi)b_C(I_C+C_C)}{N_C}S - (\omega + \eta)\sigma_c I_C - \mu I_C \\ \frac{dX_3}{dt} &= f_3 = \eta\,\sigma_c I_c - (r + \mu + d_c)C_c \end{aligned}\right\} \quad (3.100)$$

$$a = \frac{2l_2 c(1-\psi\xi)b_c(-\frac{r+\mu+d_c)w_3\Lambda}{\eta\,\sigma_c\mu} - \frac{w_3\Lambda}{\mu})(-\frac{\kappa w_3\Lambda}{\mu} - \frac{(r+\mu+d_c)w_3\Lambda}{\eta\,\sigma_c\mu})\mu^3}{\Lambda^3}$$

$$b = \frac{l_2(\eta\,\sigma_c + \mu + r + d_c)w_3 c(1-\psi\xi)}{\eta\,\sigma_c + \omega\sigma_c + \mu}$$

Theorem 2.2.6 states that because the coefficient b is always positive, the local dynamics surrounding the HCV disease-free equilibrium for $b_c = b_c^*$ are determined by the sign of the coefficient a. As a result, the following conclusion is reached:

3. if $a > 0$ a backward bifurcation happens
4. If $a < 0$, a forward bifurcation happens

The following outcomes from theorem 2.2.6 items (a) and (d) provide a summary of the preceding discussion:

Lemma 3.4:

If $R_{eC} < 1$ otherwise maintains stability, the HCV-only model of (3.55) has a positive endemic

equilibrium that is unstable.

Lemma 3.5:

The HCV-only model of (3.55), if $R_{eC} > 1$, has a unique positive endemic equilibrium that is locally asymptotically stable (LAS) and unstable otherwise he local stability of E^* implies its global stability because $a < 0$.

3.5.5 Sensitivity Indices on R_0 for HCV Only Model Case 2

To determine R_{eC} elasticity with respect to r as determined in case 1 as in Caswell (2001):

$$\frac{r}{R_{eC}}\frac{\partial R_{eC}}{\partial \mathrm{r}} = \frac{cb_c(1-\psi\xi)\eta\sigma_c)}{(r+\mu+d_c)^2(\mu+(\omega+\eta)\sigma_c)} \qquad (3.101)$$

3.6 Case 3: HIV-HCV Co-infection Disease Transmission Model

The full HIV-HCV co-infection model can be recalled from the set of equations in (3.3)

with positive initial conditions specified by:

$S(0) = S_0, H_u(0) = H_{U0,}\, H_A(0) = H_{A0,}\, H_T(0) = H_{T0,}\, A_a(0) = A_{A0,}\, I_c(0) = I_{C0,}\, C_c(0) =$

$C_{C0,}\, H_{uI}(0) = H_{uI0}, H_{AI}(0) = H_{AI0}, H_{TI}(0) = H_{TI0},\ A_{AI}(0) = A_{AI0}, H_{UC}(0) = H_{uC0}, H_{AC}(0) =$

$H_{AC0},\ H_{TC}(0) = H_{TC0}, A_{AC}(0) = A_{AC0} \in \mathbb{R}_+^{15}$ (3.103)

3.6.1 Basic Properties of the Model Case 3

It follows from the equation of $N(t)$, which represents the total population, as shown in equation (3.4) that

$N(t) = \Lambda + \mu N - H_{uI}(t) - H_{AI}(t) - H_{TI}(t) - A_{AI}(t) - H_{UC}(t) - H_{AC}(t) - H_{TC}(t) -$

$$A_{aC}(t) \leq \Lambda - \mu N, \qquad (3.103)$$

and (3.3) implies that $\lim_{t\to\infty} supN(t) \leq \frac{\Lambda}{\mu}$. Therefore, the dynamics of the system (3.3) will be looked at based on the biological factors of the region

$$\Phi = \left\{\left(S(t) + H_u(t) + H_A(t) + H_T(t) + A_a(t) + I_c(t) + C_c(t) + H_{uI}(t) + H_{AI}(t) + H_{TI}(t) + A_{AI}(t) + H_{UC}(t) + H_{AC}(t) + H_{TC}(t) + A_{aC}(t)\right) \in \mathbb{R}_+^{15} : N \leq \frac{\Lambda}{\mu}\right\},$$

This is simple to demonstrate as being positively model-invariant.

Therefore as $t \longrightarrow \infty$, $\frac{\Lambda}{\mu}$ is an upper limit of N provided that $N(0) \leq \frac{\Lambda}{\mu}$. If $N(0) > \frac{\Lambda}{\mu}$, $N(t)$ will decline to this level. As a result, the region Φ contains all possible system solutions that can enter or remain. Therefore, under the flow caused by the system, the region of biological interest Φ is positively invariant (3.3).

3.6.1.1 Positivity and Boundedness of Solution for case 3 model

With all variables and parameters being positive for all-time series as in theorem 3.14, we can regard model (3.3) to be epidemiologically and mathematically properly posed.

Theorem 3.14

For all $t > 0$, the system (3.3) with initial conditions (3.103) has solutions that satisfy

$S(t) \geq 0, H_u(t) \geq 0, H_A(t) \geq 0, H_T(t) \geq 0, A_a(t) \geq 0, I_c(t) \geq 0, C_c(t) \geq 0, H_{uI}(t) \geq 0, H_{AI}(t) \geq 0, H_{TI}(t) \geq 0, A_{AI}(t) \geq 0, H_{UC}(t) \geq 0, H_{AC}(t) \geq 0, H_{TC}(t) \geq 0, A_{aC}(t) \geq 0$. $The\ region\ \Phi \in \mathbb{R}_+^{15}$ is positively invariant and attractive to the system (3.3).

Proof:

Model's first equation (3.3) gives us:

$$\frac{dS}{dt} = (1 - \varphi H_u)\Lambda + \omega_0 \sigma_c I_c + r_1 C_c - (\lambda_H + \lambda_C + \mu)S$$

$\frac{dS}{dt} \geq -(\lambda_H + \lambda_C + \mu)S$

$\int \frac{1}{S} dS \geq \int -(\lambda_H + \lambda_C + \mu)\, dt$

$S \geq S_0 e^{-(\lambda_H + \lambda_C + \mu)t} \geq 0$

Thus, $S \geq 0$

The second equation of system (3.3) is analogous:

$\frac{dH_U}{dt} = \lambda_H S + \varphi \Lambda H_U + \omega_1 \epsilon_1 \sigma_c H_{UI} + r_2 H_{UC} - (\delta_1 \lambda_C + \alpha_1 + \rho_1 + \mu) H_U$

$\frac{dH_U}{dt} \geq -(\delta_1 \lambda_C + \alpha_1 + \rho_1 + \mu) H_U$

$\int \frac{1}{H_U} dH_U \geq \int -(\delta_1 \lambda_C + \alpha_1 + \rho_1 + \mu)\, dt$

$H_U \geq H_{U_0} e^{-(\delta_1 \lambda_C + \alpha_1 + \rho_1 + \mu)t} \geq 0$

Hence, $H_U \geq 0$

Analogously, it's easy to show that

$H_A(t), H_T(t), A_a(t), I_c(t), C_c(t), H_{uI}(t), H_{AI}(t), H_{TI}(t), A_{AI}(t), H_{UC}(t), H_{AC}(t), H_{TC}(t)\ and\ A_{aC}(t)$

for all $t > 0$,are all positive.

3.6.1.2 The Existence and Uniqueness of Solution for the Full Model

Lemma: The initial conditions and solutions to the model Equations (3.3)

$S(0) > 0, H_u(0) > 0\ H_A(0) > 0, H_T(0) > 0, A_a(0) > 0, I_c(0) > 0, C_c(0) > 0, H_{uI}(0) >$

$0, H_{AI}(0) > 0, H_{TI}(0) > 0,\ H_{UC}(0) > 0, H_{AC}(0) > 0,\ H_{TC}(0) > 0, A_{AI}(0) > 0, A_{AC}(0) >$

0 exists in $\mathbb{R}_+^{15}$

i.e., the solution of the model variable

$$S(t), H_A(t), H_T(t), A_a(t), I_c(t), C_c(t), H_{uI}(t), H_{AI}(t), H_{TI}(t), H_{UC}(t), H_{AC}(t), H_{TC}(t), A_{AI}(t), and\ A_{ac}(t)$$

exist for all t and will remain in $\mathbb{R}_+^{15}$.

According to (Derrick and Groosman, 1976) theorem as in theorem 2.1, let Φ denote the region,

$$\Phi = \left\{\left(S(t) + H_u(t) + H_A(t) + H_T(t) + A_a(t) + I_c(t) + C_c(t) + H_{uI}(t) + H_{AI}(t) + H_{TI}(t) + H_{UC}(t) + H_{AC}(t) + H_{TC}(t) + A_{AI}(t) + A_{aC}(t)\right) \in \mathbb{R}_+^{15}: N \leq \frac{\Lambda}{\mu}\right\},$$

Then equations (3.3) have a unique solution if

$\frac{\partial f_i}{\partial f_j}, i, j = 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15$ are continuous and bounded in Φ. Here, $x_1 = S(t), x_2 = H_U(t), x_3 = H_A(t), x_4 = H_T(t), x_5 = A_a(t), x_6 = I_c(t), x_7 = C_c(t), x_8 = H_{uI}(t), x_9 = H_{AI}(t), x_{10} = H_{TI}(t), x_{11} = H_{UC}(t), x_{12} = H_{AC}(t), x_{13} = H_{TC}(t), x_{14} = A_{AI}(t), and\ x_{15} = A_{aC}(t)$. The partial derivatives of the entire system of equations are shown to exist, and they are shown to be finite and bounded. The model system (3.3) therefore has a unique solution according to Theorem 3.3.

3.6.2 Equilibrium Points System of Model Case 3

By equating the derivatives of the system (3.3) to zero, the subsequent equation that is obtained can be used to find the equilibriums of the system. Thus, the HIV-HCV co-infection-free equilibrium is denoted by E_{ohc} if there are no HIV and HCV infections in the population:

$$E_{ohc} = (S^0, H_u^0, H_A^0, H_T^0, A_a^0, I_c^0, C_c^0, H_{uI}^0, H_{AI}^0, H_{TI}^0, H_{UC}^0, H_{AC}^0, H_{TC}^0, A_{AI}^0, A_{aC}^0) =$$

$$(\frac{\Lambda}{\mu}, 0,0,0,0,0,0,0,0,0,0,0,0,0,0)$$

If there is no infection, the overall population changes in proportion to the ratio of recruitment rate to the death rate.

Here, the system of equations in (3.3) is set to zero and the endemic stable states are determined. $S = S^*, H_A = H_A *, H_T = H_T *, A_a = A_A *, I_c = {I_c}^*, C_c = {C_c}^*, H_{uI} = H_{uI} *, H_{AI} = H_{AI} *, H_{TI} = H_{TI} *, , H_{UC} = H_{UC} *, H_{AC} = H_{AC} *, H_{TC} = H_{TC} * A_{AI} = A_{AI} * and A_{aC} = A_{aC} *$ so that;

$k_1 = \mu + \alpha_1 + \rho_1, k_2 = \mu + \theta_1, k_3 = \mu + \nu_1, k_4 = \mu + d_a + \theta_2, k_5 = \mu + d_c + r_1, k_6 = \eta\varepsilon_2\sigma_c + \omega\varepsilon_1\sigma_c + \mu + \alpha_2 + \rho_2, k_7 = \eta\varepsilon_2\sigma_c + \omega\varepsilon_1\sigma_c + \mu + \theta_3, k_8 = \eta\varepsilon_2\sigma_c + \omega\varepsilon_1\sigma_c + \mu + \nu_3, k_9 = r_2 + \alpha_3 + \rho_3 + \mu + d_c, k_{10} = r_3 + \theta_5 + \mu + d_c, k_{11} = r_4 + \nu_3 + \mu + d_c, k_{12} = \eta\varepsilon_2\sigma_c + \omega\varepsilon_1\sigma_c + \mu + d_a + \theta_4, k_{13} = r_5 + \theta_6 + \mu + d_a + d_c,$

$$
\begin{aligned}
S^* &= \frac{[(\omega_0+\eta_0)\sigma_c+\gamma\lambda_h+\mu]}{\lambda_c} {I_C}^* \\
{H_U}^* &= \frac{\Lambda\lambda_c(\tau\lambda_h+k_5)+\mathrm{A}}{\varphi\Lambda\tau\lambda_c(\tau\lambda_h+k_5)} {I_C}^* \\
{H_A}^* &= A_7 + A_8\, {I_C}^* \\
{H_T}^* &= A_{24} + A_{25}\, {I_C}^* \\
{A_A}^* &= A_{26} + A_{27}\, {I_C}^* \\
{I_C}^* &= \frac{\Lambda\lambda_c(\tau\lambda_h+k_5)+A}{\lambda_c(\tau\lambda_h+k_5)} + \frac{\lambda_h[(\omega_0+\eta_0)\sigma_c+\gamma\lambda_h+\mu]}{\lambda_c} + \omega\,\varepsilon_1\sigma_c(A_7+\lambda_8) + r_2(A_3+A_4) - \\
&\frac{\delta_1\,(\lambda_c\Lambda(\tau\lambda_h+k_5)+A)}{\varphi\Lambda(\tau\lambda_h+k_5)} - \frac{k_1\,(\lambda_c\Lambda(\tau\lambda_h+k_5)+A)}{\varphi\Lambda\lambda_c(\tau\lambda_h+k_5)} \\
{C_C}^* &= \frac{\eta_0\sigma_c}{(\tau\lambda_h+k_5)} {I_C}^* \\
{H_{uI}}^* &= \frac{\delta_1\lambda_c}{k_6\varphi} + \frac{(\delta_1\,A+\gamma\lambda_h\Lambda\varphi(\tau\lambda_h+k_5))}{k_6\varphi\Lambda(\tau\lambda_h+k_5)} {I_C}^* \\
{H_{AI}}^* &= A_5 + A_6 {I_C}^* \\
{H_{TI}}^* &= \frac{\theta_3(A_5+A_6A_{32})}{k_8} + \frac{\delta_3\lambda_c(A_{24}+A_{25}A_{32})}{k_8} + \frac{\theta_4\left(\frac{\eta\epsilon_2\sigma_c\delta_1\lambda_c}{k_6k_9\varphi}+A_1A_{32}\right)}{k_8} \\
{H_{uC}}^* &= \frac{\eta\,\varepsilon_2\sigma_c\delta_1\lambda_c}{k_6k_9\varphi} + A_1 {I_C}^* \\
{H_{AC}}^* &= A_3 + A_4 {I_C}^* \\
{H_{TC}}^* &= A_9 + A_{10} {I_C}^* \\
{A_{AI}}^* &= A_{30} + A_{31} {I_C}^* \\
{A_{AC}}^* &= A_{28} + A_{29} {I_C}^*
\end{aligned}
\qquad (3.104)
$$

Where

$$A = \omega_0\sigma_c\lambda_c(\tau\lambda_h + k_5) + r_1\eta_0\sigma_c\lambda_c - (\tau\lambda_h + k_5)(\lambda_h + \lambda_c + \mu)[((\omega_0 + \eta_0)\sigma_c + \gamma\lambda_h + \mu)]$$

$$A_1 = \frac{\tau\lambda_h\eta_0\sigma_c}{k_9(\tau\lambda_h+k_5)} + \frac{\delta_1 A+\gamma\lambda_h\Lambda\varphi(\tau\lambda_h+k_5)}{k_6\varphi\Lambda(\tau\lambda_h+k_5)}, A_2 = \frac{\delta_1 A+\gamma\lambda_h\Lambda\varphi(\tau\lambda_h+k_5)}{k_6\varphi\Lambda(\tau\lambda_h+k_5)}, A_3 = \frac{\delta_1\lambda_c+k_1-\varphi\Lambda(\tau\lambda_h+k_5)}{r_2\varphi\Lambda\lambda_c(\tau\lambda_h+k_5)},$$

$$A_4 = \frac{A(\delta_1\lambda_c k_1 - \varphi\Lambda)}{r_2\varphi\Lambda\lambda_c(\tau\lambda_h + k_5)} + \frac{\lambda_h\big((\omega_0 + \eta_0)\sigma_c + \gamma\lambda_h + \mu\big)}{r_2\lambda_c} - \frac{\omega\varepsilon_1\sigma_c\delta_1\lambda_c}{r_2 k_6\varphi} - \frac{\omega\varepsilon_1\sigma_c A_2}{r_2 k_6\varphi},$$

$$A_5 = \frac{k_{10}A_3k_6k_9\varphi-\alpha_3\eta\varepsilon_2\sigma_c\delta_1\lambda_c}{\eta\varepsilon_2\sigma_c k_6k_9\varphi}, A_6 = \frac{k_{10}A_4-\alpha_3A_1}{\eta\varepsilon_2\sigma_c}, A_7 = \frac{k_7k_6A_5\varphi-\alpha_2\delta_1\lambda_c}{k_6\varphi\delta_2\lambda_c},$$

$$A_8 = \frac{k_7k_6A_6\varphi\Lambda(\tau\lambda_h+k_5)-\alpha_2[\delta_1 A+\gamma\lambda_h\Lambda\varphi(\tau\lambda_h+k_5)]}{k_6\varphi\Lambda(\tau\lambda_h+k_5)}, A_9 = \frac{\varphi A_7(\delta_2\lambda_c+k_2)-\alpha_1-\varphi\omega\varepsilon_1\sigma_c A_5}{\varphi r_3},$$

$$A_{10} = \frac{\varphi\Lambda\lambda_c A_8(\tau\lambda_h+k_5)(\delta_2\lambda_c+k_2)-\alpha_1 A}{\varphi\Lambda\lambda_c r_3(\tau\lambda_h+k_5)}, A_{11} = \frac{\rho_1}{(\delta_4\lambda_h+k_4)},$$

$$A_{12} = \frac{r_5}{(\delta_4\lambda_h+k_4)}\left(\frac{\nu_1}{r_5} + \frac{\gamma_1\eta\varepsilon_2\sigma_c\delta_3\lambda_c}{k_{12}k_{13}k_8}\right), A_{13} = \frac{r_5}{(\delta_4\lambda_h+k_4)}\left(\frac{\omega\varepsilon_1\sigma_c}{r_5} + \frac{\nu_2\eta\varepsilon_2\sigma_c\theta_4}{k_{12}k_{13}k_8} + \frac{\rho_3}{k_{13}}\right),$$

$$A_{14} = \frac{r_5(\delta_4\lambda_c\Lambda\varepsilon_2\sigma_c)}{k_{12}k_{13}(\delta_4\lambda_h+k_4)}, A_{15} = \frac{r_5\rho_2\eta\varepsilon_2\sigma_c)}{k_{12}k_{13}(\delta_4\lambda_h+k_4)} \quad , \quad A_{16} = \frac{r_5\nu_2\eta\varepsilon_2\sigma_c\theta_3}{k_{12}k_{13}k_8(\delta_4\lambda_h+k_4)} \quad , \quad A_{17} = \frac{\omega\varepsilon_1\sigma_c\delta_3\lambda_c}{k_8} +$$

$$\frac{r_4k_{13}A_{12}}{\eta\varepsilon_2\sigma_c} + \theta_2A_{12} - (\delta_3\lambda_c + k_3), A_{18} = \frac{\omega\varepsilon_1\sigma_c\theta_3}{k_8} + \frac{r_4k_{13}A_{16}}{\eta\varepsilon_2\sigma_c} + \theta_2A_{16}, A_{19} = \frac{\omega\varepsilon_1\sigma_c\theta_4}{k_8} + \frac{r_4k_{13}A_{13}}{\eta\varepsilon_2\sigma_c} -$$

$$\frac{r_4\rho_3}{\eta\varepsilon_2\sigma_c} + \theta_2A_{13}, \ A_{20} = \frac{r_4k_{13}A_{11}}{\eta\varepsilon_2\sigma_c} + \theta_2A_{11}, A_{21} = \frac{r_4k_{13}A_{15}}{\eta\varepsilon_2\sigma_c} + \theta_2A_{15},$$

$$A_{22} = \frac{r_4k_{13}A_{14}}{\eta\varepsilon_2\sigma_c} + \theta_2A_{14}, \ A_{23} = \frac{r_4\nu_3}{\eta\varepsilon_2\sigma_c}, A_{24} = \left(\frac{A_{23}A_9}{A_{17}} - \frac{A_{13}A_5}{A_{17}} - \frac{A_{19}\eta\varepsilon_2\sigma_c\delta_1\lambda_c}{A_{17}k_6k_9\varphi} - \frac{A_{20}}{A_{17}\varphi} - \frac{A_{21}\delta_1\lambda_c}{A_{17}k_6\varphi} -\right.$$

$$\left.\frac{A_7\theta_1}{A_{17}}\right),$$

$$A_{25} = \left(\frac{A_{23}A_{10}}{A_{17}} - \frac{A_{13}A_6}{A_{17}} - \frac{A_{19}A_1}{A_{17}k_6k_9\varphi} - \frac{A_{20}A}{A_7\varphi\Lambda\lambda_c(\tau\lambda_h+k_5)} - \frac{A_{21}(\delta_1 A+\gamma\lambda_h\Lambda\varphi(\tau\lambda_h+k_5))}{A_{17}k_6\varphi\Lambda(\tau\lambda_h+k_5)} - \frac{A_{22}}{A_{17}} - \frac{A_3\theta_1}{A_{17}}\right)$$

$$, A_{26} = \frac{A_{11}}{\varphi} + A_{12}A_{24} + \frac{A_{13}\eta\varepsilon_2\sigma_c\delta_1\lambda_c}{\varphi k_6k_9} + \frac{A_{15}\delta_1\lambda_c}{\varphi k_6} + A_{16}A_9 ,$$

$$A_{27} = \frac{A_{11}A}{\varphi\Lambda\lambda_c(\tau\lambda_h+k_5)} + A_{12}A_{25} + A_{13}A_7 + A_{14} + \frac{A_{15}(\delta_1 A+\gamma\lambda_h\Lambda\varphi(\tau\lambda_h+k_5))}{\varphi\Lambda k_6(\tau\lambda_h+k_5)} + A_{16}A_{10} ,$$

$$A_{28} = \left(\frac{\rho_2\eta\varepsilon_2\sigma_c\delta_1\lambda_c}{k_{12}k_{13}k_6\varphi} + \frac{\nu_2\eta\varepsilon_2\sigma_c\theta_3A_5}{k_{12}k_{13}k_8} + \frac{\nu_2\eta\varepsilon_2\sigma_c\delta_3\lambda_cA_{24}}{k_{12}k_{13}k_8} + \frac{\nu_2\eta^2{\varepsilon_2}^2{\sigma_c}^2\delta_1\lambda_c\theta_4}{k_{12}k_{13}k_8k_6k_9\varphi} - \frac{\nu_3A_5}{k_{13}} + \frac{\rho_3\eta\varepsilon_2\sigma_c\delta_1\lambda_c}{k_{13}k_6k_9\varphi}\right),$$

$$A_{29} = \frac{\delta_4\lambda_c\eta\varepsilon_2\sigma_c}{k_{12}k_{13}} + \frac{\rho_2\eta\varepsilon_2\sigma_c(\delta_1 A+\gamma\lambda_h\Lambda\varphi(\tau\lambda_h+k_5))}{k_{12}k_{13}k_6\Lambda\varphi(\tau\lambda_h+k_5)} + \frac{\nu_2\eta\varepsilon_2\sigma_c\theta_3A_6}{k_{12}k_{13}k_8} + \frac{\nu_2\eta\varepsilon_2\sigma_c\delta_3\lambda_cA_{25}}{k_{12}k_{13}k_8} + \frac{\nu_2\eta\varepsilon_2\sigma_c\theta_4A_{11}}{k_{12}k_{13}k_8} +$$

$$\frac{\nu_2A_6}{k_{13}} + \frac{\nu_3A_{10}}{k_{13}} + \frac{\rho_3A_1}{k_{13}}, A_{30} = \frac{k_{13}A_{28}}{\eta\varepsilon_2\sigma_c} - \frac{\nu_3A_9}{\eta\varepsilon_2\sigma_c} - \frac{\rho_3\delta_3\lambda_c}{k_6k_9\varphi},$$

$$A_{31} = \frac{k_{13}A_{29}}{\eta\varepsilon_2\sigma_c} - \frac{\nu_3A_{10}}{\eta\varepsilon_2\sigma_c} - \frac{\rho_3A_1}{\eta\varepsilon_2\sigma_c}, \quad A_{32} = \frac{\Lambda\lambda_c(\tau\lambda_h+k_5)+A}{\lambda_c(\tau\lambda_h+k_5)} + \frac{\lambda_h\left((\omega_0+\eta_0)\sigma_c+\gamma\lambda_h+\mu\right)}{\lambda_c} + \omega\epsilon_1\sigma_c(A_7+\lambda_8) +$$

$$r_2(A_3+A_4) - \frac{\delta_1(\Lambda\lambda_c(\tau\lambda_h+k_5)+A)}{\varphi\Lambda(\tau\lambda_h+k_5)} - \frac{k_1(\Lambda\lambda_c(\tau\lambda_h+k_5)+A)}{\varphi\Lambda\lambda_c(\tau\lambda_h+k_5)}$$

3.6.3 HIV-HCV Co-infection Basic Reproduction Number R_{hc} for Model Case 3

The next generation matrix approach as discussed in case 1 and case 2 was employed here. By the next-generation matrix approach, we need to enumerate the number of new infections that can arise and the transfer of infections. Thus, by considering system (3.3) there are four ways of creating new infections and transfer of infections stated below:

1. Unaware HIV humans give birth to an infected HIV offspring
2. Susceptible humans having contact with infected individuals with HIV or HCV or infectious individual with both HCV and HIV.
3. When an infectious individual with HIV has an unprotected sex with an infected HCV or

an infected individual with HCV is in contact with infectious individual with HIV or an infectious individual with HCV is in contact with an infectious individual having both HCV and HIV diseases.

4. When a susceptible HCV have a contact with an infectious individual with HCV or both HCV and HIV.

By next-generation-matrix (NGM)

$R_{hc} = FV^{-1}$

where F is the newly formed infection matrix and V is the transferred infection matrix. Based on the submission in (1) – (4) above.

Therefore, at the co-infection disease free equilibrium E_{ohc}

See appendix I for the value of $F\ and\ V$

Then,

$\rho = FV^{-1}$

$$\lambda_1 = \lambda_2 = \lambda_3 = \lambda_4 = \lambda_5 = \lambda_6 = \lambda_7 = \lambda_8 = \lambda_9 = \lambda_{10} = \lambda_{11} = \lambda_{12} = 0,$$

$$\lambda_{13} = \frac{cb_c(\eta\psi\xi\sigma_c - \psi\xi k_5 - \eta_0\sigma_c + k_5)}{k_5(\eta_0\sigma_c + \omega_0\sigma_c + \mu)},$$

$$\lambda_{14} = \frac{cb_h(1-\psi\xi)(\alpha_1\theta_1\upsilon_1 + k_2k_3k_4 + k_2k_3\rho_1 - k_2\theta_2\upsilon_1)}{k_2(k_3k_4 - \upsilon_1\theta_2)(\Lambda\varphi - k_1)}$$

There are two dominant eigenvalues of FV^{-1} namely:

$$\lambda_{13} = \frac{cb_c(\eta\psi\xi\sigma_c - \psi\xi k_5 - \eta_0\sigma_c + k_5)}{k_5(\eta_0\sigma_c + \omega_0\sigma_c + \mu)},$$

$$\lambda_{14} = \frac{cb_h(1-\psi\xi)(\alpha_1\theta_1\upsilon_1 + k_2k_3k_4 + k_2k_3\rho_1 - k_2\theta_2\upsilon_1)}{k_2(k_3k_4 - \upsilon_1\theta_2)(\Lambda\varphi - k_1)}$$

Therefore,

R_{HC}

$$= max\left\{\frac{cb_h(1-\psi\xi)(\alpha_1\theta_1\upsilon_1 + k_2k_3k_4 + k_2k_3\rho_1 - k_2\theta_2\upsilon_1)}{k_2(k_3k_4 - \upsilon_1\theta_2)(\Lambda\varphi - k_1)}, \frac{cb_c(\eta\psi\xi\sigma_c - \psi\xi k_5 - \eta_0\sigma_c + k_5)}{k_5(\eta_0\sigma_c + \omega_0\sigma_c + \mu)}\right\}$$

$$= \{R_{\mathrm{H}}, R_{\mathrm{C}}\} \quad (3.105)$$

Let R_{HC} denote the basic reproduction number for HIV and HCV co-infection defined thus

$$R_{HC} = max\{R_H, R_C\}$$

3.6.4 Stability Analysis of the Co-infection Model

3.6.4.1 Analysis of the HIV-HCV Free Equilibrium $E_o's$ Local Stability

At the HIV-HCV disease-free equilibrium E_0, the local stability of the HIV-HCV free equilibrium was explored. Theorem 3.15 shows that the HCV disease-free equilibrium E_0 is locally stable.

Theorem 3.15:

The virus-free equilibrium E_o is asymptotically stable locally if R_{HC}< 1, otherwise it is unstable.

Proof:

The linearized model yields $\frac{dX}{dt} = AX$ as the Jacobian matrix of (3.3) at E_o.

$$X = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9, x_{10}, x_{11}, x_{12}, x_{13}, x_{14}, x_{15})^T,$$

$$(x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9, x_{10}, x_{11}, x_{12}, x_{13}, x_{14}, x_{15}) \in R_+^{15}$$

See appendix II for the resulting Jacobian matrices

Hence, from eqaution (3) in appendix II

$\lambda_1 = -\mu;\ \lambda_2 = -k_6;\ \lambda_3 = -k_7;\ \lambda_4 = -k_8;\ \lambda_5 = -k_9;\ \lambda_6 = -k_{10};\ \lambda_7 = -k_{11};\ \lambda_8 = -k_{12};\ \lambda_9 = -k_{13};$

so that the remaining eigenvalues are obtained from the remaining 6 x 6 matrix from eqaution (4) in appendix II using the Routh_Hurwitz condition which states that :

(1) Trace $J(E_0) < 0$ (2) Determinant $J(E_0) > 0$`

$$\text{Trace } J(E_0) = \Lambda\varphi + cb_h(1-\psi\xi) - k_1 - k_2 - k_3 - k_4 - 6\lambda + cb_c(1-\psi\xi) - (\omega_0 + \eta_0)\sigma_c - \mu - k_5 < 0 \quad (3.106)$$

$$\text{Determinant } J(E_0) = (b_h c\,\lambda^3\psi\xi + b_h c\,\lambda^2\psi\xi k_2 + b_h c\,\lambda^2\psi\xi k_3 + b_h c\,\lambda^2\psi\xi k_4 + b_h c\,\lambda^2\psi\xi\rho_1 + b_h c\lambda\psi\xi k_2 k_3 + b_h c\lambda\psi\xi k_2 k_4 + b_h c\lambda\psi\xi k_2\rho_1 + b_h c\lambda\psi\xi k_3 k_4 + b_h c\lambda\psi\xi k_3\rho_1 - b_h c\lambda\psi\xi\theta_2\upsilon_1 + b_h c\psi\xi\alpha_1\theta_1\upsilon_1 + b_h c\psi\xi k_2 k_3 k_4 + b_h c\psi\xi k_2 k_3\rho_1 - b_h c\psi\xi k_2\theta_2\upsilon_1 - \Lambda\,\lambda^3\varphi - \Lambda\,\lambda^2\varphi k_2 - \Lambda\,\lambda^2\varphi k_3 - \Lambda\,\lambda^2\varphi k_4 - \Lambda\lambda\varphi k_2 k_3 - \Lambda\lambda\varphi k_2 k_4 - \Lambda\lambda\varphi k_3 k_4 + \Lambda\lambda\varphi\theta_2\upsilon_1 - \Lambda\varphi k_2 k_3 k_4 + \Lambda\varphi k_2\theta_2\upsilon_1 - b_h c\,\lambda^3 - b_h c\,\lambda^2 k_2 - b_h c\,\lambda^2 k_3 - b_h c\,\lambda^2 k_4 - b_h c\,\lambda^2\rho_1 - b_h c\lambda k_2 k_3 - b_h c\lambda k_2 k_4 - b_h c\lambda k_2\rho_1 - b_h c\lambda k_3 k_4 - b_h c\lambda k_3\rho_1 + b_h c\lambda\theta_2\upsilon_1 - \alpha_1 c b_h\upsilon_1\theta_1 - b_h c k_2 k_3 k_4 - b_h c k_2 k_3\rho_1 + b_h c k_2\theta_2\upsilon_1 + \lambda^4 + \lambda^3 k_1 + \lambda^3 k_2 + \lambda^3 k_3 + \lambda^3 k_4 + \lambda^2 k_1 k_2 + \lambda^2 k_1 k_3 + \lambda^2 k_1 k_4 + \lambda^2 k_2 k_3 + \lambda^2 k_2 k_4 + \lambda^2 k_3 k_4 - \lambda^2\theta_2\upsilon_1 + \lambda k_1 k_2 k_3 + \lambda k_1 k_2 k_4 + \lambda k_1 k_3 k_4 - \lambda k_1\theta_2\upsilon_1 + \lambda k_2 k_3 k_4 - \lambda k_2\theta_2\upsilon_1 + k_1 k_2 k_3 k_4 - k_1 k_2\theta_2\upsilon_1)(b_c c\eta\psi\xi\sigma_c + b_c c\lambda\psi\xi + b_c c\psi\xi k_5 - cb_c\eta\sigma_c - b_c c\lambda - b_c c k_5 + \lambda\eta_0\sigma_c + \lambda\omega_0\sigma_c + \eta_0 k_5\sigma_c + k_5\omega_0\sigma_c + \lambda^2 + \lambda\mu + \lambda k_5 + \mu k_5) > 0\ since\ R_{HC} < 1 \quad (3.107)$$

The disease-free equilibrium is stable since the conditions in (3.106) and (3.107) have been met.

Now, $\lambda_{10}, \lambda_{11}, \lambda_{12}, \lambda_{13}, \lambda_{14}, \lambda_{15}<$ since the values are considered to be positive. If $R_{HC}<1$, therefore, E_o is stable and unstable when $R_{HC}>1$.

From Determinant $J(E_0)$ in (3.107)

$$(b_h c\psi\xi\alpha_1\theta_1\upsilon_1 + b_h c\psi\xi k_2 k_3 k_4 + b_h c\psi\xi k_2 k_3\rho_1 - b_h c\psi\xi k_2\theta_2\upsilon_1 - \Lambda\varphi k_2 k_3 k_4 + \Lambda\varphi k_2\theta_2\upsilon_1 - \alpha_1 c b_h\upsilon_1\theta_1 - b_h c k_2 k_3 k_4 - b_h c k_2 k_3\rho_1 + b_h c k_2\theta_2\upsilon_1 + k_1 k_2 k_3 k_4 - k_1 k_2\theta_2\upsilon_1)(b_c c\eta\psi\xi\sigma_c + b_c c\psi\xi k_5 - c b_c\eta\sigma_c - b_c c k_5 + \eta_0 k_5\sigma_c + k_5\omega_0\sigma_c + \mu k_5) = 0 \quad (3.108)$$

3.6.4.2 Model Case 3 Global Stability of HIV-HCV Free Equilibrium

Using the Comparison theorem at the HIV-HCV disease-free equilibrium E_0, it was determined whether the HIV-HCV free equilibrium was globally stable. The global stability of the HIV-HCV disease-free equilibrium, E_0, is demonstrated by theorem (3.16).

Theorem 3.16:

The global asymptotically stable HIV-HCV disease-free equilibrium E_0 of the system (3.3) is unstable if $R_{HC} > 1$ and stable if $R_{HC} < 1$.

Proof:

The Lashmkantham *et al* (1989) and Mushayabasa *et al* (2011) Comparison approach is employed here. The rate of change of the system's exposed and infected components (3.3) can be represented as:

See appendix III the complete proof.

J is a non-negative matrix since $S(t) \leq \frac{\Lambda}{\mu}$ in the invariant set. Hence, it follows that

$$\frac{dx}{dt} \leq (F - V)X$$

The eigenvalues of the matrix $F - V$ have negative results when $R_{\mathrm{HC}} < 1$. It follows that the linearized differential inequality (3.3) is stable whenever $R_{HC} < 1$. Consequently, $(H_A, H_T, A_a, I_c, C_c, H_{uI}, H_{AI}, H_{TI}, H_{UC}, H_{AC}, H_{TC}, A_{AI}, A_{aC}) \rightarrow (0,0,0,0,0,0,0,0,0,0,0,0,0,0)$ as $t \rightarrow \infty$. Evaluating system (3.3) at $H_A = H_T = A_a = I_c = C_c = H_{uI} = H_{AI} = H_{TI} = H_{UC} = H_{AC} = H_{TC} = A_{AI} = A_{aC} = 0$ gives, $S_h \rightarrow 1$ and $S_C \rightarrow 1$ for $R_{HC} < 1$. Hence, the HIV diseases free equilibrium E_0 of the system (3.3) is globally asymptotically stable if $R_{HC} < 1$. The result also follows immediately that the HIV-HCV disease-free equilibrium E_0 of the system (3.3) is unstable if $R_{HC} > 1$.

3.6.4.3 Local Asymptotic Stability of HIV-HCV Endemic Equilibrium

Here, the local stability of the HIV-HCV endemic equilibrium was investigated at the HIV-HCV disease-endemic equilibrium ${E_0}^*$. Theorem 3.17 prove the local stability of the co-infection disease - endemic equilibrium ${E_0}^*$.

Theorem 3.17:

If $R_{HC} > 1$, then the endemic equilibrium is locally asymptotically stable.

Proof:

The endemic equilibria of the system (3.3), denoted by

$(S^*, H_U^*, H_A^*, H_T^*, A_A^*, I_C^* \; C_C^*, H_{UI}^*, H_{AI}^*, H_{TI}^*, H_{UC}^*, H_{AC}^*, H_{TC}^*, A_{AI}^*, A_{AC}^*)$, can be rewritten as:

Let $S = x + S^*, H_U = y + H_U^*, H_A = z + H_A^*, H_T = p + H_T^*, A_A = q + A_A^*, I_C = r + I_C^*, C_C = u + C_C^*, H_{uI} = v + H_{uI}^*, H_{AI} = w + H_{AI}^*, H_{TI} = a + H_{TI}^*, H_{UC} = b + H_{UC}^*, H_{TC} = d + H_{TC}^*, A_{AI} = e + A_{AI}^*, A_{AC} = f + A_{AC}^*$

See appendix IV for the proof

Now from eqaution (10) in appendix IV,

$\lambda_1 = -a_{11},\ \lambda_2 = -a_{22},\ \lambda_3 = -a_{33},\ \lambda_4 = -a_{44},\ \lambda_5 = -a_{55},\ \lambda_6 = -a_{66},\ \lambda_7 = -a_{77},\ \lambda_8 = -a_{88},\ \lambda_9 = -a_{99},\ \lambda_{10} = -a_{1010},\ \lambda_{11} = -a_{1111},\ \lambda_{12} = -a_{1212},\ \lambda_{13} = -a_{1313},\ \lambda_{14} = -a_{1414},\ \lambda_{15} = -a_{1515}$.

Since all eigenvalues along the diagonal are negative; If R_{HC}< 1, therefore, E_o is stable and unstable when R_{HC}> 1.

$$\text{Trace} = a_{11} + a_{22} + a_{33} + a_{44} + a_{55} + a_{66} + a_{77} + a_{88} + a_{99} + a_{1010} + a_{1111} + a_{1212} + a_{1313} + a_{1414} + a_{1515} \quad (3.109)$$

$$\text{Determinant} = a_{11}a_{22}a_{33}a_{44}\, a_{55}a_{66}a_{77}a_{88}a_{99}a_{1010}a_{1111}a_{1212}a_{1313}a_{1414}a_{1515} \quad (3.110)$$

` (1) Trace $(E_0) < 0$ (2) Determinant $(E_0) > 0$

From equation (3.109) and (3.110) 1 and 2 are satisfied.

Therefore, endemic equilibrium of the co-infection model is locally asymptotically stable.

3.6.4.4 Global Stability of Endemic Equilibrium and Bifurcation Analysis of HIV-HCV

The HIV–HCV co-infection model of (3.3) has a positive distinctive endemic equilibrium whenever $R_{HC} > 1$, which is said to be globally asymptotically stable and unstable if $R_{HC} < 1$ whenever item (d) of theorem 2.3 in subsection 2.2.6 is satisfied.

Using a regular perturbation argument together with Lyapunov function theory as was done in model cases 1 and 2, and applying the Lasalle Theorem as in case 1 and case 2 is employed here. Recall that R_{HC} is defined to be $R_{HC} = max\{R_H, R_C\}$.

In summary, by the Lasalle theorem, the HIV-HCV equilibrium is globally asymptotically stable in the positive region R_+^{15}.

The case $R_{HC} = 1$ is considered and the assumption that $R_H < R_C = 1$. Also, let

$b(h) = b(h)^*$ be a bifurcation parameter.

Indeed, for some simple epidemiologic models, backward bifurcation with multiple endemic equilibria and Hopf bifurcation yielding a periodic solution can occur, (Hadler and Castillo-Chavez, 1995; Alexander and Moghades; 2004; 2005)

When R_{HC} is greater than but close to one in a model with only forward bifurcation, the level (number of the fraction) of infective individuals is low; however, when R_{HC} is less than but close to one in a system with backward bifurcation, the model has two endemic equilibria, one of which is a saddle and the other which is locally asymptotically stable. While the model with forward bifurcation has a unique endemic equilibrium, when R_{HC} is more than but near to one, the level (number or fraction) of infective individuals is higher. There are usually two thresholds for systems

with backward bifurcation: $R_{eHC} = R_{Hc}(0 < R_{Hc} < 1)$. There is a saddle-node bifurcation at $R_{eHC} = R_{Hc}$, and a backward bifurcation at $R_{eHC} = 1$.

The center manifold theory is used in this study to perform bifurcation analysis at the disease-free equilibrium as presented in (Buonomo and Lacitignola, 2011).

The focus is now on the HIV-HCV disease-free equilibrium E_0, with the transcritical bifurcation at $R_{eHC} = 1$ being investigated same as in case 1 and case 2.

The Centre Manifold Theorem as stated in Theorem 2.2.6 is now applied to ascertain if the system (3.3) exhibits a backward or forward bifurcation at $R_{ehC} = 1$.

It follows that the HIV-HCV disease-free equilibrium E_0 is locally stable when

$b_c < {b_c}^* and\ b_h < {b_h}^*$, whereas it loses its stability when $b_c > {b_c}^*\ and\ b_h < {b_h}^*$. So, the critical value $b_c = {b_c}^*$ and $b_h = {b_h}^*$is a bifurcation value.

The nature of the bifurcation involving the HCV disease-free equilibrium E_0 at $b_{c_C} = {b_c}^* and\ b_{c_h} = {b_h}^*$ (or equivalently at $R_{eC} = 1$) is investigated same as in case 1 and 2.

3.6.5 The Effect of Condom on HIV and HCV Disease Transmission Dynamics

The aim and ultimate goal of a public health worker are to change the transmission dynamics of disease in such a way that if an infected individual enters a community he/she will not trigger an epidemic in the community. Mathematically, it is reasonable to assume that if

$R_0 < 1$, then

$$\frac{dI}{dt} < 0 \tag{3.111}$$

For HIV and HCV, intervention can be in the following ways:

(i) Counselling and testing for the uninfected or unaware infected individual

(ii) Treatment using HAART and DAA drugs for HIV and HCV respectively

(iii) Reducing the rate of contact between susceptible individuals and infected individual and vice-versa and also reducing contact rate between HIV infected populace and HCV infected populace and vice-versa.

The latter can be achieved through use of condom, abstinence, avoid risk factors as a preventive measure, etc.

The system of equations in (3.3) introduces the functions $(1-\psi\xi)$ to describe the effect of condom usage on the HIV and HCV transmission respectively.

Let $Z = (1-\psi\xi)$

$Z > 0, if\ \psi\xi < 1\ and\ Z < 0, if\ \psi\xi > 1$

Here

$$\frac{\partial R_H}{\partial Z} = \frac{c_h b_h M}{k_2(\Lambda\varphi - k_1)(\theta_2\mu + (\mu+\nu_1)(\mu+d_a))} \tag{3.112}$$

$$\frac{\partial R_C}{\partial Z} = \frac{c_c b_c(\eta_0\sigma_c - k_5)}{k_5((\eta_0\sigma_c + \omega_0\sigma_c + \mu))} \tag{3.113}$$

Hence,

$$b_h(\xi) = c_{h_{max}} - \psi\xi \tag{3.114}$$

$$b_c(\xi) = c_{c_{max}} - \psi\xi \tag{3.115}$$

The functions $b_h(\xi)$ and $b_c(\xi)$ in equations (3.114) and (3.115) predicts that HIV and HCV transmissions are reduced proportionally to the strict abstinence and condom usage conditions. ψ is the coefficient of the condom use/effectiveness level ξ in the population. ξ is defined to be $\xi \in [0,1]$, so that if $\xi = 0$, then there is maximum transmission of HIV and HCV diseases in the population and if $\xi = 1$, means that there is access to maximum condoms in the population, hence, minimum transmission rate of HIV and HCV are achieved.

Using the functions defined in (3.112) and (3.113), a required level of condom use to prevent the outbreak and low transmission of HIV and HCV respectively are established as follows:

If $R_h < 1$

$$\frac{c_h b_h M}{k_2(\Lambda\varphi - k_1)\big(\theta_2\mu + (\mu + \nu_1)(\mu + d_a)\big)} < 1 \tag{3.116}$$

$$b_h < \frac{c_h M}{k_2(\Lambda\varphi - k_1)(\theta_2\mu + (\mu + \nu_1)(\mu + d_a))} \tag{3.117}$$

$$b_{h_{max}} - \psi\xi < \frac{c_h M}{k_2(\Lambda\varphi - k_1)\big(\theta_2\mu + (\mu + \nu_1)(\mu + d_a)\big)} \tag{3.118}$$

Thus, the level of condom protection required for HIV reduction/eradication is

$$\xi > \frac{1}{\psi}\left[b_{h_{max}} - \frac{c_h M}{k_2(\Lambda\varphi - k_1)(\theta_2\mu + (\mu + \nu_1)(\mu + d_a))}\right] \tag{3.119}$$

Also, if $R_c < 1$

$$\frac{c_c b_c(\eta_0\sigma_c - k_5)}{k_5\big((\eta_0\sigma_c + \omega_0\sigma_c + \mu)\big)} < 1 \tag{3.120}$$

$$b_c < \frac{c_c(\eta_0\sigma_c - k_5)}{k_5((\eta_0\sigma_c + \omega_0\sigma_c + \mu))} \tag{3.121}$$

$$b_{h_{max}} - \psi\xi < \frac{c_c(\eta_0\sigma_c - k_5)}{k_5\big((\eta_0\sigma_c + \omega_0\sigma_c + \mu)\big)} \tag{3.122}$$

Thus, the level of condom required for HCV reduction/eradication is

$$\xi > \frac{1}{\psi}\left[b_{c_{max}} - \frac{c_c(\eta_0\sigma_c - k_5)}{k_5((\eta_0\sigma_c + \omega_0\sigma_c + \mu))}\right] \tag{3.123}$$

3.6.6 The Effect of HIV on HCV Disease Transmission Dynamics

The work of a public health worker is to change the transmission dynamics of disease in such a way that if an infected individual enters a community he/she will not trigger an epidemic in the community. Mathematically, it is reasonable to assume that if

$R_0 < 1$, then

$$\frac{dI}{dt} < 0 \tag{3.124}$$

From (3.106)

$$R_{\mathrm{C}} = \frac{c_c b_c(1 - \psi\xi)(\eta_0\sigma_c - k_5)}{k_5(\eta_0\sigma_c + \omega_0\sigma_c + \mu)} \tag{3.125}$$

$$R_{\mathrm{H}} = \frac{c_h b_h(1 - \psi\xi)(\alpha_1\theta_1\upsilon_1 + k_2k_3k_4 + k_2k_3 - k_2\theta_2\upsilon_1)}{k_2(k_3k_4 - \upsilon_1\theta_2)(\Lambda\varphi - k_1)} \tag{3.126}$$

Where

$$k_1 = \mu + \alpha_1 + \rho_1, k_2 = \mu + \theta_1, k_3 = \mu + \nu_1, k_4 = \mu + d_a + \theta_2, k_5 = \mu + d_c + r_1$$

Then

$$R_{\mathrm{H}} = \frac{c_h b_h (1 - \psi\xi)(\alpha_1 \theta_1 \upsilon_1 + k_2 k_3 \rho_1 + k_2(\mu + \nu_1)(\mu + d_a) + k_2 \theta_2 \mu)}{k_2(\theta_2 \mu + (\mu + \nu_1)(\mu + d_a))(\Lambda\varphi - k_1)} \qquad (3.127)$$

Observe from (3.127) that

$$(1 - \psi\xi) = \frac{k_5(\eta_0 \sigma_c + \omega_0 \sigma_c + \mu)}{c_c b_c (\eta_0 \sigma_c - k_5)} R_{\mathrm{C}} \qquad (3.128)$$

Using (3.128) in (3.129)

$$R_{\mathrm{H}} = \frac{c_h b_h M k_5(\eta_0 \sigma_c + \omega_0 \sigma_c + \mu)}{k_2(\Lambda\varphi - k_1)(\theta_2 \mu + (\mu + \nu_1)(\mu + d_a)) c_c b_c (\eta_0 \sigma_c - k_5)} R_{\mathrm{C}} \qquad (3.130)$$

Provided $\eta_0 \sigma_c > k_5 \; and \; \Lambda\varphi > k_1$

Where $M = (\alpha_1 \theta_1 \upsilon_1 + k_2 k_3 \rho_1 + k_2(\mu + \nu_1)(\mu + d_a) + k_2 \theta_2 \mu)$

We want to consider how the reproduction number of HCV, R_{C} and reproduction number of R_{H} impact one another as follows:

$$\frac{\partial R_H}{\partial C} * \frac{\partial C}{\partial R_C} = \frac{\partial R_H}{\partial R_C}$$

$$= \frac{b_h M k_5(\eta_0 \sigma_c + \omega_0 \sigma_c + \mu)}{k_2(\Lambda\varphi - k_1)\big(\theta_2 \mu + (\mu + \nu_1)(\mu + d_a)\big) b_c (\eta_0 \sigma_c - k_5)} \qquad (3.131)$$

From (3.131) since the partial derivatives with respect to R_C is positve, this implies that as the reproduction number of HCV, R_C increase, it impacts the reproduction number of HIV R_H. Then,

we should simply allow HCV infection to reduce to avoid increased viral load in HIV-infected individuals because any slight increase in HCV will make HIV increase.

3.7 Application of Optimal Control to HIV-HCV Co-infection Model

The main objective of this study is to suggest possible(s) optimal method of reducing/minimizing HIV and HCV transmission. Many mathematical model already exist describing HIV infection or HCV infection but the best control for HIV infection, HCV infection and the co-infection of both diseases still remain a subject of debate.

Previous mathematical models have considered public health education, treatment and behavioural change through total abstinence as controls also maintaining a balanced nutritional supplementation. However, these have their limitations.

Generally, abstinence and balanced nutritional supplementation are not 100% effective in controlling HIV and HCV, and therefore only a proportion of aware individuals or informed via public health education can abstain and those who can afford the cost of maintaining balanced nutritional supplementation, then some proportion of the unaware individuals may are at the high risk of disease progression (Rabiu *et al.*, 2021).

However, testing and treatment will be more effective in a well-informed population hence, the inclusion of enhancement of the strength of treatment for the infected individuals and awareness source among the unaware infective as a control in the present work (Naik *et al.*, 2020). The latter control by (Naik *et al.*, 2020) will be more effective in a closed area, hence, the inclusion of condom usage, counselling and testing and HAART as a control in the present work as HIV testing remains an essential gateway to HIV prevention, treatment, care and support services

The preventive and treatment control for HCV includes abstinence or use of condom, testing at various infectious stage and appropriate treatment (Scott *et al.*, 2016). It is believed that, if appropriate preventive measures were instituted globally, liver cirrhosis will be reduced greatly in HCV infected individual as early testing will help reduce mortality rate through liver cirrhosis (WHO, 2020b) and also help in reducing disease progression HIV infected individual. Also, if HCV testing and proper treatment were universally available for people living with HIV and vice versa disease progression and deaths could be decreased by 65% in co-infection individual and new infections could be reduced by 54% (Garcia-Broncano *et al.*, 2018).

3.7.1 Formulation of Optimal Control Model for HIV-HCV Co-infection

We now introduce into the system (3.3) time-dependent preventive measures $\left(u_1(t), u_2(t)\right)$ and treatment efforts $\left(u_3(t), u_4(t)\right)$ as controls to curtail the spread of HIV and HCV co-infection. Thus, system (3.3) becomes

where

$u_1(t)$: is the time preventive control using a condom for HIV and HCV for control

$u_2(t)$: is the time preventive control using counselling and testing on unaware HIV and HCV infected

$u_3(t)$: is the treatment effort using pEp/ PrEp or HAART drugs for HIV/AIDS

$u_4(t)$: is the treatment effort using DAAs drugs for HCV

In the present work, the following cases are considered:

Case 4: The optimal control strategy for the HIV transmission model

Case 5: The optimal control strategy for the HCV transmission model

$$\left.\begin{aligned}
S_{hc}'(t) &= (1-\varphi H_U)\Lambda + \omega_0\sigma_c \mathrm{I}_C + u_4 C_C - ((1-u_1)\lambda_H + (1-u_1)\lambda_C + \mu)S \\
H_U'(t) &= \varphi H_U\Lambda + (1-u_1)\lambda_H S + \omega\epsilon_1\sigma_c H_{UI} + u_4 H_{AC} - \big((1-u_1-u_2)\delta_1\lambda_C + \mu + u_2 + \rho_1\big)H_U \\
H_A'(t) &= u_2 H_U + \omega\epsilon_1\sigma_c H_{AI} + r_3 H_{AC} - ((1-u_1)\delta_2\lambda_C + \mu + u_3)H_A \\
H_T'(t) &= u_3 H_A + \omega\epsilon_1\sigma_c H_{TI} + r_4 A_{AI} + u_3\theta_2 A_A - \big((1-u_1)\delta_3\lambda_C + \mu + \upsilon_1\big)H_T \\
A_A'(t) &= \rho_1 H_U + \upsilon_1 H_T + \omega\epsilon_1\sigma_c H_{UC} + r_5 A_{AC} - \big((1-u_1)\delta_4\lambda_C + \mu + d_a + u_3\theta_2\big)A_A \\
I_C'(t) &= (1-u_1)\lambda_C S - (\omega_0+\eta_0)\sigma_c \mathrm{I}_C - \big((1-u_2)\gamma\lambda_H + \mu\big)I_C \\
C_C'(t) &= \eta_0\sigma_c I_C - \big((1-u_1)\tau\lambda_H + \mu + d_c + u_4\big)C_C \\
H_{UI}'^{(t)} &= (1-u_1-u_2)\delta_1\lambda_C H_U + (1-u_2)\gamma\,\lambda_H \mathrm{I}_C - (\eta\epsilon_2\sigma_c + \omega\epsilon_1\sigma_c + \mu + \rho_2 + u_2)H_{UI} \\
H_{AI}'(t) &= u_2 H_{UI} + (1-u_1)\delta_2\lambda_C H_A - (\eta\epsilon_2\sigma_c + \omega\epsilon_1\sigma_c + \mu + u_1 + 2u_3)H_{AI} \\
H_{TI}'(t) &= u_3 H_{AI} + (1-u_1)\delta_3 H_T + u_3\theta_4 A_{AI} - (\eta\epsilon_2\sigma_c + \omega\epsilon_1\sigma_c + \mu + \upsilon_3)H_{TI} \\
H_{UC}'(t) &= (1-u_1)\tau\lambda_H C_C + \eta\epsilon_2\sigma_c H_{UI} - (u_4 + u_2 + \rho_3 + \mu + d_c)H_{UC} \\
H_{AC}'(t) &= u_2 H_{UC} + \eta\epsilon_2\sigma_c H_{AI} - (u_4 + u_3 + \mu + d_c)H_{AC} \\
H_{TC}'(t) &= u_3 H_{AC} + \eta\epsilon_2\sigma_c H_{TI} + u_3\theta_6 A_{AC} - (\upsilon_3 + \mu + d_c + u_4)H_{TC} \\
A_{AI}'(t) &= (1-u_1)\delta_4\lambda_C A_A + H_{UI}\rho_2 + \upsilon_2 H_{TI} - (\eta\epsilon_2\sigma_c + \omega\epsilon_1\sigma_c + u_3\theta_4 + \mu + d_a)A_{AI} \\
A_{AC}'(t) &= \eta\epsilon_2\sigma_c A_{AI} + H_{TC}\upsilon_3 + \rho_3 H_{UC} - (u_3\theta_6 + \mu + d_a + d_c + u_4)A_{AC}
\end{aligned}\right\} \quad (3.132)$$

$$\lambda_H = \frac{c_h(1-\psi\xi)b_h\big(H_U + A_A + \kappa_1(H_{UI} + H_{UC})\big)}{S + H_U + H_A + H_T + A_A + \mathrm{I}_C + C_C + H_{UI} + H_{AI} + H_{TI} + H_{UC} + H_{AC} + H_{TC} + A_{AI} + A_{AC}},$$

$$\lambda_C = \frac{c_c(-\psi\xi+1)b_c\big(\mathrm{I}_C + C_C + \kappa_2(H_{UI} + H_{UC})\big)}{S + H_U + H_A + H_T + A_A + \mathrm{I}_C + C_C + H_{UI} + H_{AI} + H_{TI} + H_{UC} + H_{AC} + H_{TC} + A_{AI} + A_{AC}}$$

3.8 The Optimal Control Strategy for HIV Transmission Model

Here, the formulation of the optimal control problem, analysis of the optimal control problem, adjoint conditions, optimality conditions and the optimality system for the HIV model case 4 are considered.

3.8.1 The Optimal Control Formulation for HIV Transmission Model

Let $I_C(t) = C_C(t) = H_{UI}(t) = H_{AI}(t) = H_{TI}(t) = H_{UC}(t) = H_{AC}(t) = H_{TC}(t) = A_{AI}(t) = A_{AC}(t) = 0$ in a model system (3.132) gives the following system of equations

$$\left.\begin{aligned} S'(t) &= (1-\varphi H_U)\Lambda - \left(\frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)}{S+H_U+H_A+H_T+A_A}+\mu\right)S \\ H_U'(t) &= \Lambda\varphi H_U + \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S}{S+H_U+H_A+H_T+A_A} - (\mu+u_2+\rho_1)H_U \\ H_A'(t) &= u_2H_U-(\mu+u_3)H_A \\ H_T'(t) &= H_Au_3+u_3\theta_2A_A-(\mu+v_1)H_T \\ A_A'(t) &= \rho_1H_U+H_Tv_1-(u_3\theta_2+\mu+d_a)A_A \end{aligned}\right\} \quad (3.133)$$

The controls used in the system (3.133) represent effective time-dependent preventive measures (u_1, u_2) and treatment efforts (u_3) to curtail the spread of HIV. The controls u in (3.133) is defined to be $u \in [0,1]$, where u ranges from no control $(u = 0)$ to maximum control $(u = 1)$.Note that $u_1, u_2, u_3 \in u$.

One of the objectives of this research is to find the optimal control strategy u throughout the length of $0 \le t \le t_f$ such that the number of HIV-infected individuals is minimized while minimizing the cost of control u. Thus, the objective function is

$$J(u_1,u_2,u_3) = \int_0^{tf}(G_1H_U + G_2H_A + G_3H_T + G_4A_A + G_5u_1^2 + G_6u_2^2 + G_7u_3^2)dt \quad (3.134)$$

where coefficients $G_1, G_2, G_3, G_4, G_5, G_6,\ and\ G_7$ are positive weights to balance the factors.

Thus, we seek an optimal control

$$u^* = \{u_1{}^*, u_2{}^*, u_3{}^*\}$$

such that

$$J(u_1{}^*, u_2{}^*, u_3{}^*) = \min_{u_1,u_2,u_3}\left\{J(u_1,u_2,u_3)|_{u_1,u_2,u_3} \in u\right\} \quad (3.135)$$

where

$$u = \left\{(u_1,u_2,u_3)|_{u_1,u_2,u_3}: [0,t_f] \to [0,1]\right\} \quad (3.136)$$

is Lebesgue measurable and convex on u, then there exists an optimal control u satisfying the conditions in section 2.2.8.1.

3.8.2 The Analysis of the HIV Optimal Control Problem Model

Since there exist an optimal control for minimizing the functional (3.133) subject to system of equations (3.124), the Pontryagins' Maximum Principle (Fleming and Rishel, 1975) is used to derive necessary conditions for this optimal control.

The Hamiltonian is defined as follows:

$$\bar{H} = G_1 H_U + G_2 H_A + G_3 H_T + G_4 A_A + G_5 u_1^2 + G_6 u_2^2 + G_7 u_3^2 + \lambda_1[(1-\varphi H_U)\Lambda - \left(\frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)}{S+H_U+H_A+H_T+A_A} + \mu\right)S] + \lambda_2[\varphi H_U \Lambda + \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S}{S+H_U+H_A+H_T+A_A} - (\mu+u_2+\rho_1)H_U] + \lambda_3[u_2 H_U - (\mu+u_3)H_A] + \lambda_4[u_3 H_A + u_3\theta_2 A_A - (\mu+\upsilon_1)H_T] + \lambda_5[\rho_1 H_U + H_T\upsilon_1 - (u_3\theta_2 + \mu + d_a)A_A] \quad (3.137)$$

3.8.3 The Adjoint Conditions for HIV Model

To attach the system of ordinary differential equation in (3.133) to the objective function in (3.134), the adjoint functions (or co-state variables) were used. The Pontryagins' Maximum Principle gives the necessary conditions that the adjoint functions must satisfy. Thus, the differential equations satisfied by system (3.133) are

$$\frac{d\lambda_1}{dt} = -\frac{\partial \bar{H}}{\partial S} = \left(\frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2} - \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)}{S+H_U+H_A+H_T+A_A} - \mu\right)\lambda_1 - \left(-\frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2} + \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)}{S+H_U+H_A+H_T+A_A}\right)\lambda_2$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial \bar{H}}{\partial H_U} = \left(-\varphi\Lambda - \left(\frac{(1-u_1)c(1-\psi\xi)b_h}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)}{(S+H_U+H_A+H_T+A_A)^2}\right)S\right)\lambda_1 - \left(\varphi\Lambda + \frac{(1-u_1)c(1-\psi\xi)b_hS}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2} - \mu - u_2 - \rho_1\right)\lambda_2 - u_2\lambda_3 - \rho_1\lambda_5 - G_1$$

$$\frac{d\lambda_3}{dt} = -\frac{\partial \bar{H}}{\partial H_A} = \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S\lambda_1}{(S+H_U+H_A+H_T+A_A)^2} + \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S\lambda_2}{(S+H_U+H_A+H_T+A_A)^2} - (-\mu-u_3)\lambda_3 - u_3\lambda_4 - G_2$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial \bar{H}}{\partial H_T} = \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S\lambda_1}{(S+H_U+H_A+H_T+A_A)^2} + \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S\lambda_2}{(S+H_U+H_A+H_T+A_A)^2} - (-\mu-v_1)\lambda_4 - v_1\lambda_5 - G_3 \quad (3.138)$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial \bar{H}}{\partial A_A} = \left(\frac{(1-u_1)c(1-\psi\xi)b_h}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)}{(S+H_U+H_A+H_T+A_A)^2}\right)S\lambda_1 - \left(\frac{(1-u_1)c(1-\psi\xi)b_hS}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2}\right)\lambda_2 - u_3\theta_2\lambda_4 - (-u_3\theta_2-\mu-d_a)\lambda_5 - G_4$$

with the boundary conditions (or Transversality conditions) at the final time, t_f:

$$\lambda_1(t_f) = 0,\ \lambda_2(t_f) = 0,\ \lambda_3(t_f) = 0,\ \lambda_4(t_f) = 0,\ \lambda_5(t_f) = 0$$

3.8.4 The Optimality Conditions for HIV Model

The Hamiltonian in (3.137) is minimized with respect to the controls $u_1, u_2, and\ u_3$ separately in order to obtain the optimal value of u_1^*, u_2^*, u_3^*. At these controls values, the maximum Hamiltonian is obtained. The derivative of the Hamiltonian with respect to $u_1, u_2, and\ u_3$ is thus zero, since at the absolute minimum or maximum the slope of a function is zero. Thus,

$$\frac{\partial \bar{H}}{\partial u_1} = 2G_5u_1 + \frac{c(1-\psi\xi)b_h(H_U+A_A)S\lambda_1}{S+H_U+H_A+H_T+A_A} - \frac{c(1-\psi\xi)b_h(H_U+A_A)S\lambda_2}{S+H_U+H_A+H_T+A_A} = 0$$

Thus,

$$u_1 = \frac{c(\psi\xi - 1)b_h(H_U + A_A)S(\lambda_1 - \lambda_2)}{2(S + H_U + H_A + H_T + A_A)G_5} \tag{3.139}$$

Similar reasoning gives

$$\frac{\partial \bar{H}}{\partial u_2} = \frac{\partial \bar{H}}{\partial u_3} = 0$$

Thus

$$u_2 = \frac{H_U(\lambda_2 - \lambda_3)}{2G_6} \tag{3.140}$$

$$u_3 = -\frac{A_A\lambda_4\theta_2 - \theta_2 A_A\lambda_5 - H_A\lambda_3 + H_A\lambda_4}{2G_7} \tag{3.141}$$

At the absolute minimum $u = u^*$, therefore the optimality conditions are

$$\left.\begin{aligned} u_1^* &= min\{1, max(0, u_1)\} \\ u_2^* &= min\{1, max(0, u_2)\} \\ u_3^* &= min\{1, max(0, u_3)\} \end{aligned}\right\} \tag{3.142}$$

3.8.5 The optimality system for the HIV model

The optimality system consists of the state system, the adjoint system, initial conditions and the transversality conditions.

$$
\left.\begin{aligned}
S'(t) &= (1-\varphi H_U)\Lambda - \left(\frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)}{S+H_U+H_A+H_T+A_A}+\mu\right)S \\
H_U'(t) &= \Lambda\varphi H_U + \frac{(1-u_1)c(1-\psi\xi)b_h(H_U+A_A)S}{S+H_U+H_A+H_T+A_A} - (\mu+u_2+\rho_1)H_U \\
H_A'(t) &= u_2 H_U - (\mu+u_3)H_A \\
H_T'(t) &= H_A u_3 + u_3\theta_2 A_A - (\mu+\upsilon_1)H_T \\
A_A'(t) &= \rho_1 H_U + H_T\upsilon_1 - (u_3\theta_2+\mu+d_a)A_A \\
\lambda_1{}'(t) &= \left(\frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2} - \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)}{S+H_U+H_A+H_T+A_A} - \mu\right)\lambda_1 \\
&\quad -\left(-\frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2} + \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)}{S+H_U+H_A+H_T+A_A}\right)\lambda_2 \\
\lambda_2{}'(t) &= \left(-\varphi\Lambda - \left(\frac{(1-u_1)c(-\psi\xi+1)b_h}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)}{(S+H_U+H_A+H_T+A_A)^2}\right)S\right)\lambda_1 \\
&\text{Thus,} -\left(\varphi\Lambda + \frac{(1-u_1)c(-\psi\xi+1)b_h S}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2} - \mu - u_2 - \rho_1\right)\lambda_2 \\
&\quad -u_2\lambda_3 - \rho_1\lambda_5 - G_1 \\
\lambda_3{}'(t) &= \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S\lambda_1}{(S+H_U+H_A+H_T+A_A)^2} + \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S\lambda_2}{(S+H_U+H_A+H_T+A_A)^2} \\
&\quad -(-\mu-u_3)\lambda_3 - u_3\lambda_4 - G_2 \\
\lambda_4{}'(t) &= \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S\lambda_1}{(S+H_U+H_A+H_T+A_A)^2} + \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S\lambda_2}{(S+H_U+H_A+H_T+A_A)^2} \\
&\quad -(-\mu-\upsilon_1)\lambda_4 - \upsilon_1\lambda_5 - G_3 \\
\lambda_5{}'(t) &= \left(\frac{(1-u_1)c(-\psi\xi+1)b_h}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)}{(S+H_U+H_A+H_T+A_A)^2}\right)S\lambda_1 \\
&\quad -\left(\frac{(1-u_1)c(-\psi\xi+1)b_h S}{S+H_U+H_A+H_T+A_A} - \frac{(1-u_1)c(-\psi\xi+1)b_h(H_U+A_A)S}{(S+H_U+H_A+H_T+A_A)^2}\right)\lambda_2 \\
&\quad -u_3\theta_2\lambda_4 - (-u_3\theta_2-\mu-d_a)\lambda_5 - G_4
\end{aligned}\right\} \quad (3.143)
$$

The optimality system in (3.143) was solved numerically by using both the forward and backward finite difference scheme.

3.9 The Optimal Control Strategy for HCV Transmission Model

In this section, the formulation of the optimal control problem, analysis of the optimal control problem, adjoint conditions, optimality conditions and the optimality system for the HCV model case 5 are considered.

3.9.1 The Optimal Control Formulation for HCV Transmission Model

If $H_U(t) = H_A(t) = H_T(t) = A_A(t) = H_{UI}(t) = H_{UC}(t) = H_{AI}(t) = H_{AC}(t) = H_{TI}(t) = H_{TC}(t) = A_{AI}(t) = A_{AC}(t) = 0$ in model system (3.132) gives the following system of equations

$$\left.\begin{aligned} S'(t) &= \Lambda + \omega_0\sigma_c \mathrm{I}_C + u_4 C_C - \left(\frac{(1-u_1-u_2)c(1-\psi\xi)b_c(\mathrm{I}_C + C_C)}{S + \mathrm{I}_C + C_C} + \mu\right)S \\ I_C'(t) &= \frac{(1-u_1-u_2)c(1-\psi\xi)b_c(I_C + C_C)S}{S + I_C + C_C} - (\omega_0 + \eta_0)\sigma_c I_C - \mu I_C \\ C_C'(t) &= \sigma_c \mathrm{I}_C \eta_0 - (\mu + d_c + u_4)C_C \end{aligned}\right\} \quad (3.144)$$

The controls used in system (3.144) represent effective time dependent preventive measures (u_1, u_2) and treatment efforts (u_4) to curtail the spread of HCV. The controls u in (3.144) is defined to be $u \in [0,1]$, where u ranges from no control $(u = 0)$ to maximum control $(u = 1)$.Note that $u_1, u_2, u_4 \in u$.

The main objective of this research is to find the optimal control strategy u throughout the length of $0 \leq t \leq t_f$ such that the numbers of infected humans with HCV $I_C \; and \; C_C$ is minimized while minimizing the cost of control u. Thus, the objective function is defined as

$$J(u_1, u_2, u_4) = \int_0^{tf} (G_1 I_C + G_2 C_C + G_3 {u_1}^2 + G_4 {u_2}^2 + G_5 {u_4}^2)dt \quad (3.145)$$

where coefficients $G_1, G_2, G_3, G_4 \; and \; G_5$ are positive weights to balance the factors.

Thus, we seek an optimal control

$$u^* = \{{u_1}^*, {u_2}^*, {u_4}^*\}$$

such that

$$J({u_1}^*, {u_2}^*, {u_4}^*) = \min_{u_1, u_2, u_4} \left\{J(u_1, u_2, u_4)|_{u_1, u_2, u_4} \in u\right\} \quad (3.146)$$

where

$$u = \left\{(u_1, u_2, u_4)|_{u_1, u_2, u_4} : [0, t_f] \to [0,1]\right\} \quad (3.147)$$

is Lebesgue measurable and convex on u, then there exist an optimal control u satisfying the conditions in section 2.2.8.1.

3.9.2 The Analysis of the HCV Optimal Control Problem Model

Since there exist an optimal control for minimizing the functional (3.145) subject to system of equations (3.144), the Pontryagin Maximum Principle is used to derive necessary conditions for this optimal control.

The Hamiltonian is defined as follows:

$$\bar{H} = G_1 I_C + G_2 C_C + G_3 {u_1}^2 + G_4 {u_2}^2 + G_5 {u_4}^2 + \lambda_1 \Big[\Lambda + \omega_0 \sigma_c \mathrm{I}_C + u_4 C_C - \Big(\frac{(1-u_1-u_2)c(1-\psi\xi)b_c(\mathrm{I}_C+C_C)}{S+\mathrm{I}_C+C_C} + \mu\Big) S\Big] + \lambda_2 \Big[\frac{(1-u_1-u_2)c(1-\psi\xi)b_c(I_C+C_C)S}{S+I_C+C_C} - (\omega_0+\eta_0)\sigma_c I_C - \mu I_C\Big] + \lambda_3[\sigma_c \mathrm{I}_C \eta_0 - (\mu + d_c + u_4)C_C] \quad (3.148)$$

3.9.3 The Adjoint Conditions for HCV Model

In order to attach the system of ordinary differential equation in (3.144) on to the objective function in (3.145), the adjoint functions (or co-state variables) were used. The Pontryagins maximum principle gives the necessary conditions that the adjoint functions must satisfy. Thus, the differential equations satisfied by system (3.144) are:

$$\left.\begin{aligned} \frac{d\lambda_1}{dt} &= -\frac{\partial \bar{H}}{\partial S} = \lambda_1 - \left(\frac{(1-u_1-u_2)c(1-\psi\xi)b_c(I_C+C_C)S}{(S+I_C+C_C)^2} - \frac{(1-u_1-u_2)c(1-\psi\xi)b_c(I_C+C_C)}{S+I_C+C_C} - \mu\right)\lambda_1 \\ \frac{d\lambda_2}{dt} &= -\frac{\partial \bar{H}}{\partial I_C} = \lambda_2 - \left(\omega_0\sigma_c - \left(\frac{(1-u_1-u_2)c(1-\psi\xi)b_c}{S+I_C+C_C} - \frac{(1-u_1-u_2)c(1-\psi\xi)b_c(I_C+C_C)}{(S+I_C+C_C)^2}\right)S\right)\lambda_1 - G_1 \\ \frac{d\lambda_3}{dt} &= -\frac{\partial \bar{H}}{\partial C_C} = \lambda_3 - \left(u_4 - \left(\frac{(1-u_1-u_2)c(1-\psi\xi)b_c}{S+I_C+C_C} - \frac{(1-u_1-u_2)c(1-\psi\xi)b_c(I_C+C_C)}{(S+I_C+C_C)^2}\right)S\right)\lambda_1 - G_2 \end{aligned}\right\} \quad (3.149)$$

with the boundary conditions (or Transversality conditions) at the final time, t_f:

$$\lambda_1(t_f) = 0,\ \lambda_2(t_f) = 0,\ \lambda_3(t_f) = 0 \quad (3.150)$$

3.9.4 The Optimality Conditions for HCV Model

The Hamiltonian in (3.148) is minimized with respect to the controls $u_1, u_2\ and\ u_4$ separately in order to obtain the optimal value of u_1^*, u_2^*, u_4^*. At these controls values, the maximum Hamiltonian is obtained. The derivative of the Hamiltonian with respect to $u_1, u_2\ and\ u_4$ is thus zero, since at the absolute minimum or maximum the slope of a function is zero. Thus,

$$\frac{\partial \bar{H}}{\partial u_1} = 2G_3u_1 + \frac{c(1-\psi\xi+1)b_c(\mathrm{I}_C + C_C)S\lambda_1}{S + \mathrm{I}_C + C_C} = 0$$

Thus

$$u_1 = \frac{c(1-\psi\xi)b_c(\mathrm{I}_C + C_C)S\lambda_1}{2(S + \mathrm{I}_C + C_C)G_3} \tag{3.151}$$

Similar reasoning gives

$$\frac{\partial \bar{H}}{\partial u_2} = \frac{\partial \bar{H}}{\partial u_4} = 0$$

Therefore

$$u_2 = \frac{c(1-\psi\xi)b_c(I_C + C_C)S\lambda_1}{2(S + I_C + C_C)G_4} \tag{3.152}$$

$$u_4 = -\frac{C_C\lambda_1}{2G_5} \tag{3.153}$$

At the absolute minimum $u = u^*$, therefore the optimality conditions are

$$\left.\begin{aligned} u_1^* &= min\{1, max(0, u_1)\} \\ u_2^* &= min\{1, max(0, u_2)\} \\ u_4^* &= min\{1, max(0, u_4)\} \end{aligned}\right\} \tag{3.154}$$

3.9.5 The Optimality System for HCV Model

The optimality system consists of the state system, the adjoint system, initial conditions and the

transversality conditions. Thus

$$\left.\begin{aligned}
S'(t) &= \Lambda + \omega_0\sigma_c \mathrm{I}_C + u_4 C_C - \left(\frac{(1-u_1-u_2)c(1-\psi\xi)b_c(\mathrm{I}_C+C_C)}{S+\mathrm{I}_C+C_C} + \mu\right)S \\
I_C'(t) &= \frac{(1-u_1-u_2)c(-\psi\xi+1)b_c(\mathrm{I}_C+C_C)S}{S+\mathrm{I}_C+C_C} - (\omega_0+\eta_0)\sigma_c \mathrm{I}_C - \mu \mathrm{I}_C \\
C_C'(t) &= \sigma_c \mathrm{I}_C \eta_0 - (\mu + d_c + u_4)C_C \\
\lambda_1'(t) &= -\left(\frac{(1-u_1-u_2)c(-\psi\xi+1)b_c(\mathrm{I}_C+C_C)S}{(S+\mathrm{I}_C+C_C)^2} - \frac{(1-u_1-u_2)c(-\psi\xi+1)b_c(\mathrm{I}_C+C_C)}{S+\mathrm{I}_C+C_C} - \mu\right)\lambda_1 \\
\lambda_2'(t) &= -\left(\omega_0\sigma_c - \left(\frac{(1-u_1-u_2)c(-\psi\xi+1)b_c}{S+\mathrm{I}_C+C_C} - \frac{(1-u_1-u_2)c(-\psi\xi+1)b_c(\mathrm{I}_C+C_C)}{(S+\mathrm{I}_C+C_C)^2}\right)S\right)\lambda_1 - G_1 \\
\lambda_3'(t) &= -\left(u_4 - \left(\frac{(1-u_1-u_2)c(-\psi\xi+1)b_c}{S+\mathrm{I}_C+C_C} - \frac{(1-u_1-u_2)c(-\psi\xi+1)b_c(\mathrm{I}_C+C_C)}{(S+\mathrm{I}_C+C_C)^2}\right)S\right)\lambda_1 - G_2 \\
S(0) &= 700,\ I_C(0) = 100,\ C_C(0) = 0,\ \lambda_1(t_f) = 0, \lambda_2(t_f) = 0, \lambda_3(t_f) = 0
\end{aligned}\right\} \quad (3.155)$$

The optimality system in (3.155) was solved numerically by using the forward and backward finite difference scheme.

CHAPTER FOUR

4.0 RESULT AND DISCUSSION OF FINDINGS

The HIV, HCV, and HIV-HCV co-infection models and their corresponding optimal control models are studied numerically in this section. For the various population dynamics, the complete solutions of the study are numerically demonstrated in tables and graphs.

Numerical computations of the mathematical models are carried out by simulating the model systems (3.3), (3.5), (3.55), (3.133), and (3.144) along with optimal control analysis using values from other literature to gain a comprehensive understanding of the transmission process of HCV, HIV, and their co-infection. The population size are in thousand and time (t) in months unless otherwise stated on the plot time axis.

4.1 HIV Model

4.1.1 Case 1

In order to gain comprehensive understanding of the HIV transmission process, numerical computation of the mathematical analysis is performed alongside optimal control analysis. The default parameter value listed in table 3.1 are used, unless otherwise stated on each graph.

Therefore, the HIV mathematical formulation results for Case 1 are as follows:

Table 4.1: Sensitivity Indices on R_{eH} for HIV model formulation of case 1

Parameter	**Sensitivity index**	**Parameter**	**Sensitivity index**
Λ	+ 0.8895705522	α	-0.6688284395
φ	+0.8895705522	μ	-0.4268936102
b_{h}	+ 1	ρ	-0.4163470396
c	+ 1	d_a	-0.001941123870
υ	+0.01802050218	θ_1	-0.3024797593
ξ	-0.04166666667	θ_2	-0.09110108292
ψ	-0.04166666667		

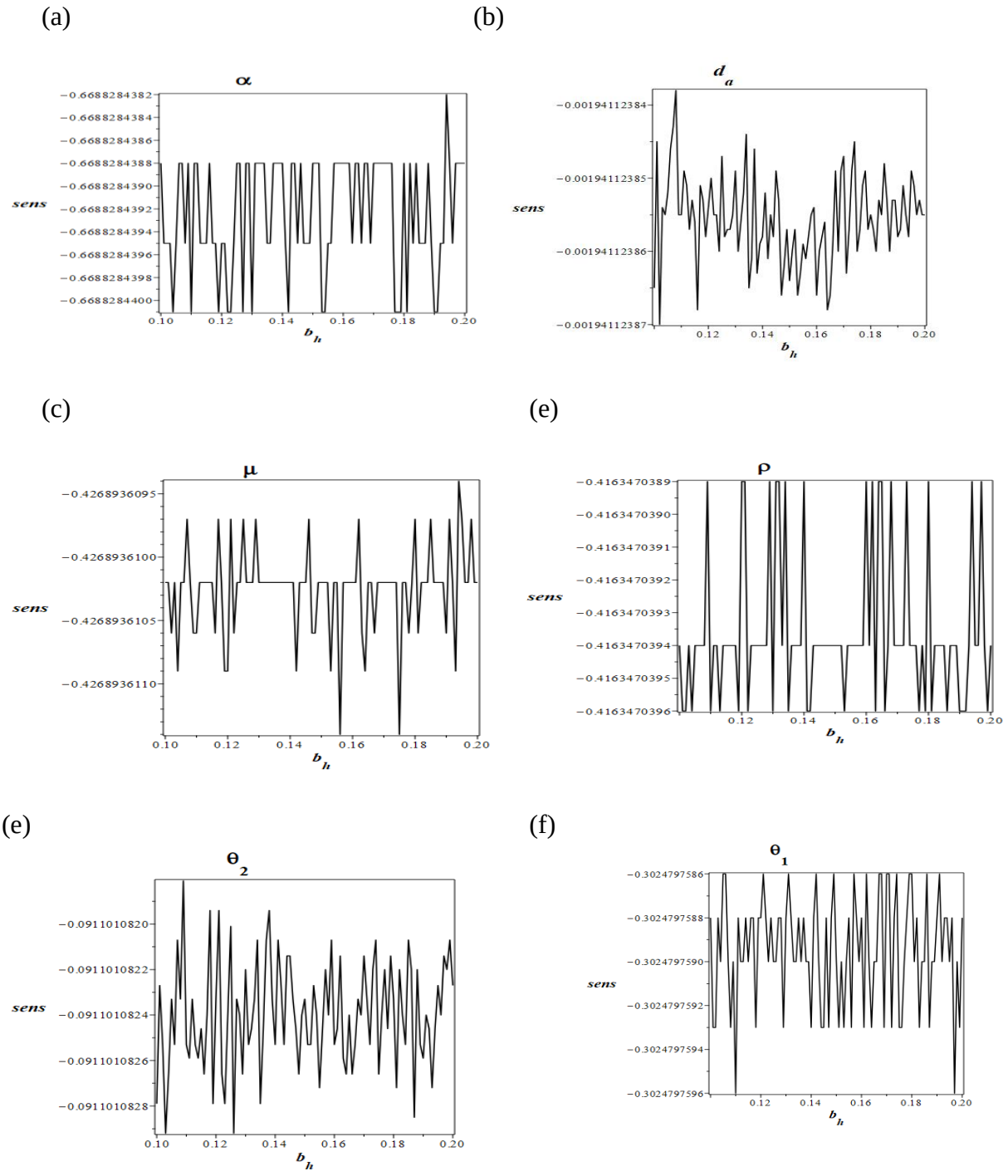

Figure 4.1: Results of sensitivity analysis on reproduction number showing the effects of (a: testing; b: treatment of AIDS, c: natural death, d: progression rate; e: death due to AIDS, f: treatment for HIV) on HIV new infections.

The sensitivity indices in Table 4.1 are read as follows: For parameters with positive indices, it means that the corresponding basic reproduction number increases (decreases) when those parameters $(\Lambda, \varphi, b_{\mathrm{h}}, c, \upsilon, \xi, \psi)$ increase (decrease). Negative indices, on the other hand, indicate that when those parameters $(\alpha, \mu, \rho, d_a, \theta_1, and\ \theta_2)$ are increased (decreased), the associated basic reproduction number decreases (increases). When the values of $b_h, \upsilon, and\ c$ are increased, the endemicity of HIV infection increases and when the values of $\alpha, \theta_1, and\ \theta_2$ are decreased, the endemicity of HIV infection decreases.

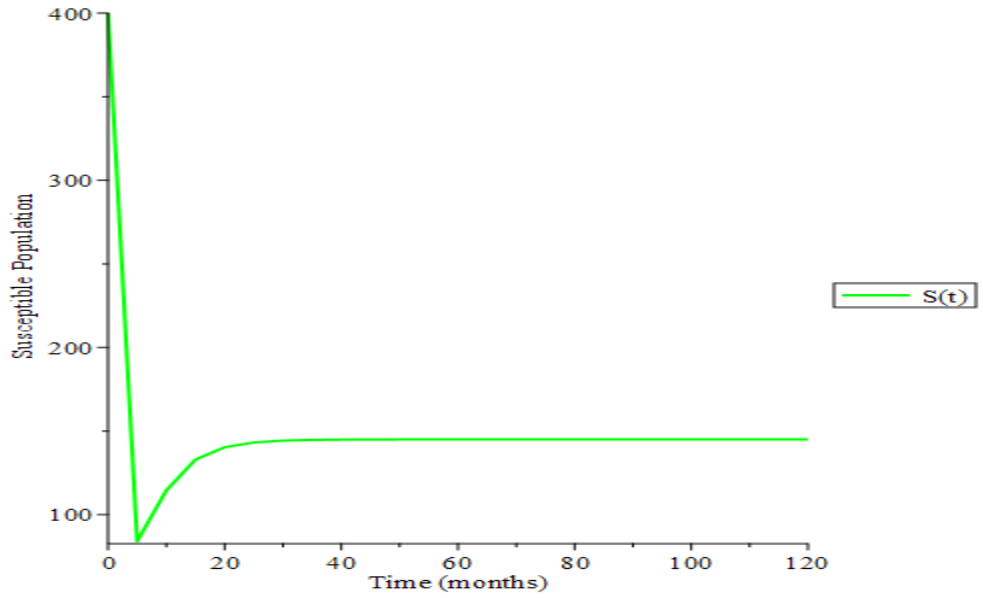

Figure 4.2: Behavioral dynamics of the susceptible population at DFE when $R_0 < 1$

As noticed in Figure 4.2, a strong early asymptotic decrease toward a limiting zero of the susceptible population exists. However, over time, a gradual increase in the susceptible population is obtained, which later remains stable and does not tend to zero. This indicates that the susceptible population will never be zero and endemicity will not exist. As such, the disease will die out over time due to the basic reproduction number being less than unity, which authenticates the analysis

shown in section 3.4.2.

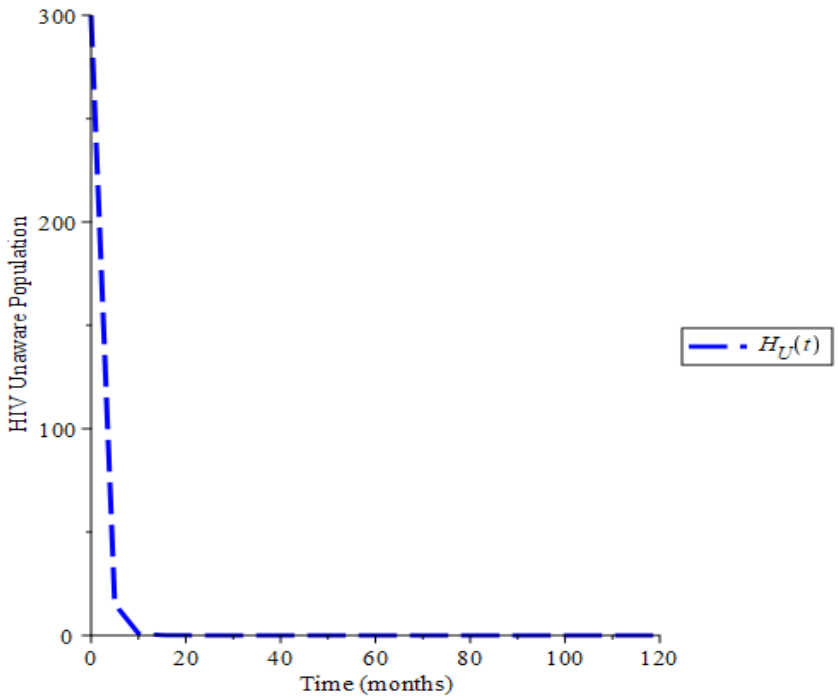

Figure 4.3: Behavioral dynamics of HIV Unaware population at DFE when $R_0 < 1$

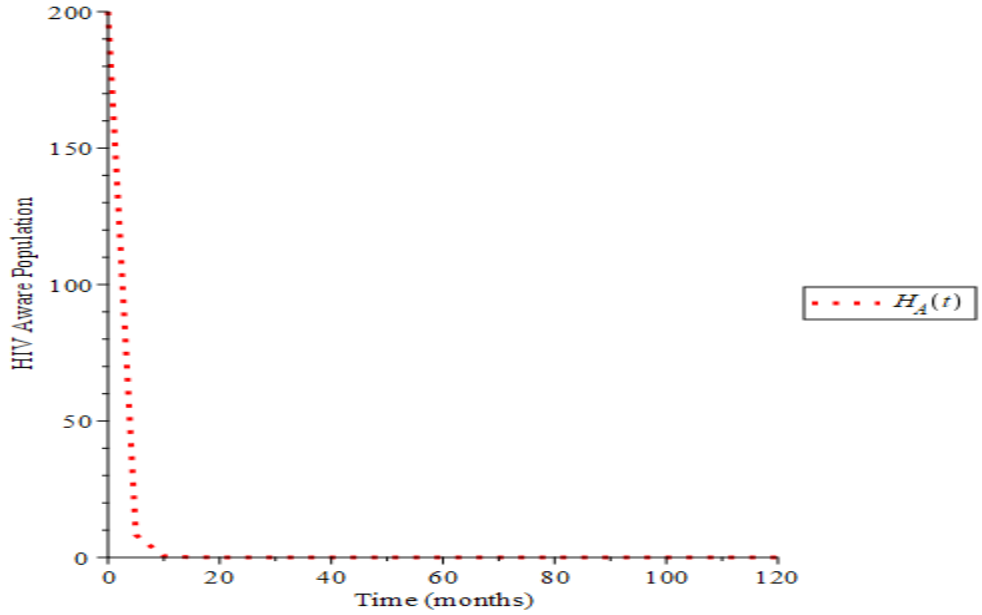

Figure 4.4: Behavioral dynamics of Aware HIV population at DFE when $R_0 < 1$

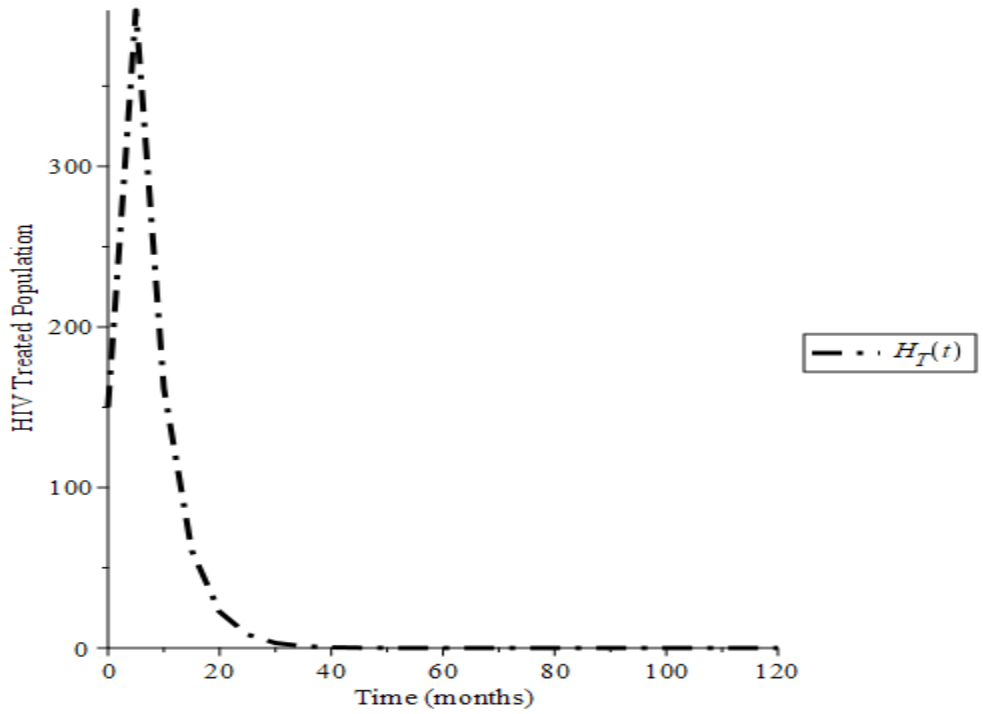

Figure 4.5: Behavioral dynamics of HIV on Treatment population at DFE when $R_0 < 1$

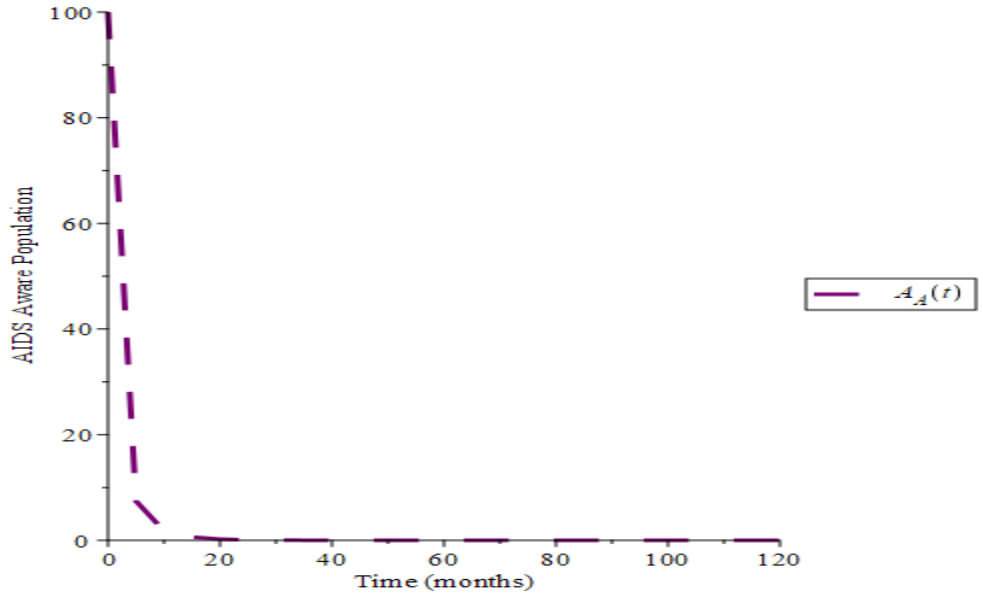

Figure 4.6: Behavioral dynamics of AIDS population at DFE when $R_0 < 1$

Figures 4.3 - 4.6 depict the dynamical performance of the HIV unaware, HIV aware, HIV on treatment, and the AIDS population respectively. A downward momentous decrease is observed in the population at the early time of the disease as depicted in Figures 4.3 - 4.6. As the time progresses, an insignificant variation in the population dynamics is noticed indicating that the disease dies out early due to the reproduction number that is less than unity. Though, the behaviour is influenced by effective condom use and other intervention strategies that resist the upsurge in the spread of the disease. This resulted in overall declination in the population which tends to zero over time. The results complement existing reports on HIV and basic reproduction numbers.

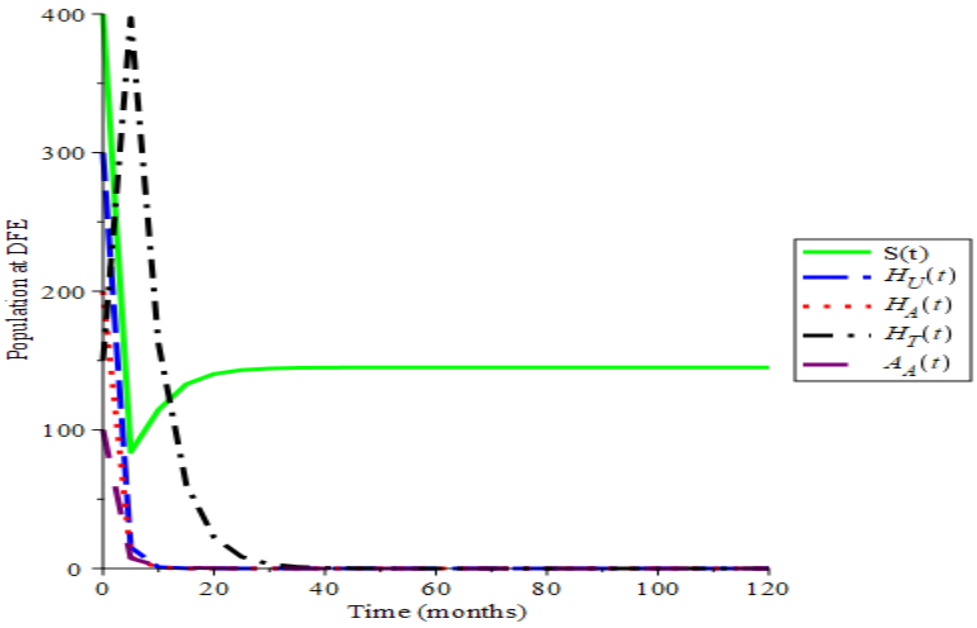

Figure 4.7: Proportion of different Population at DFE when $R_0 < 1$

By choosing 100 different initial conditions, Figure 4.7 show that the trajectories of the solutions converge to (145, 0, 0, 0, 0), hence, $R_{eH} = 0.712$. This supports the result in Theorem 3.5 that the disease-free equilibrium is globally asymptotically stable if $R_{eH} < 1$ in section 3.4.3.

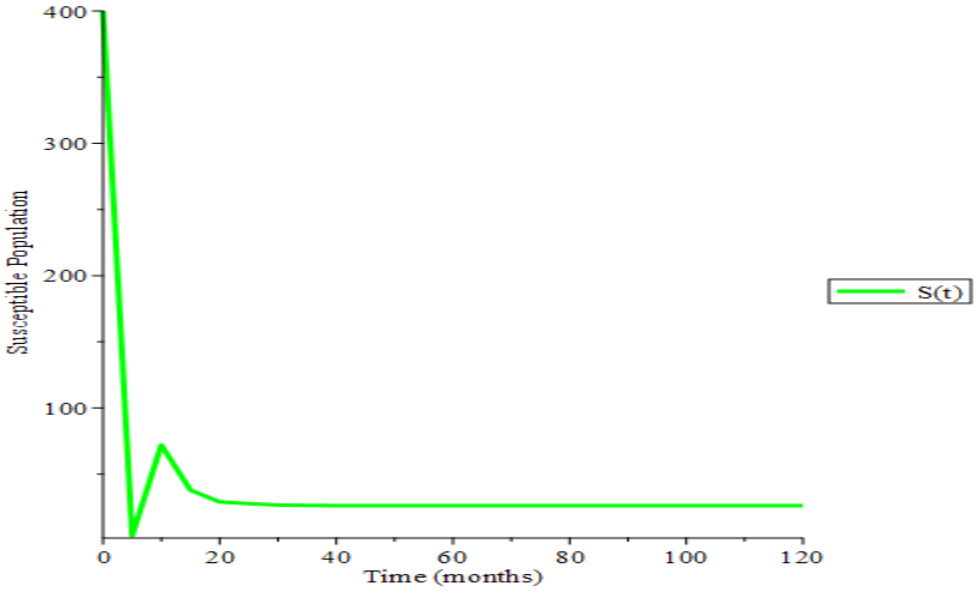

Figure 4.8: Behavioral dynamics of Susceptible population at EE when R_0>1

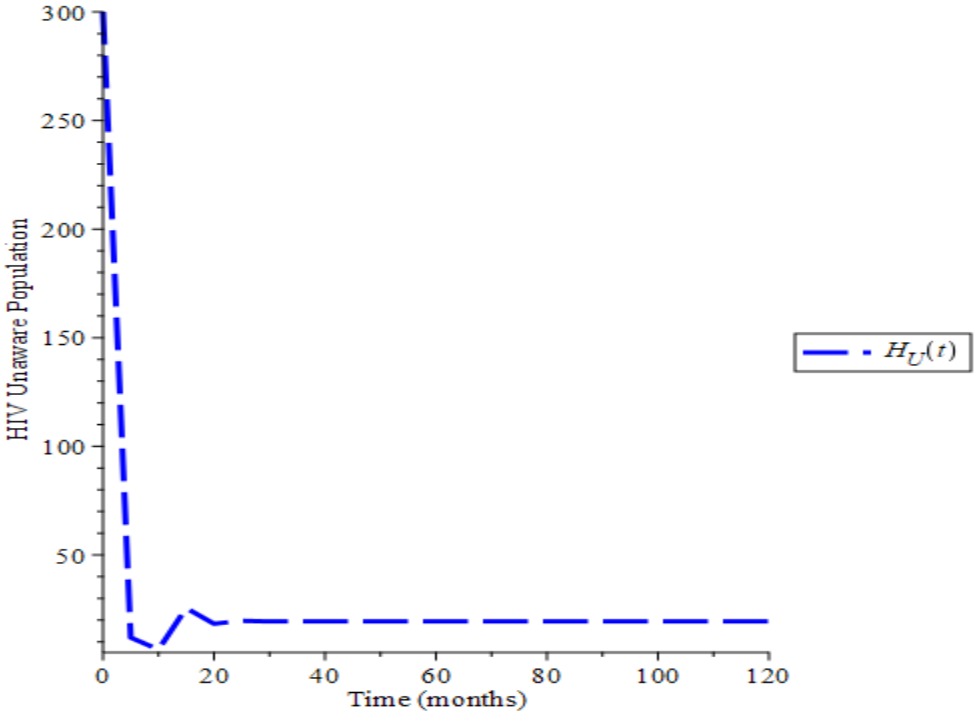

Figure 4.9: Behavioral dynamics of unaware HIV population at EE when R_0>1

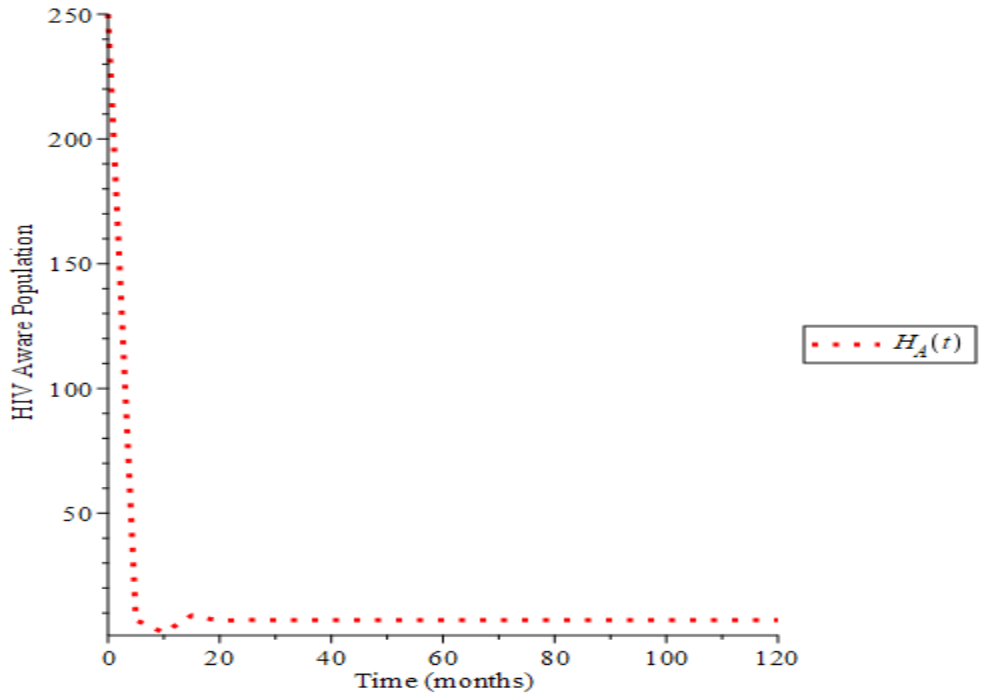

Figure 4.10: Behavioral dynamics of aware HIV population at EE when R_0>1

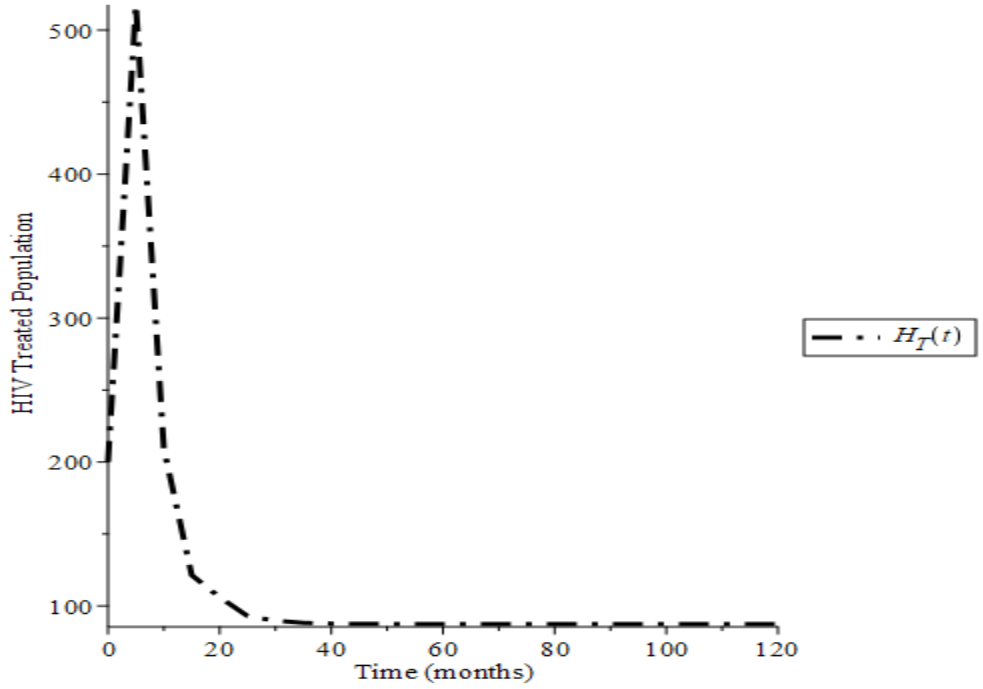

Figure 4.11: Behavioral dynamics of HIV on treatment population at EE when R_0>1

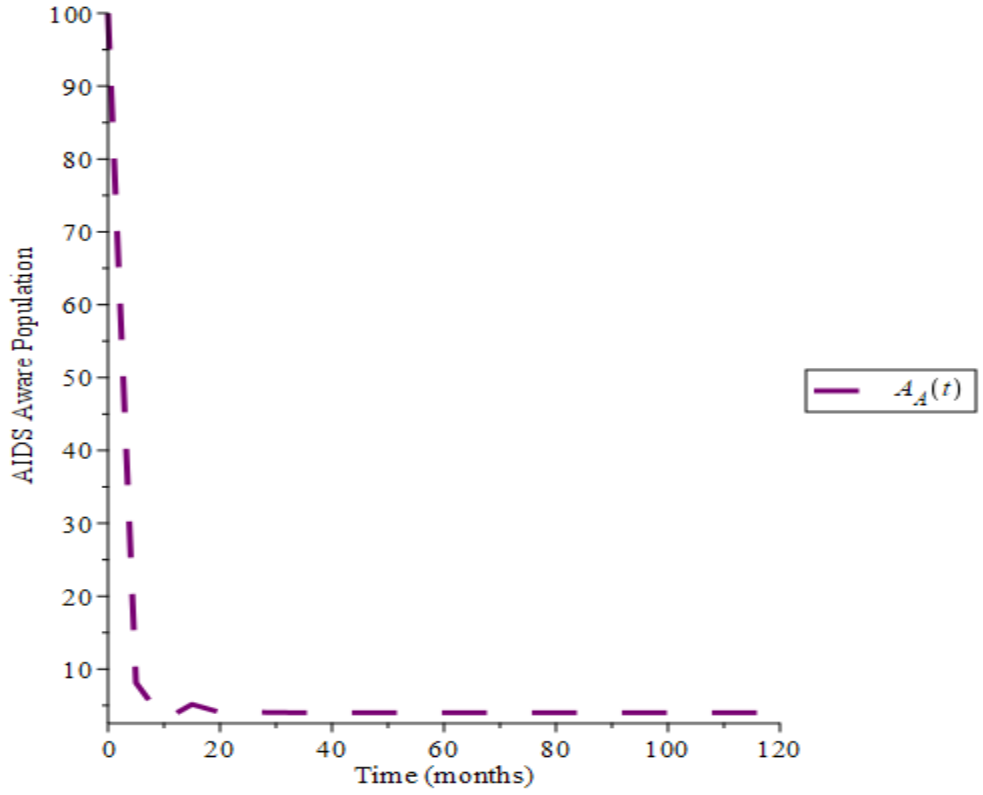

Figure 4.12: Behavioral dynamics of AIDS population at EE when R_0>1

Figures 4.8-4.12 shows the behavioural dynamics of the Susceptible, HIV unaware, HIV aware, HIV on treatment and AIDS population at endemic state when the transmission rate, $b_{\mathrm{h}} = 0.50$, each system approaches asymptotically the stable HIV endemic equilibrium. Moreover, the endemic equilibrium trajectories of the solutions converge to

$(8.420; 22.353; 17.485; 91.452; 4.534)$:

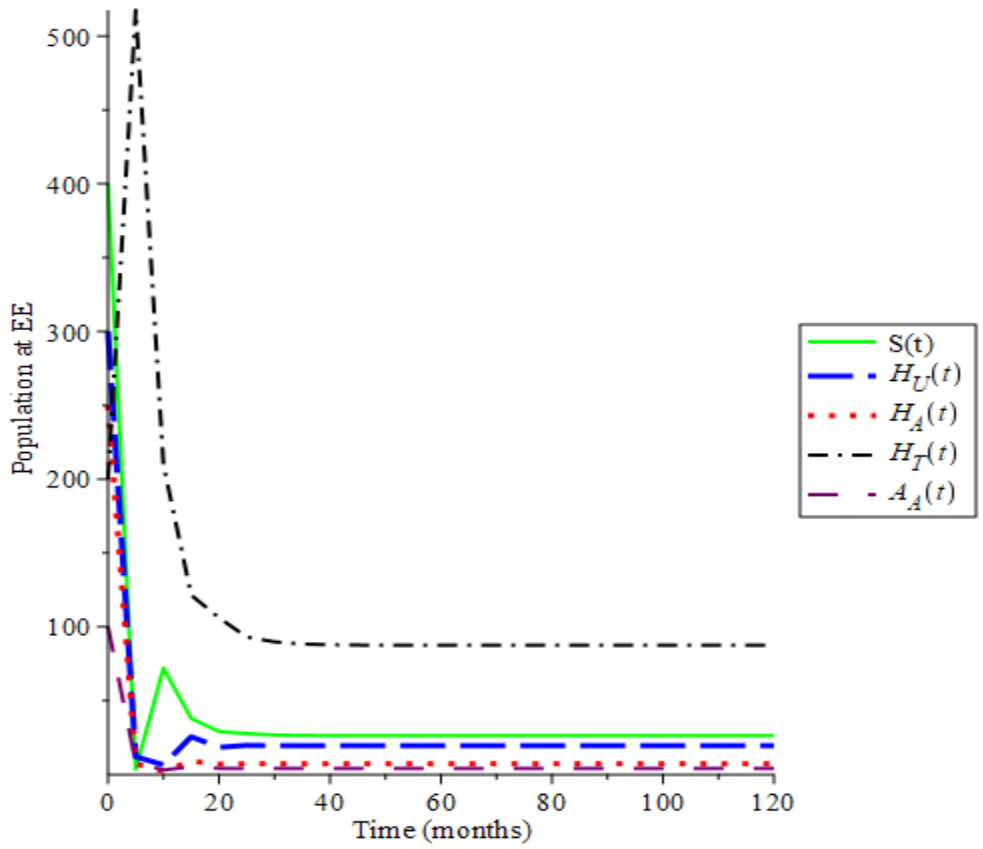

Figure 4.13: Proportion of different Population at EE when R_0>1

Choosing different initial conditions, for given parameter values in Table 4.1, and given initial conditions in Figure 4.13, hence $R_{eH} = 7.1234$. This again supports Theorem 3.7 that the endemic equilibrium is globally asymptotically stable if $R_{\mathrm{eH}} > 1$:

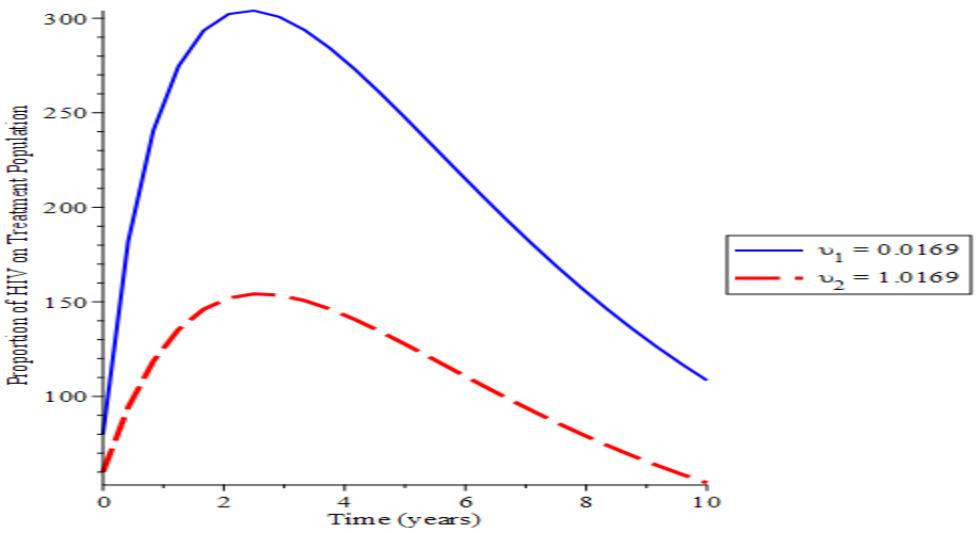

Figure 4.14: Behavioral dynamics of HIV on treatment population when varying the fallout

The effect of varying defaulter lost to follow-up (υ) on the HIV on treatment population is investigated in Figures 4.14. HIV on-treatment population diminishes as the parameters are increased upon defaulting from treatment, because treated individuals leave the treatment class and move to the AIDS class upon defaulting from treatment.

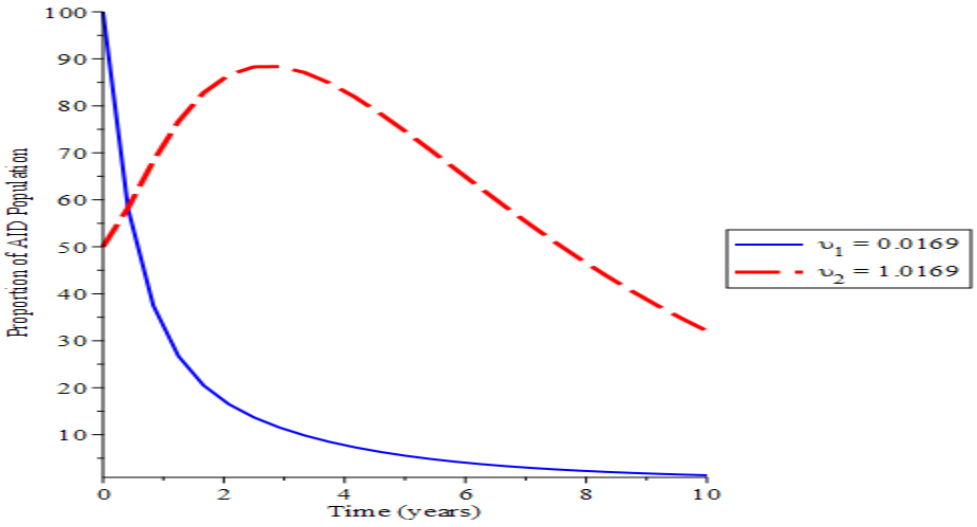

Figure 4.15: Behavioral dynamics of AIDS population when varying the fallout

Meanwhile, the AIDS population in Figure 4.15, depicts a highly significant influence of HIV on treatment individuals over time, as such, the individuals are exposed to persistent liver inflammation due to increased viral load. Thus if aware infected population adhere to treatment, the overall infective population will remain under control thus reducing the HIV aware and AIDS population.

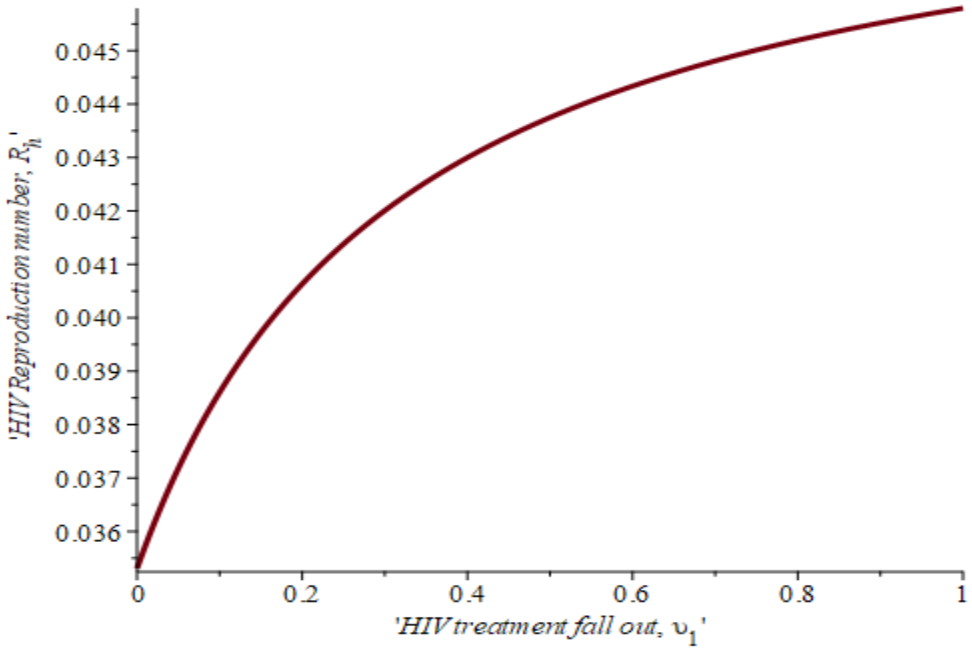

Figure 4.16: Impact of treatment fall-out population on HIV reproduction number R_{eH}

As the proportion of the fallout population increases in Figure 4.16, HIV reproduction also increases. For example, if the proportion of the population that fall-out of treatment is $16.4\%, R_{eH} = 0.04, if\ \upsilon = 30\%, R_{eH} = 0.042\ and\ when\ \upsilon = 50\%\ R_{eH} = 0.044$. This means that if the proportion of the population that fall out of treatment increase, the rate number of secondary infection that will be transmit will be on the high side.

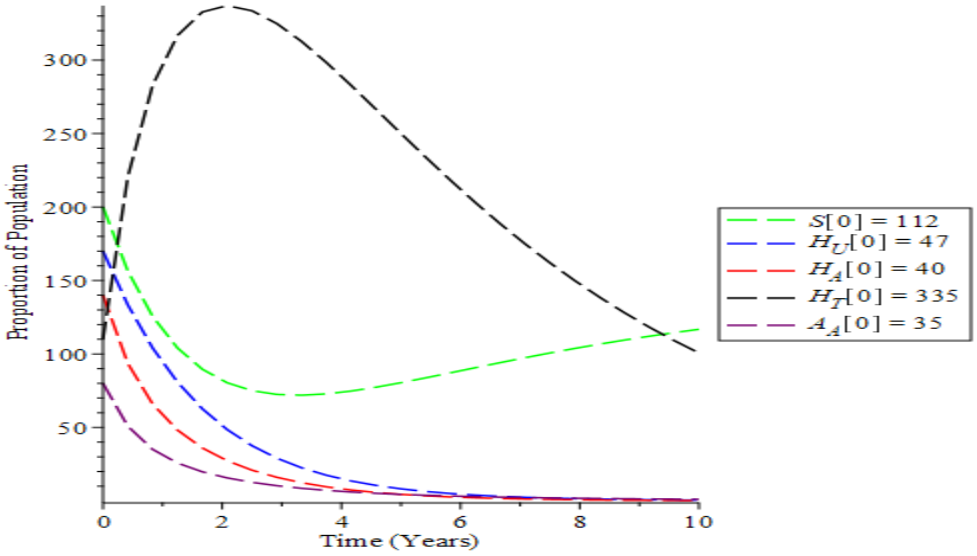

Figure 4.17: Proportion of Population when $\alpha = 0.7$ *and* $\theta_i, i = 1,2 = 1.6949$

The increasing effect of testing and treatment on the model is examined in Figures 4.17-4.20 with initial population size $112, 47, 40, 335, 35$ for $S(t), H_U(t), H_A(t), H_T(t), A_A(t)$ respectively.

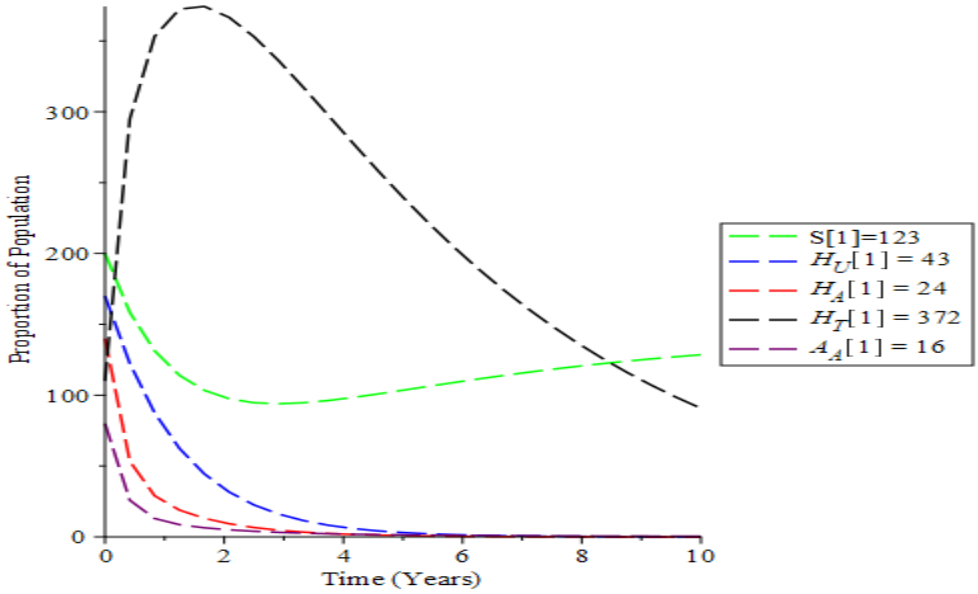

Figure 4.18: Proportion of Population when $\alpha = 0.9$ *and* $\theta_i, i = 1,2 = 3.9649$

In figure 4.17, as the testing rate increase, the proportion of the unaware population reduces from 47 to 43 in size as they move from HIV unaware to HIV aware. Also, as the treatment rate increase, the population size of those who aware of their HIV status reduces while the increasing impact reflects on HIV on treatment individuals from size 335 to 372. On the other hand, due to treatment effect, the population size of AIDS reduces from 35 to 16 in figure 4.18.

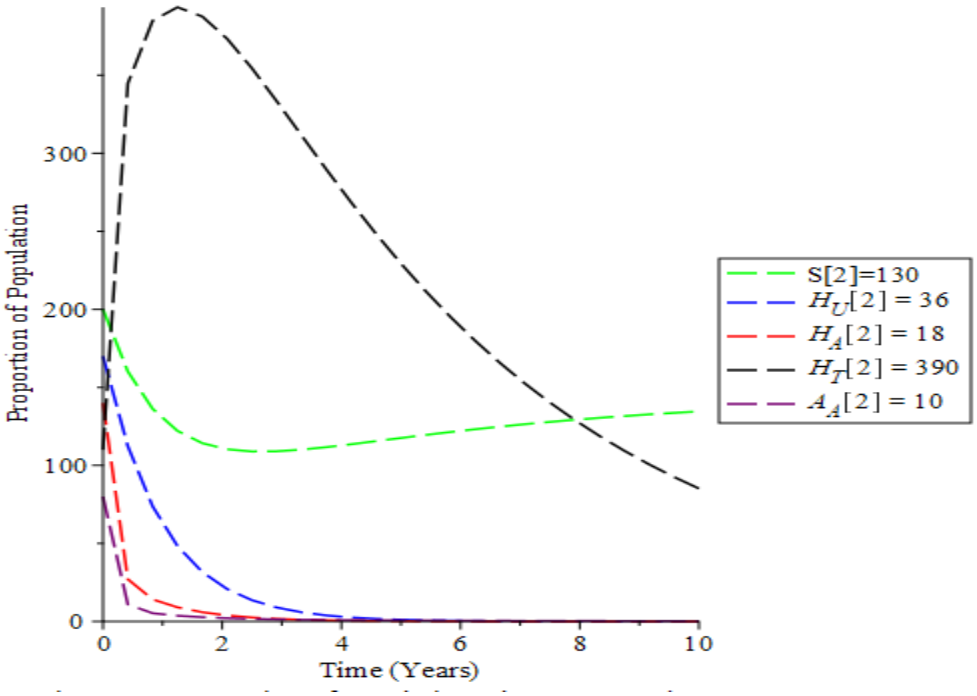

Figure 4.19: Proportion of Population when $\alpha = 1.1\ and\ \theta_i, i = 1{,}2 = 6.9649$

From Figure 4.19, as the rate at which HIV-aware infected individuals are placed on ART, the proportion of the population in HIV treatment class increases, this, in turn, reduces the progression rate to AIDS which leads to a reduction in the AIDS populace in Figure 4.20 which established the fact that the impact of the testing and treatment reduces the transmission rate.

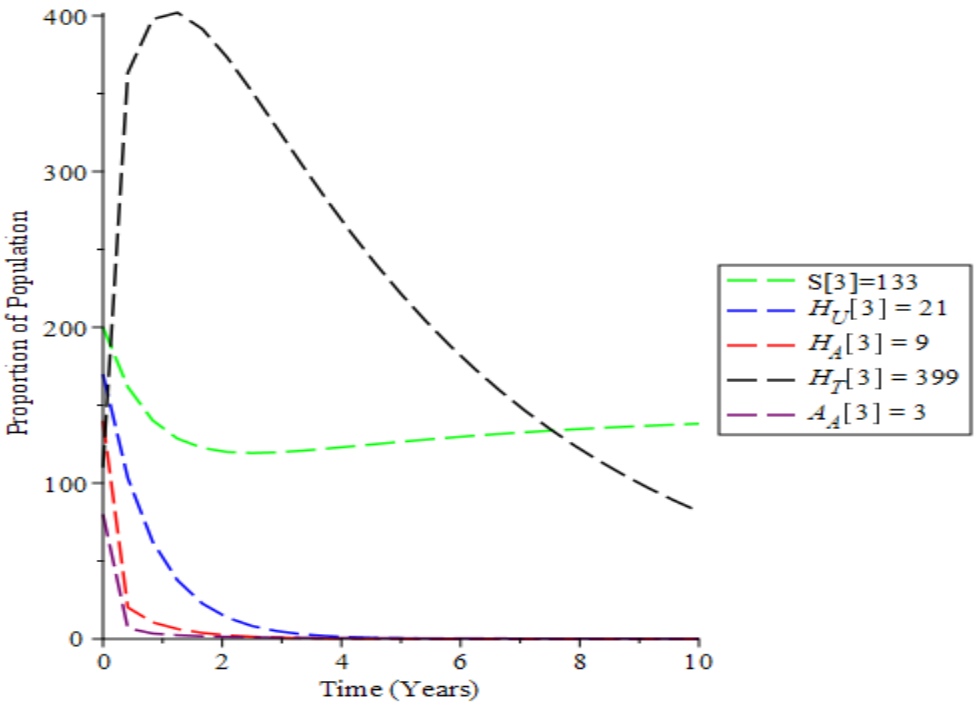

Figure 4.20: Proportion of Population when $\alpha = 1.3\ and\ \theta_i, i = 1{,}2 = 8.9649$

It is observed from Figure 4.20 that if the testing and treatment rates are increasing, the number of unaware HIV individuals decreases with time due to treatment. Furthermore, the number of susceptible individuals increases, and as treatment increases, so does the population of HIV patients on treatment. It also showed that it is possible to reduce the number of unaware and AIDS individuals by increasing the testing and treatment rates, respectively. As a result, increasing HIV screening and treatment is the first step to UNAIDS' 90-90-90 aspirations (UNAIDS, 2021).

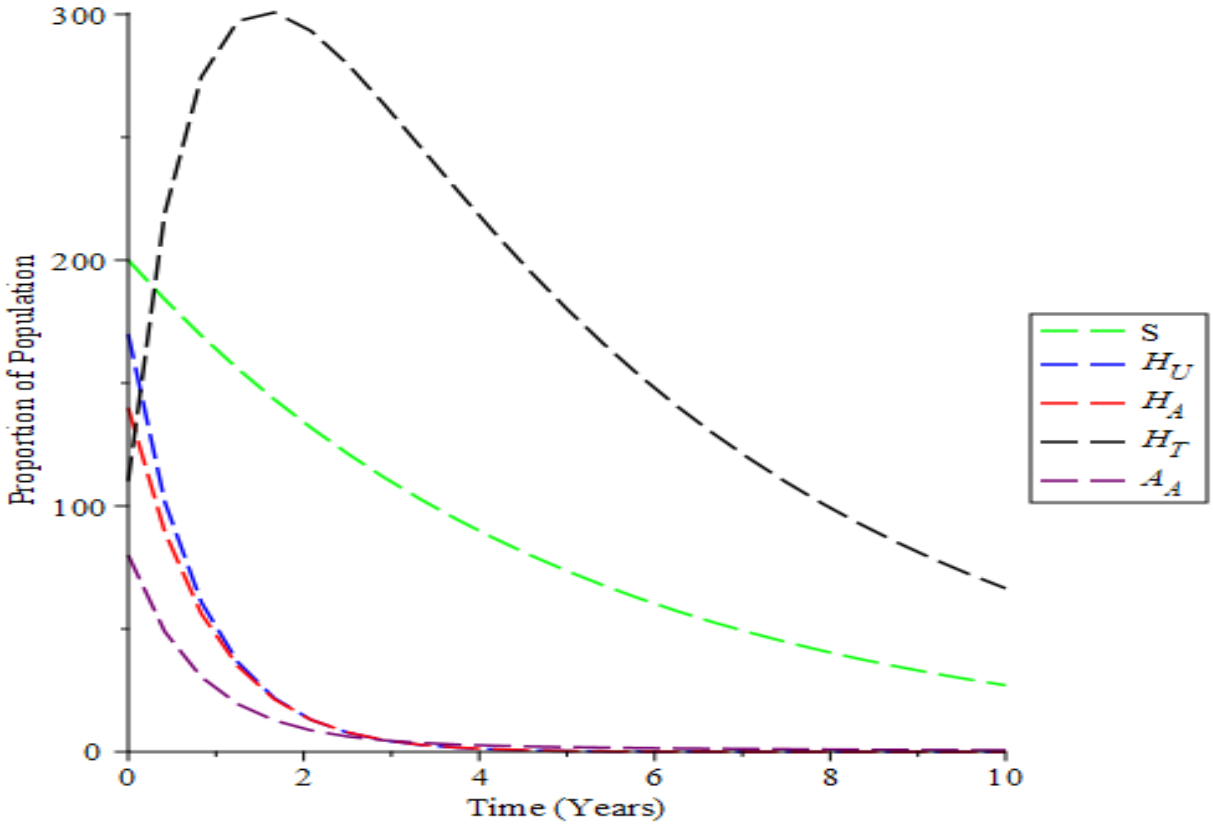

Figure 4.21: Proportion of the population with time in different classes with neither new infected children φ into the population nor recruitment Λ and contact c i.e. taking $c = 0, \varphi = 0, \Lambda = 0$ when $\psi = 1\ and\ \xi = 1$, (condom usage and effectiveness) i.e when there is full protection, keeping every other values at endemic equilibrium constant, the value of $R_0 = 0$.

Figure 4.21 shows the behavioral dynamics of different populations when there is no vertical transmission, no recruitment and there is maximum protection by a condom. Since no one is infected, the infective classes approach zero, which means only susceptible and HIV treatment classes from the population. Therefore, the total infectious groups will be better controlled.

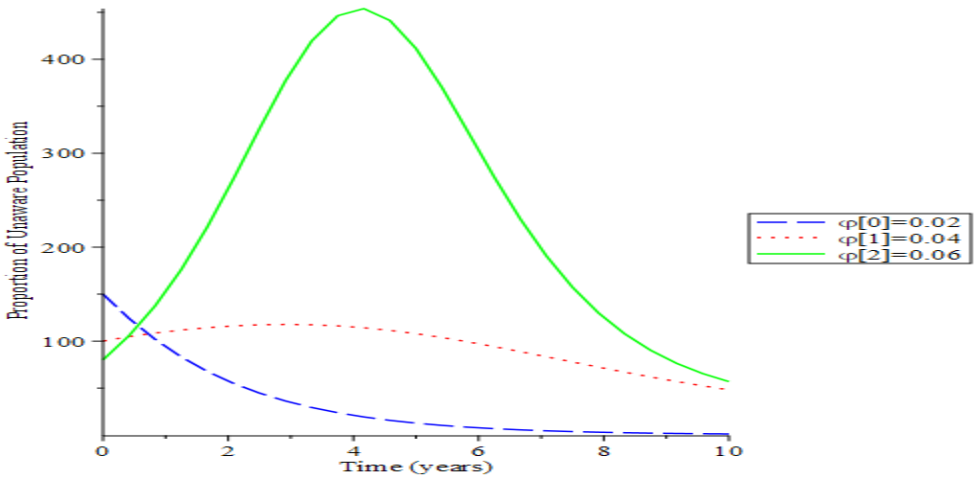

Figure 4.22: Behavioral dynamics of Infected HIV unaware when varying vertical transmission φ with time.

Figure 4.22-4.25 shows the impact of vertical transmission on the dynamics of the HIV/AIDS infected classes.

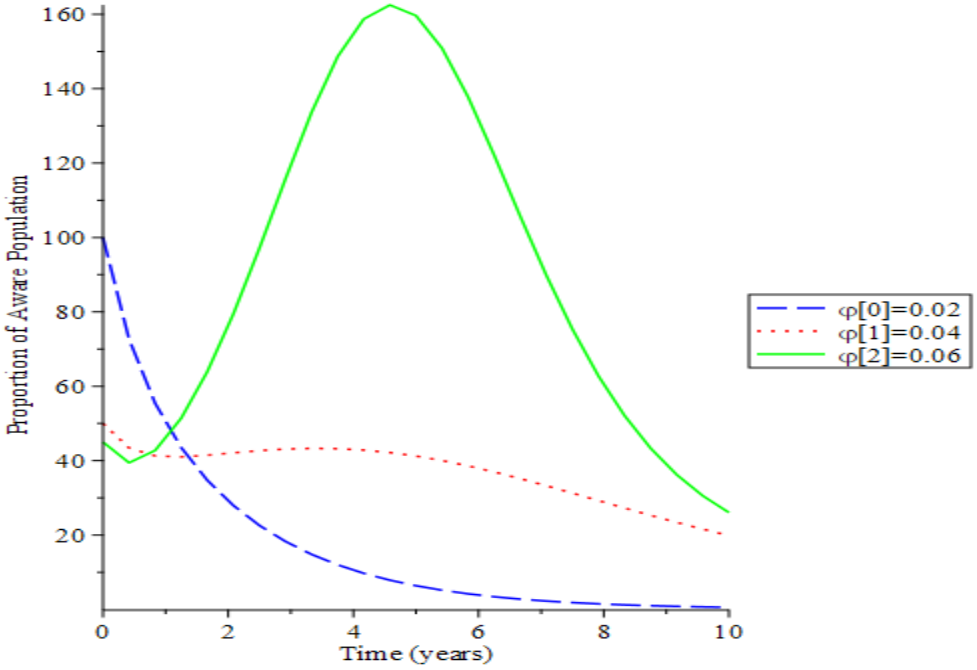

Figure 4.23: Behavioral dynamics of Infected HIV awareness when varying vertical transmission φ with time

When 2% of children born are infected with HIV, there is no significant difference in the HIV unaware, but when the rate increases to 6%, there is a great impact on the unaware population.

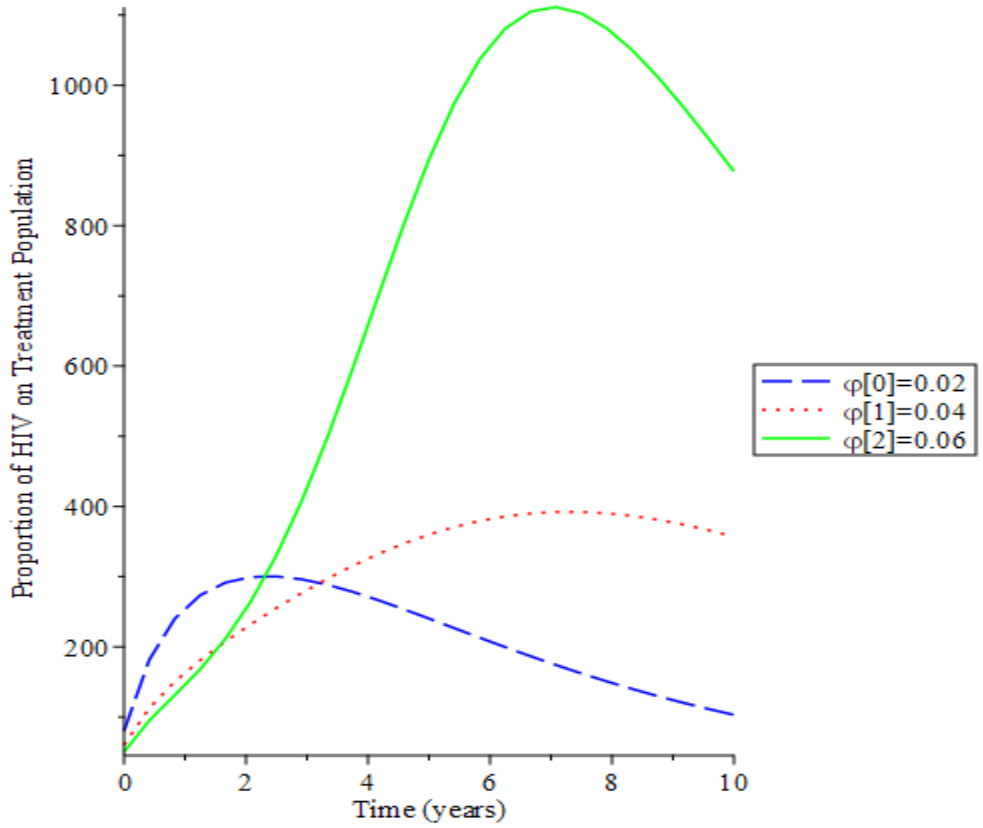

Figure 4.24: Behavioral dynamics of Infected HIV on treatment population when varying vertical transmission φ with time.

In figure 4.24, the HIV on treatment, the sharp rise signifies that more infected children will progress to treatment after testing. From the figures, there is a big change in the dynamics of the infected class even if the population grows by only 2%.

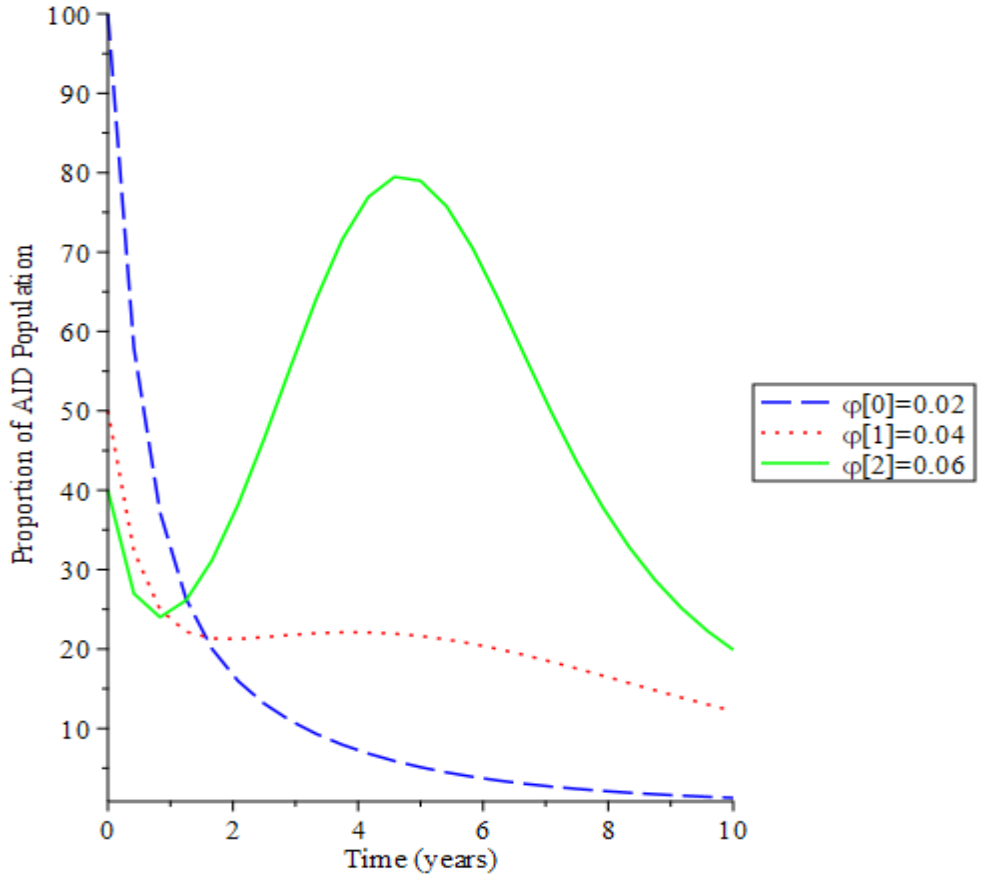

Figure 4.25: Behavioral dynamics of AIDS population when varying vertical transmission φ with time.

In Figure 4.25, there is a steady decline in the AIDS populace due to treatment intervention for the children born of infected mothers.

Figures 4.26-4.30 depicted an optimal control model for HIV transmission dynamics using time preventive (condom on susceptible, counselling and testing on HIV unaware) and treatment preventive (HART on HIV on treatment and AIDs Aware) strategies. The controls are first used to optimize the objective function, then the effect of those controls on various compartments.

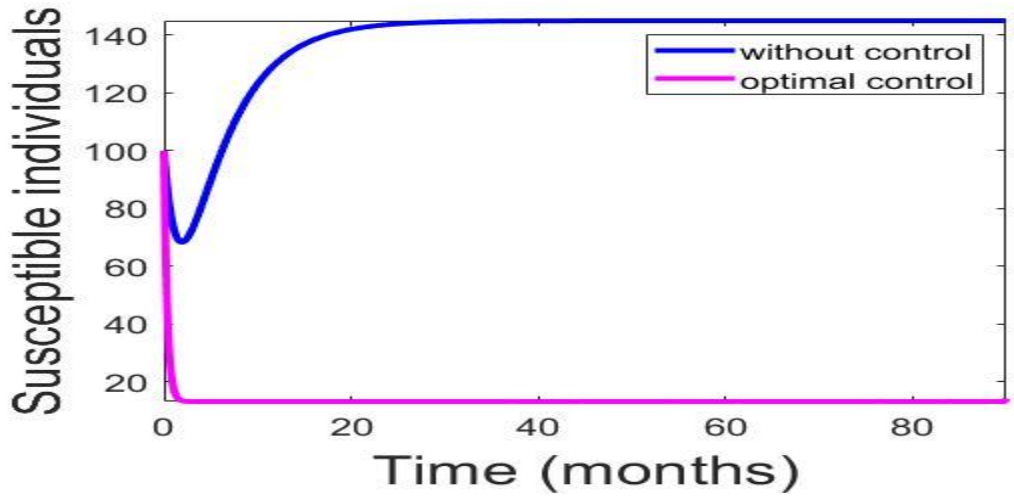

Figure 4.26: The effect of control on susceptible individuals for HIV model case1

In Figure 4.26, the impact of the control on the susceptible population was considered. When there is no control, the plot shows that there is a high possibility that the susceptible class will be infected while control is being adopted. The plot shows that few or no susceptible classes were infected. This agrees with the result of (Naik *et al*., 2020) who suggested that promoting condom use is a crucial component of combination interventions.

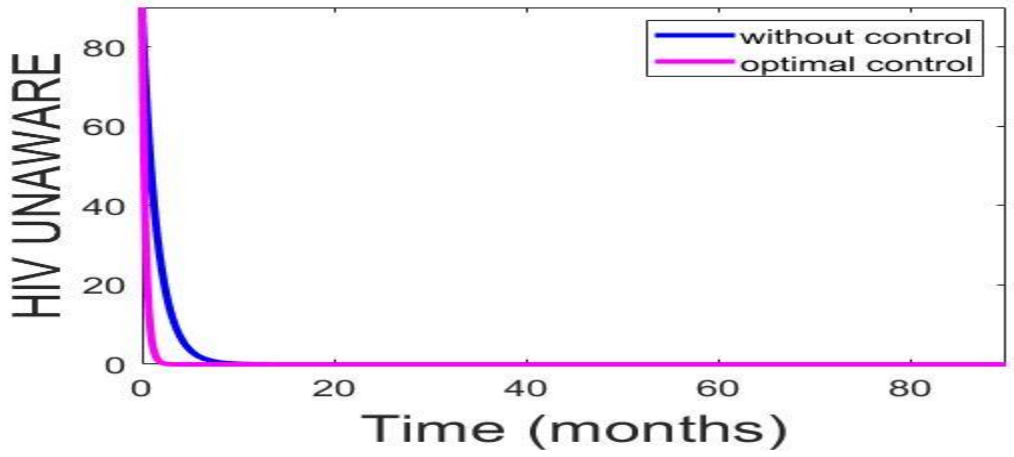

Figure 4.27: The effect of control on HIV unaware individuals for HIV model case1

In Figure 4.27, the effect of the control was observed on the HIV unaware class. There is a slight increase in the uncontrolled plot than in the controlled plot. Since the control strategies were properly implemented, the HIV unaware control plot approaches zero. That is, those that were unaware of their status are now aware of their status, thereby reducing their transmission rate.

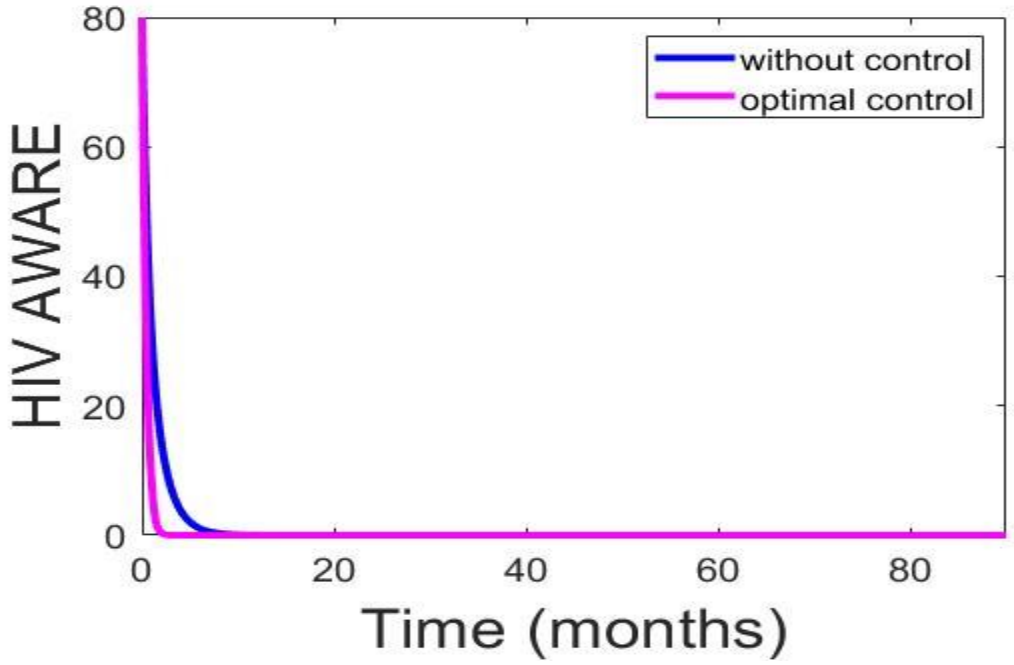

Figure 4.28: The effect of control on HIV-aware individuals for HIV model case1

Figure 4.28 shows the impact of the treatment preventive control on the HIV-aware populace. It was observed that there was a slight difference between the uncontrolled and controlled populations (that is, there was a decline in the population of the controlled plot compared to that of the uncontrolled plot). This means that the way the aware class treats the disease has a big effect on the model of how HIV spreads.

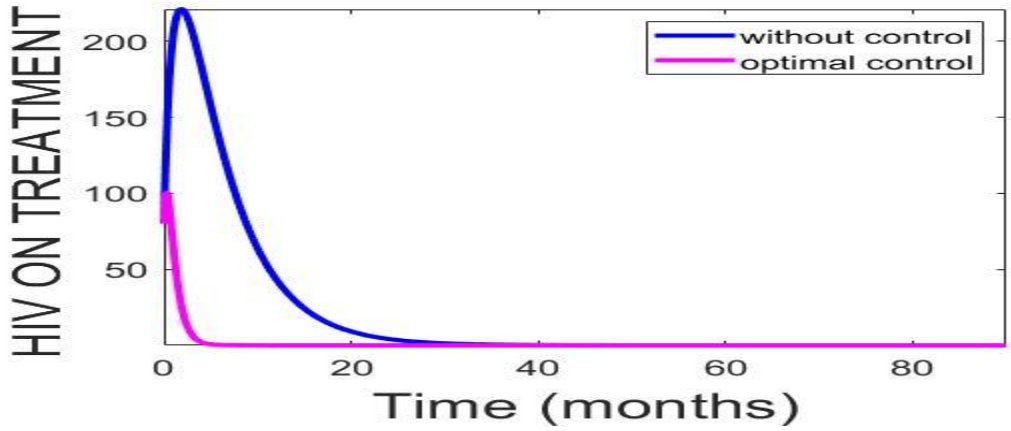

Figure 4.29: The effect of control on HIV on treatment individuals for HIV model case1

Figure 4.29 shows the effect of the control measure on HIV on treatment individuals that was considered. There is a significant difference between the controlled and uncontrolled classes. From the early stage, we observed a decline in the control population plot compared to that of the uncontrolled. That means there is a high rate of response to treatment by the HIV infective class, thereby reducing the chance of increased CD4 count and possibly progression to AIDs.

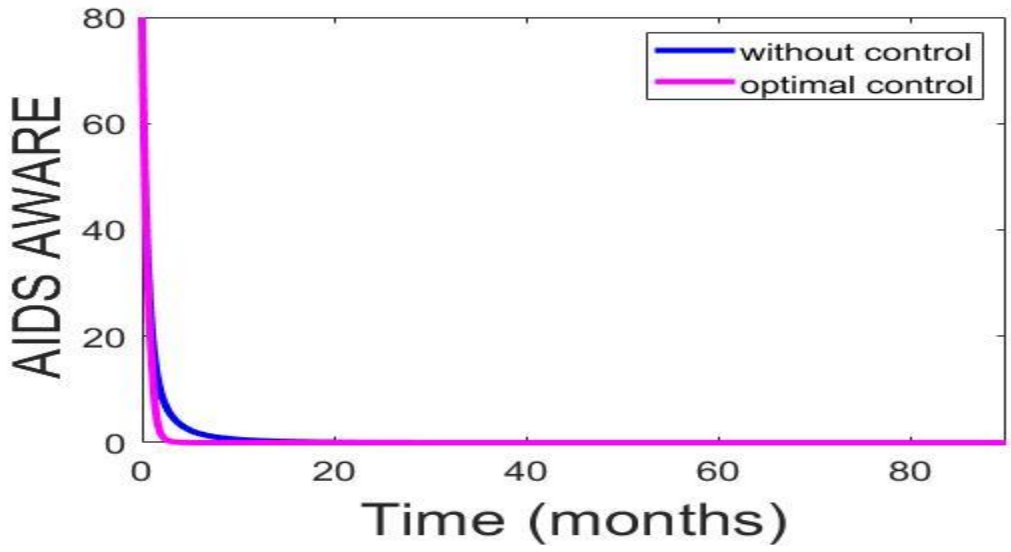

Figure 4.30: The effect of control on AIDS individuals for HIV model case1

The effect of treatment as a control measure on the AIDs individual is displayed in Figure 4.30. It was observed that the number of AIDs individuals at the control level was greater than those without controls. This is an indication that with proper control of a large proportion of AIDs on treatment, individuals maintain their good state of health, which implies that treatment can eradicate the virus in the population with many successfully treated individuals. Therefore, there is a reduction in the death rate due to the disease, making the treatment cost-effective, that is, profit will be maximized. According to (WHO, 2020a), treatment remains the best way of reducing the transmission process of HIV/AIDS.

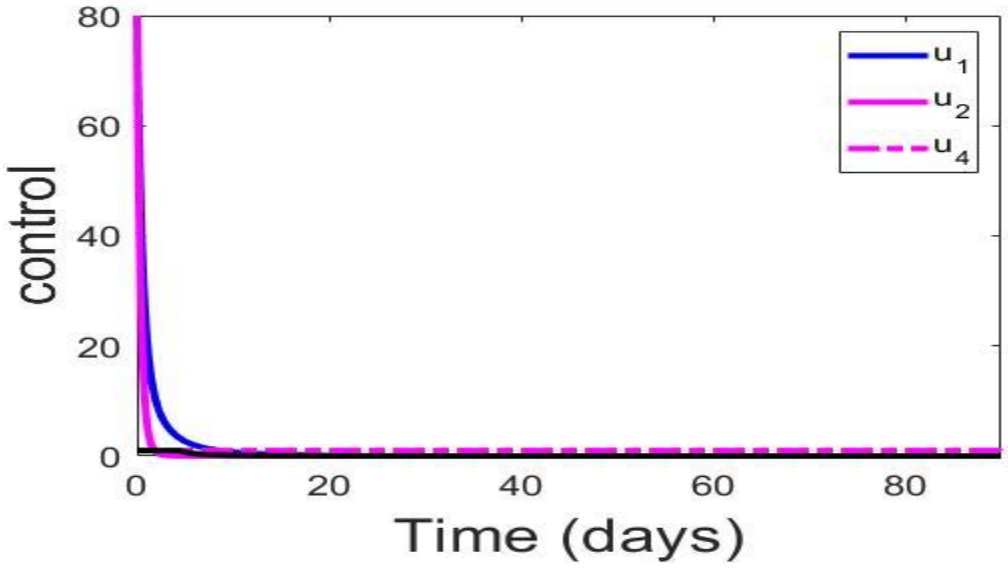

Figure 4.31: The control profile for HIV model case1

Figure 4.31 shows the control profile for the HIV model case I. As HIV testing and treatment are continuously scaled up, we expect that a larger proportion of the people receiving treatment will be in the early stage of infection, and the fatality rate will drop. Therefore, reducing high-risk behaviors, mainly through education for adherence to treatment, is the top choice to control the total number of HIV/AIDS patients.

4.2 HCV Model

4.2.1 Case 2

For a comprehensive understanding of the transmission process of the Hepatitis C virus, numerical computation of the mathematical analysis is carried out along with optimal control analysis. The default parameter values listed in table 3.2 are used, unless otherwise stated on each graph.

Hence, the HCV mathematical formulation solutions for case 2 are presented as follows:

Table 4.2: Sensitivity Indices on R_{eC} for HCV model formulation of case 2

Parameter	**Sensitivity index**	**Parameter**	**Sensitivity index**
κ	+0.3660521878	σ_c	-0.6289024038
c	+1	μ	- 0.006740055502
b_c	+1	d_c	-0.08474081441
r	-0.2796167259	ω	-0.3657921292
η	-0.2631102746	$[\psi, \xi]$	-0.04166666667

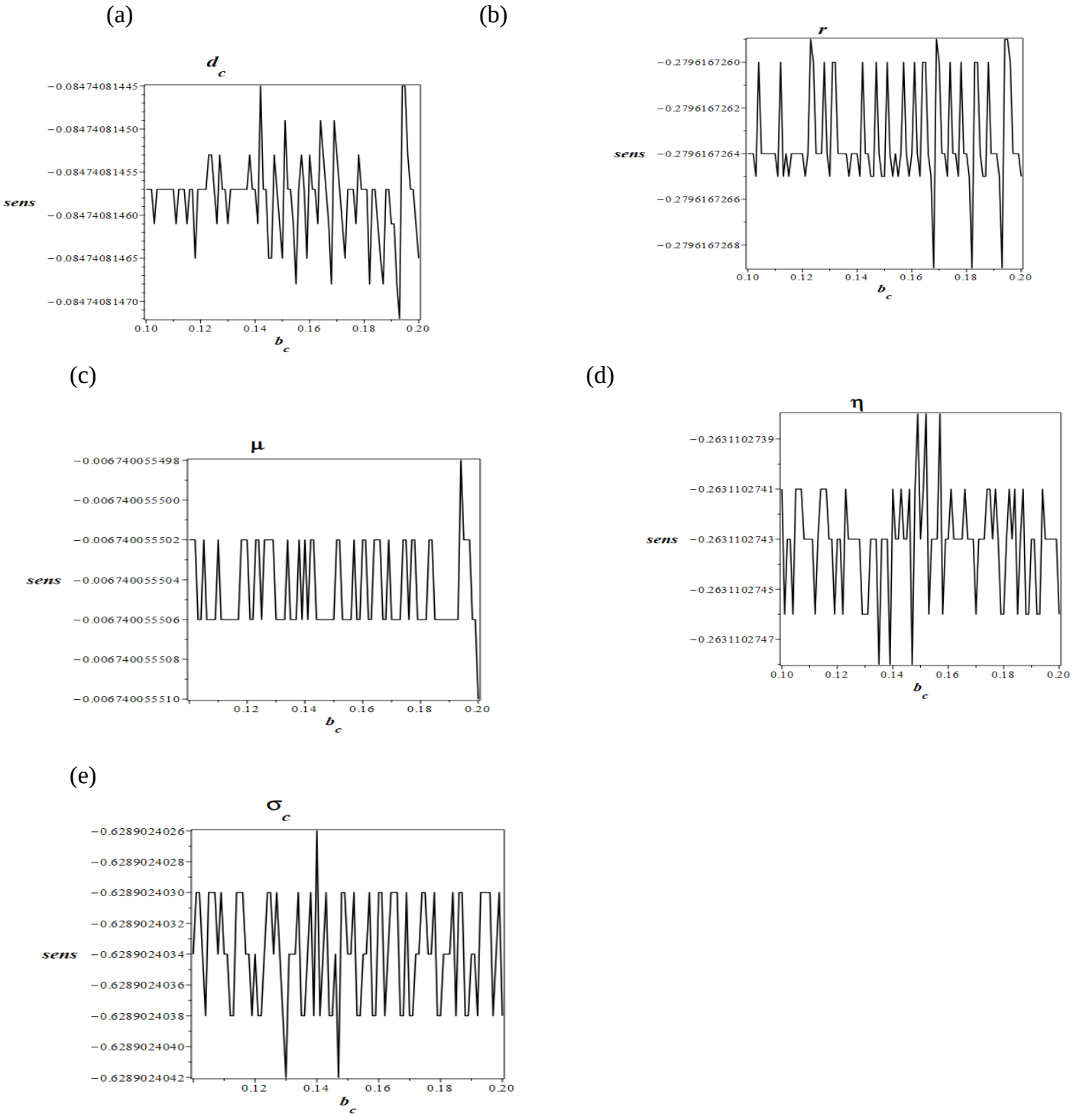

Figure 4.32: Results of sensitivity analysis on reproduction number show the effect of (a: death due to HCV; b: HCV treatment; c: natural death; d: spontaneous clearance, e: time spent in acute state) for HCV new infections with respect to model parameters.

The sensitivity indices in Table 4.2 and plotted in Figure 4.32 are read as follows: For parameters with positive indices, it means that the corresponding basic reproduction number increases (decreases) when those parameters increase (decrease). Negative indices, on the other hand, indicate that when those parameters are increased (decreased), the associated basic reproduction number decreases (increases). When the values of b_c, υ and c are increased, the endemicity of HCV infection increases; when the values of r, η_0 and μ are decreased, the endemicity of HCV infection decreases. As a result, interventions should target and concentrate on reducing the values of the average number of sexual partners acquired per year c, the number of risk factors, and HCV transmission probability per sexual contact b_c, since the increasing rate of non-spontaneous clearance ω_0, would imply fast progression to chronic HCV; C_C. Also, the effective use of condoms should be enforced as a precaution to reduce the transmission rate of HCV.

Figure 4.33–4.35 depicts the behavioural dynamics of the proportion of the HCV population at disease-free equilibrium, that is, when $R_{ec} < 1$.

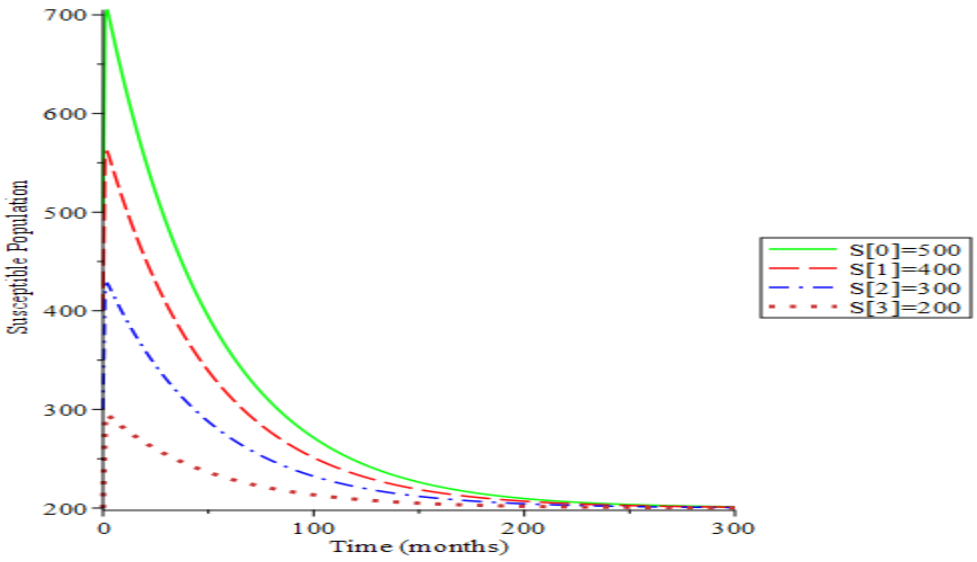

Figure 4.33: Behavioral dynamics of HCV susceptible population when $R_0 < 1$

Figure 4.33 shows the behavioral dynamics of the susceptible populations when $R_{ec} < 1$. Over time, a gradual increase in the susceptible population is obtained, which later remains stable and does not tend to zero. This is an indication that the susceptible population will never be zero and that endemicity will not exist. As such, the disease will die over time due to the basic reproduction number of less than one, and the trajectories of the solution converge to $(200,0,0)$. Hence $R_{ec} = 0.101$, which authenticates the analysis shown in section 3.5.3 Theorem 3.11 that the disease-free equilibrium is globally asymptomatically stable if $R_{ec} < 1$

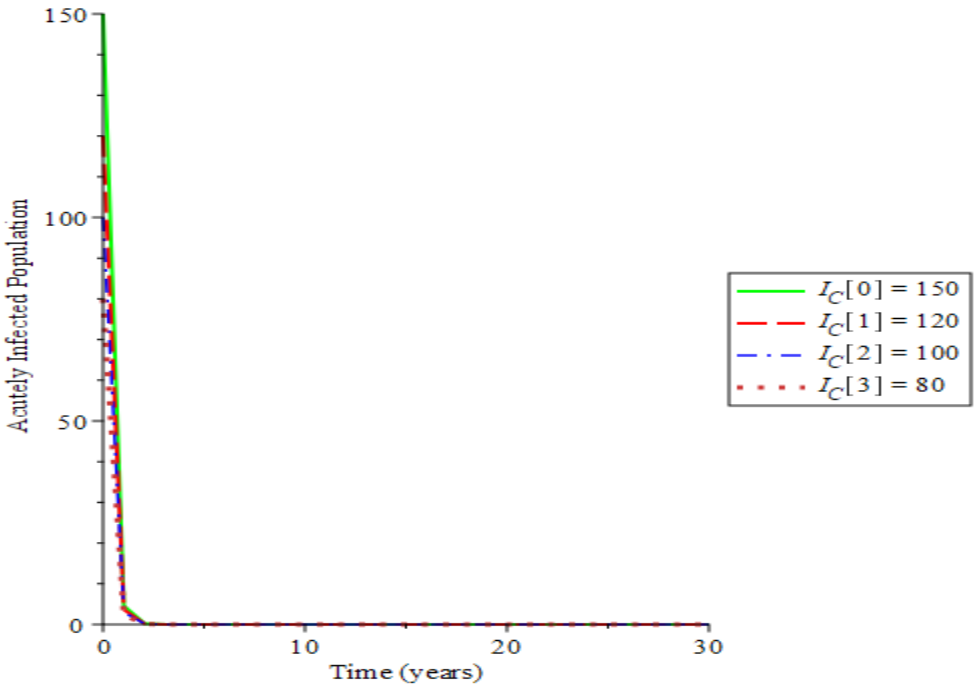

Figure 4.34: Behavioral dynamics of acute HCV population when $R_0 < 1$

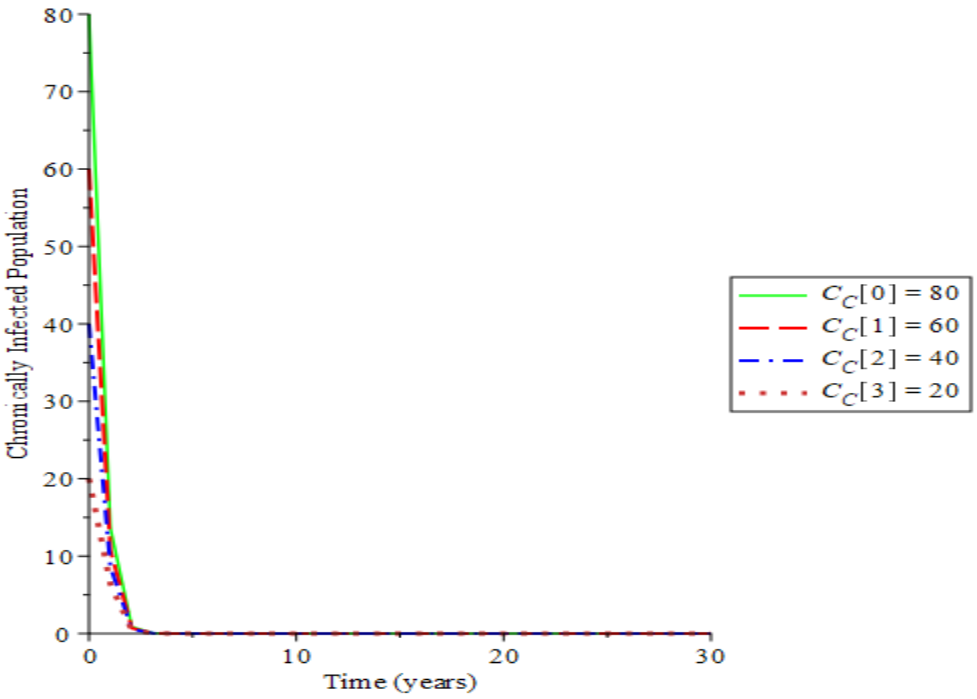

Figure 4.35: Behavioral dynamics of chronic HCV population when $R_0 < 1$

Figure 4.34-4.35 shows the behavioural dynamics of acute HCV and chronic HCV. Since there is no disease in the population, the figure shows that population tend to zero when R_{ec} is less than unity. This indicates that the disease dies out early, which is influenced by effective condom use and other strategies.

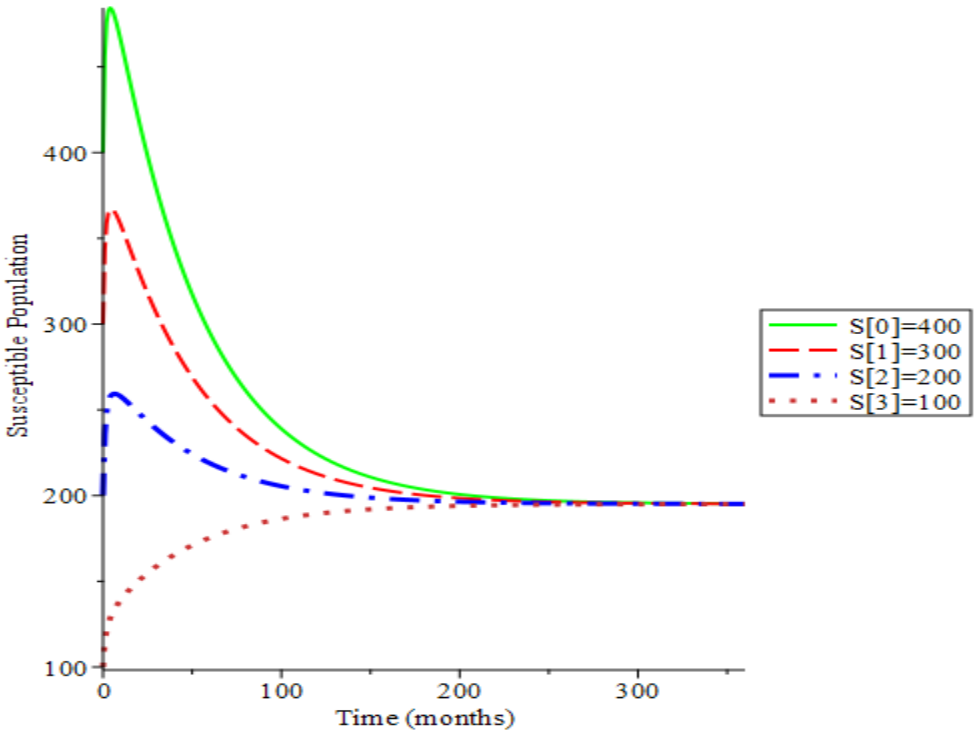

Figure 4.36: Behavioral dynamics of susceptible HCV population when $R_0 > 1$ at $b_c = 0.80$

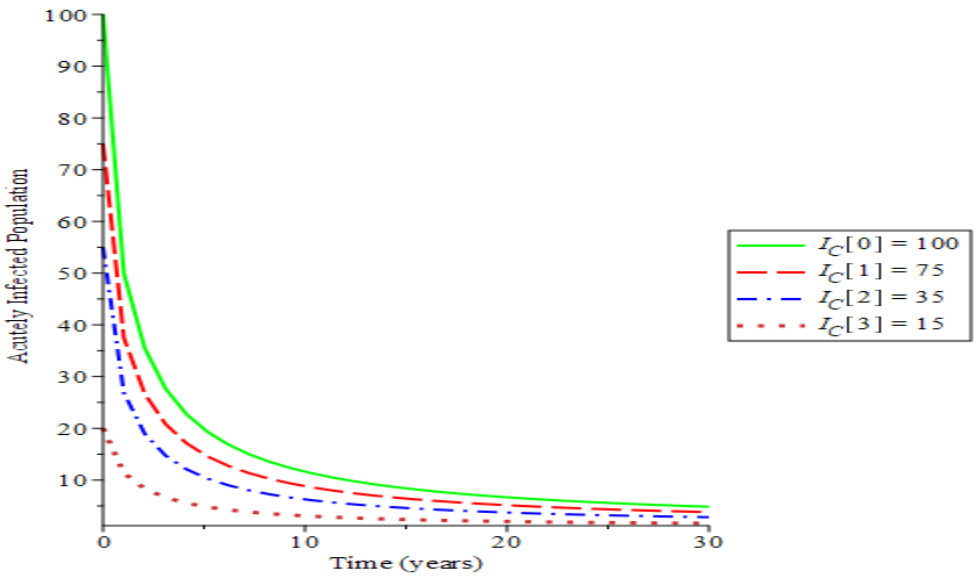

Figure 4.37: Behavioral dynamics of acute HCV population when $R_0 > 1$ at $b_c = 0.80$

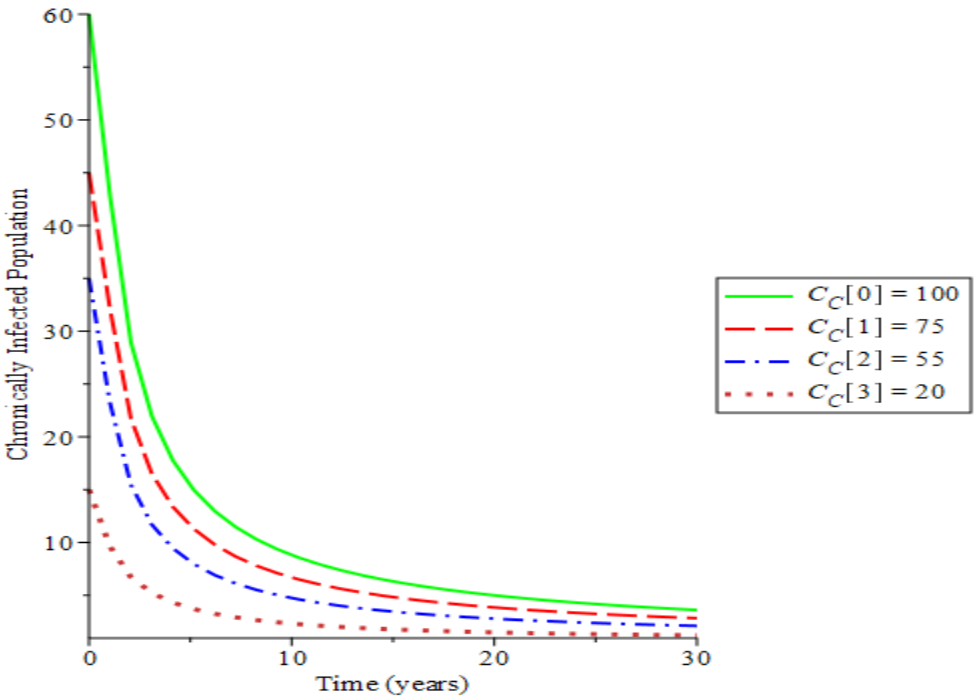

Figure 4.38: Behavioral dynamics of chronic HCV population when $R_0 > 1$ when $b_c = 0.80$

The behavioural dynamics of the susceptible, acute HCV and chronic HCV populations in endemic states was shown in Figures 4.36-4.38. Considering an increase in HCV transmission rate, $b_c = 0.80$, keeping all other parameters in Table 4.3. Each system approached asymptotically the stable HCV endemic equilibrium state of system 3.50. Moreover, the endemic equilibrium trajectories of the solution converge to $(234.034, 120.894, 89.469)$ by choosing different initial conditions for given parameters in Table 4.33. Hence, $R_{ec} = 1.011$. This again supports Theorem 3.12 that the endemic equilibrium is globally asymptomatically stable if $R_{ec} > 1$.

Figure 4.39-4.42, shows the behavioural dynamics of different populations of HCV when varying treatment rate, r.

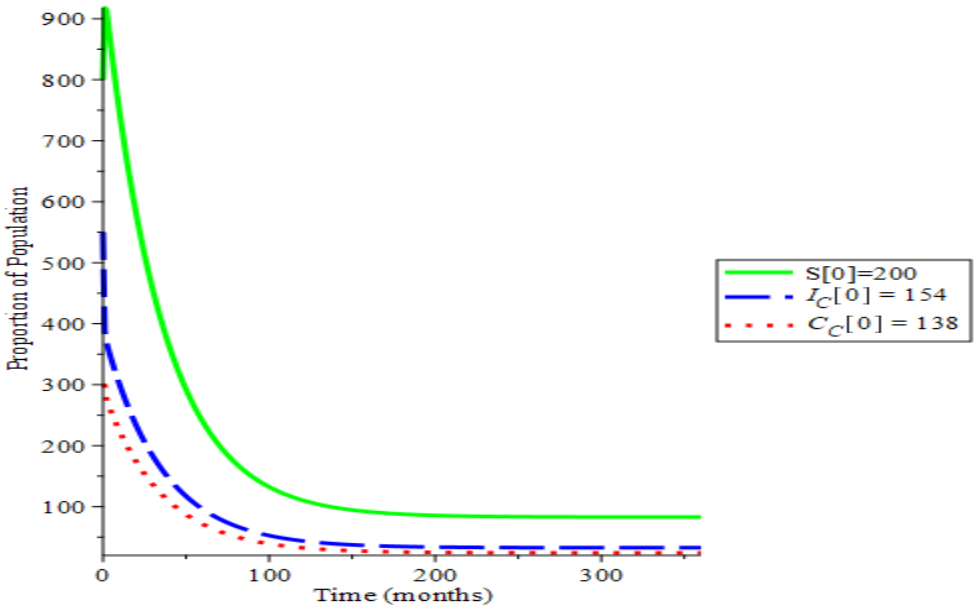

Figure 4.39: Behavioral dynamics of different populations of HCV at endemic when varying treatment rates, $c = 5, b_c = 0.8, r = 3.3$

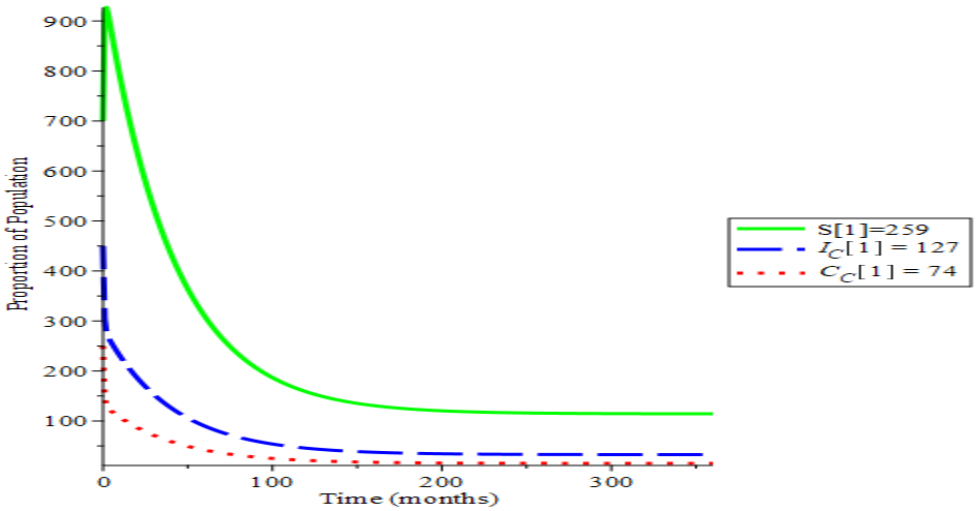

Figure 4.40: Behavioral dynamics of different populations of HCV when varying treatment rate $c = 5, b_c = 0.8, r = 5.3$

From Figure 4.39, it is seen that the susceptible initial population is 200, the acute population is

154 and the chronic HCV population is 138. On increasing treatment rate r, from 3.3 to 5.3, the susceptible population increases to 259, the acute population reduces to 127 while the chronic population decline 174 with time.

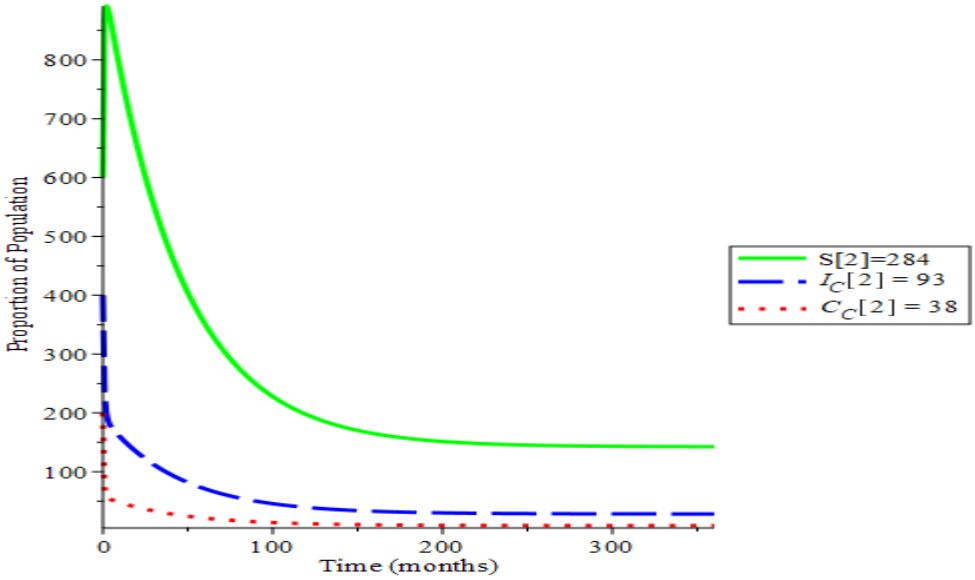

Figure 4.41: Behavioral dynamics of different populations of HCV when varying treatment rate $c = 5, b_c = 0.8, r = 8.3$

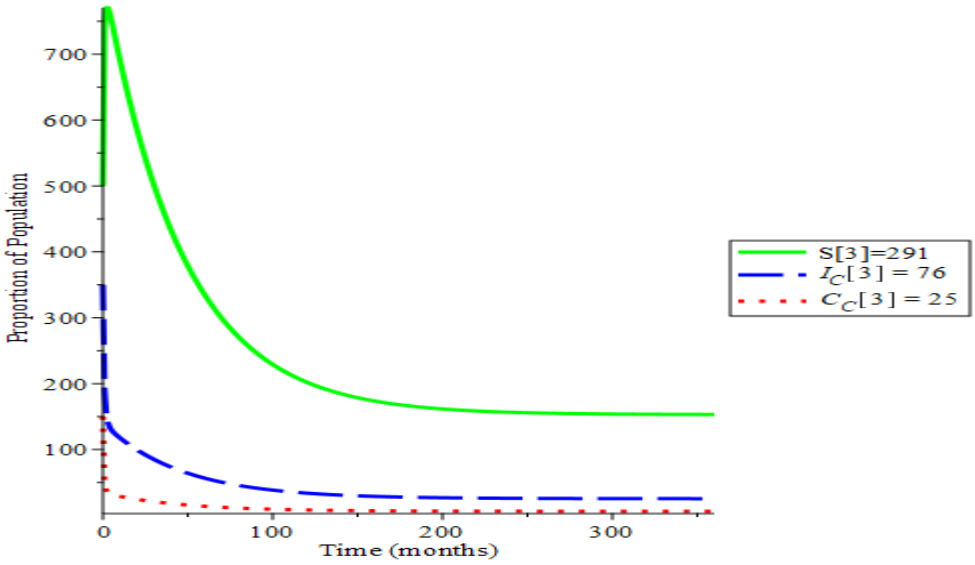

Figure 4.42: Behavioral dynamics of different populations of HCV when varying treatment rate, $c = 5, b_c = 0.8, r = 10.3$

The same trend which is an increase in susceptible populations and a decrease in acute and chronic populations is observed in Figures 4.41 and 4.42 when taking r to 8.3 and 10.3 respectively. This implies that as the treatment rate increases on the transmission dynamic of HCV the chronic population reduces due to successful treatment while the susceptible population increases because some chronically infected individuals who are treated engage in risk factors (such as unprotected sex, drinking, having more than one sexual partner) can be re-infected if sustained virologic response; SVR after 12 weeks of treatment is not attained.

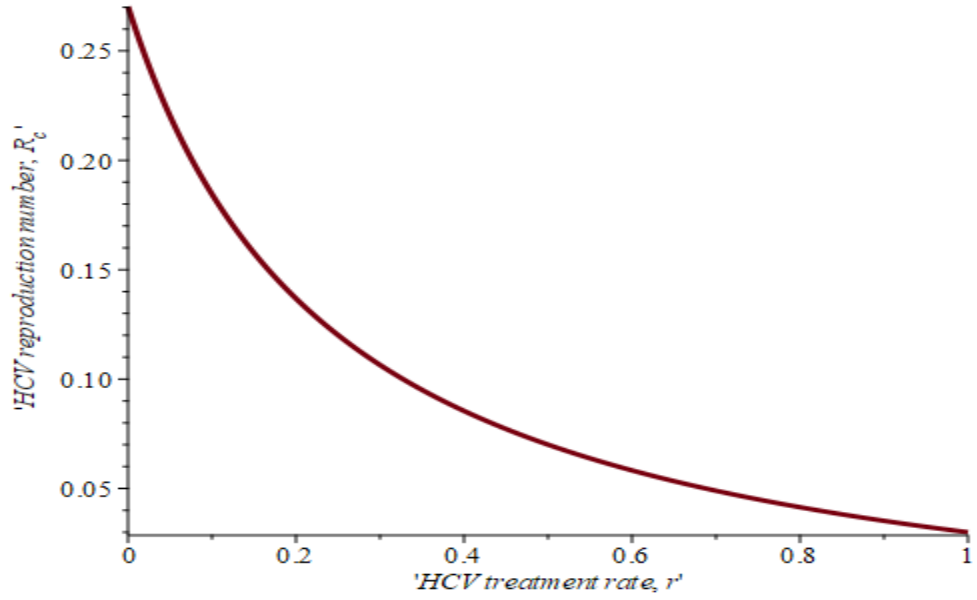

Figure 4.43: Impact of HCV treatment rate on HCV reproduction number

Figure 4.43 support the numerical variation in figure 4.40-4.43. From the contour plot, it was observed that as the HCV treatment rate increase, the rate at which the virus will be transmitted, R_{ec}, is reducing. The plot shows that when 10% of HCV infected population is treated

the R_{ec} is 18.8%, also when 20% of the population were placed on treatment, R_{ec} reduces to 13.4%, likewise, 40% treated gives 8.5% R_{ec}. This implies that with approximately, a 10% increase in treatment of HCV there is a 5% reduction in HCV reproduction number, R_{ec} which will in turn reduce the progression rate from acute to chronic and also the risk of liver fibrosis or cirrhosis which can lead to death due to HCV.

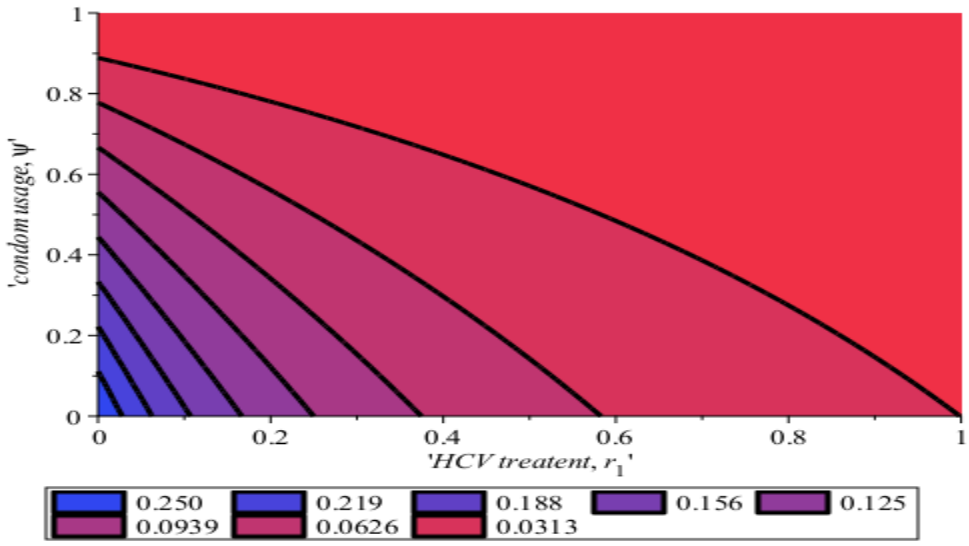

Figure 4.44: The effect of treatment and condom use on HCV reproduction number for HCV model case 2

In Figure 4.44, the effect of treatment and condom use on HCV reproduction numbers for the HCV model was shown on a contour plot. From the plot, if the treatment rate, r is 100% and the use of condoms is 90% it means that the reproduction number of HCV, R_{ec} will reduce to 0.0313. Likewise, if 57% of the population is treated and 77% of the population use condoms R_{ec} will be 0.0626 compared to when 0.7% of the HCV infected population is treated while 10.4% used the condom then R_{ec} rises to 0.250. This implies that to reduce the incidence of HCV transmission by the values of reproduction number, there is a need for more successful treatment where people

attain SVR and avoid risk factors such as unprotected sex by use of condom, drinking, and multiple sexual partners which can make them re-infected.

Figures 4.45-4.47 shows an optimal control plot with time preventive (condom at the susceptible state, counselling, and testing at the acute and chronic state, treatment at the chronic state) strategies as a control measure. So, these three controls are used to optimise the objective function of HCV transmission dynamics. The effect of the control measure on different systems is discussed.

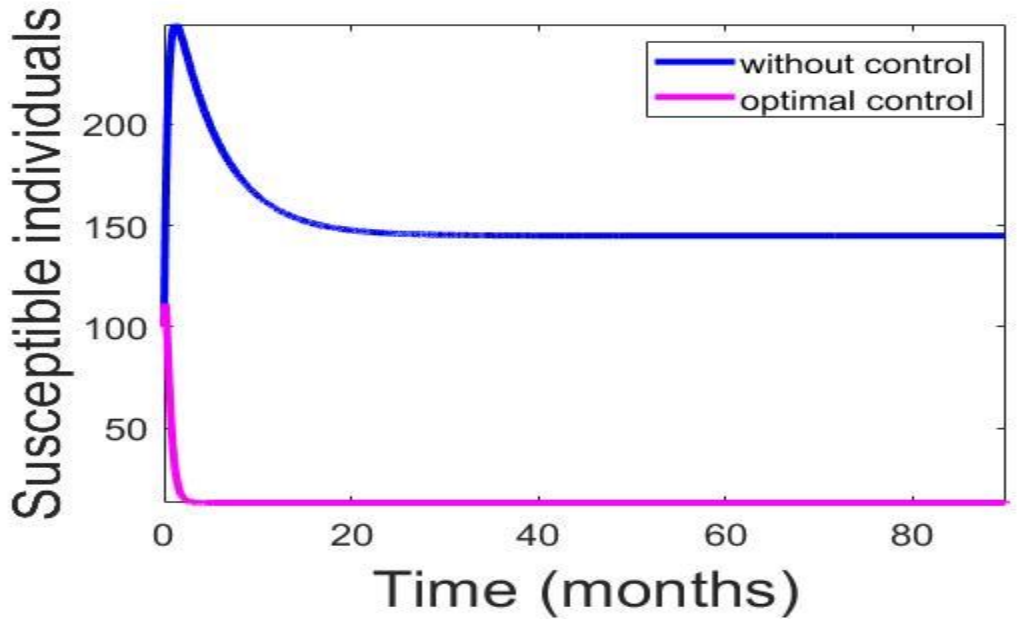

Figure 4.45: The effect of control on susceptibility to HCV for HCV model case2

Fig 4.45 shows the impact of the control on the susceptible population. It was observed from the figure that the population of the susceptible in the control plot is lower than that of those individuals not under control. Awareness is a form of testing that is an important control tool that helps in the reduction of those who will be prone to the virus because as they are informed, they

take all preventive measures to guard against the virus.

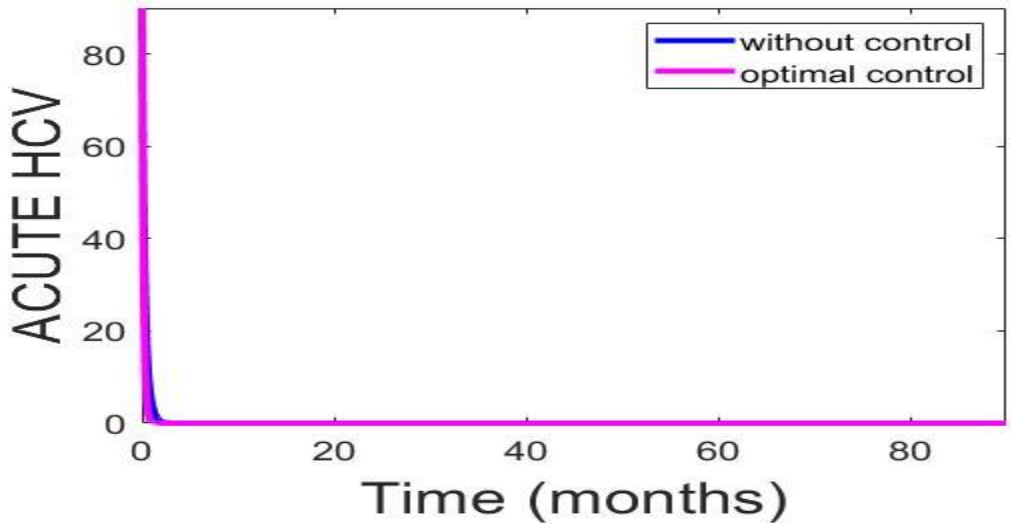

Figure 4.46: The effect of control on Acute HCV for HCV model case2

The effects of the controls on the HCV acute populations are shown in Figure 4.46. From the figure, there is no visible difference between the control plot and the uncontrolled plot because, in the acute stage, there can be few or no control measures that can be put in place at that time.

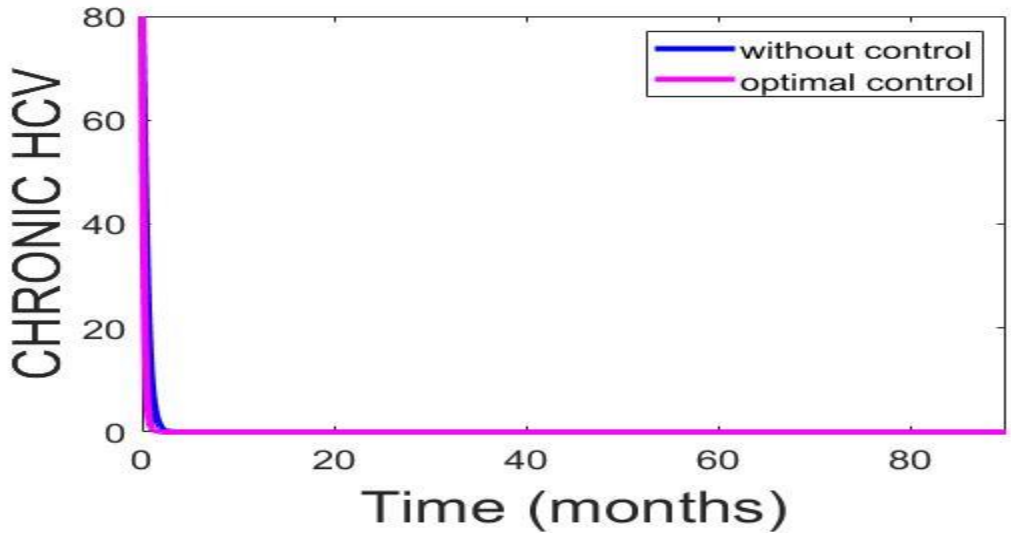

Figure 4.47: The effect of control on Chronic HCV for HCV model case 2

From Figure 4.47, there is a decline in the population of chronic individuals under control over time than the uncontrolled as observed on the plot. The treatment preventive control measures' impact on the chronic individuals reduces the effect of liver cirrhosis or fibrosis.

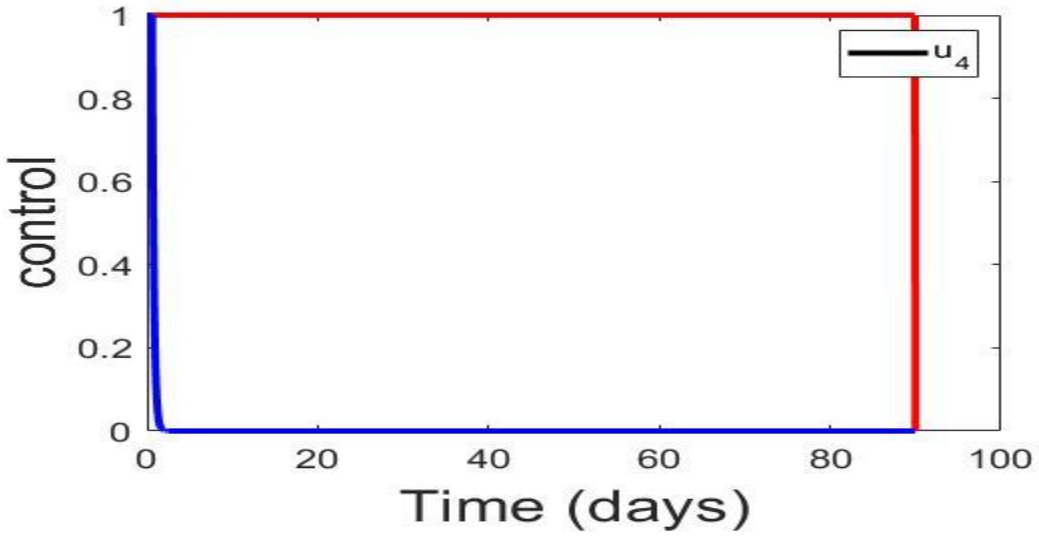

Figure 4.48: The control profile for HCV model case2

Figure 4.48 gives the control profiles for all the different combinations of the optimal control strategies for HCV transmission.

4.3 HIV-HCV Model

4.3.1 Case 3

For a comprehensive understanding of the transmission process of the co-infection of Hepatitis C and Human immunodeficiency virus, numerical computation of the mathematical analysis is carried out along with optimal control analysis to explain the interaction between HIV and hepatitis

C and how the transmission impacts each other. The default parameter values listed in table 3.3 are used, unless otherwise stated on each graph. The outcomes of treating HCV-infected first in people with co-infection are numerically checked.

Hence, the mathematical formulation solutions for case 3 are presented as follows:

Table 4.3: Sensitivity Indices on R_{eCH} for HIV-HCV model formulation of case 3

Parameter	**Sensitivity index**	**Parameter**	**Sensitivity index**
Λ	+ 0.9034267912	η	-3.476194427
φ	+0.9034267912	ω	-0.3657921292
c_h	+1	σ_c	-3.841986553
c_c	+1	$\rho_i, i = 1,2,3$	-0.3525175013
b_h	+1	$\alpha_1, i = 1,2,3..$	-1.070739778
b_c	+1	μ_h	-0.3641946643
μ_c	0.01185092345	$\psi\ \xi$	-0.04166666667
$v_{i,} i = 1,2,3$	0.02950877467	$\theta_1, i = 2,3..$	-0.1467380474
θ_1	0.004381026371	d_a	-0.003126600878
d_c	0.04224083035	$r_i, i = 1,2, \ldots$	2.787894802

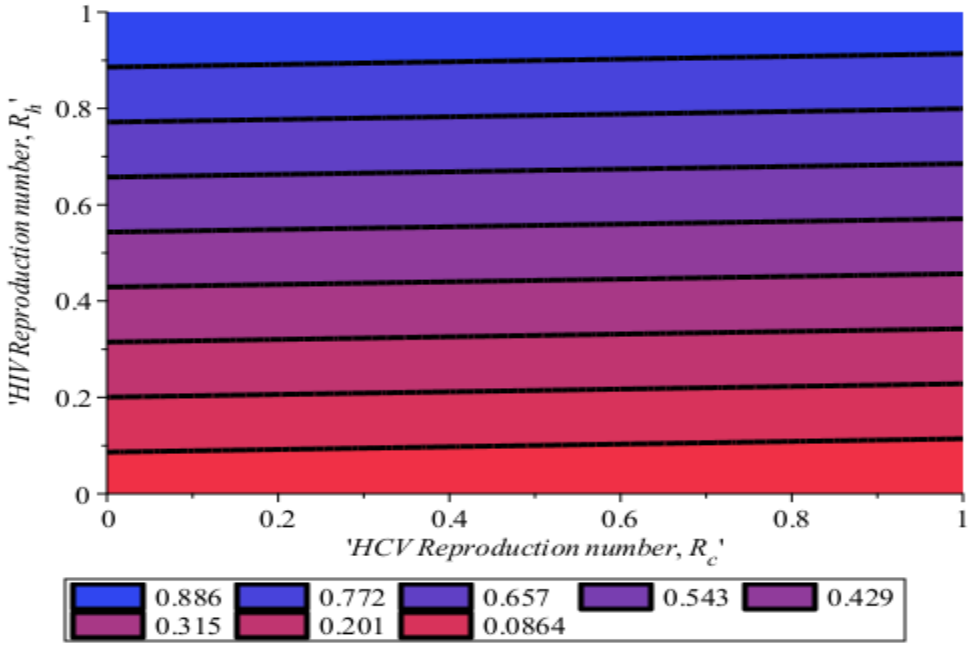

Figure 4.49: Impact of HCV reproduction number on HIV reproduction number for model case3

In figure 4.49, the impact of the HCV reproduction number on the HIV reproduction number for model case 3 is shown on a contour plot. From the figure, it is seen that when 20% of the population is infected with HCV and 9% of the population is infected with HIV, then the reproduction number of the co-infection R_{ech} will be 0.0864 (8.64%). In the same manner, if we repeat 20% of the HCV population and 20% of HIV, then R_{ech} is 0.201 (20.1%). This simply means that as the reproduction number of HCV, R_{ec} increase it, in turn, increase the reproduction number of HIV R_{eh}.

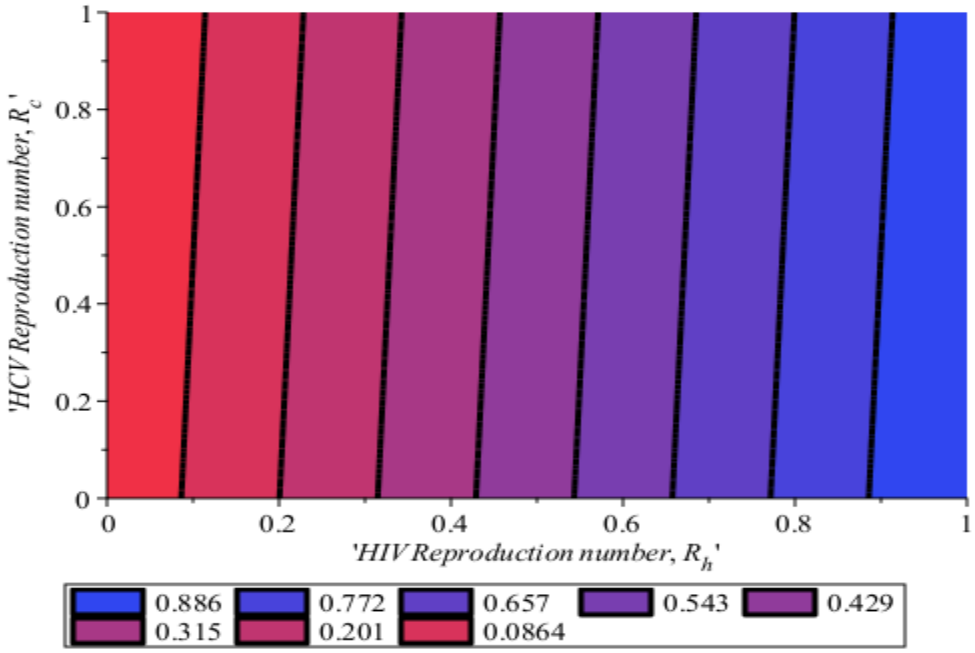

Figure 4.50: Impact of HIV reproduction number on HCV reproduction number for model case3

Moreover, in figure 4.50, the impact of HIV reproduction number on HCV reproduction number is represented by a contour plot, just as seen in figure 4.49. When we have 10% of the HIV population, there are 8.1% of the HCV population and the co-infection R_{ech} is 0.0861 (8.61%). Also, when 20% of the HIV is in the population and 2.73%of the HCV is in the population, we have R_{ech} to be 0.201 (20.1%). This also means that as HIV increases in the population, HCV also increases. This simply implies that to control HCV, HIV cases will be reduced, which is attributed to the same transmission process, and it is vice versa. Hence, to ensure the existence of the co-infection in the population, if HCV is reduced, it will in turn impact HIV, and if the two viruses $R_{ec}\ and\ R_{eh}$ are low, then there will be a reduction in the co-infection reproduction number, R_{ech}.

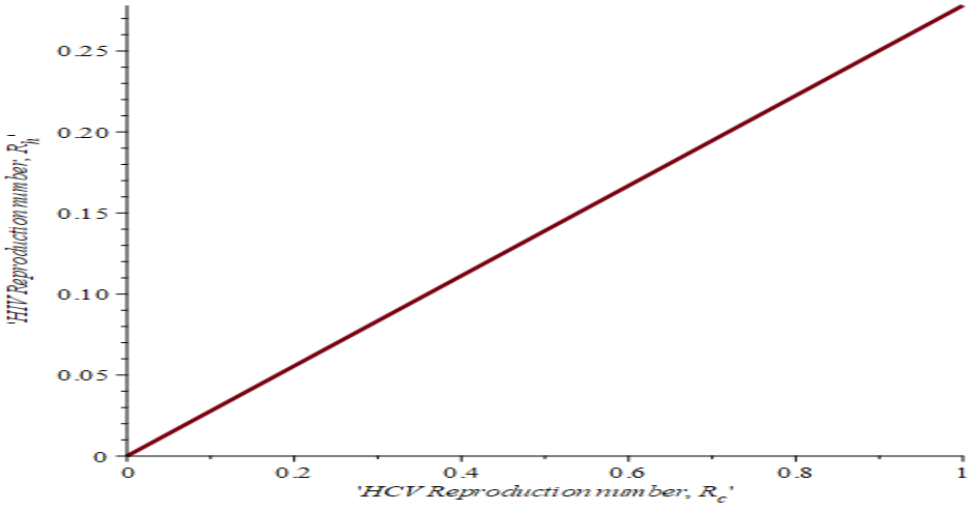

Figure 4.51: Impact of HCV reproduction number on HIV reproduction number for model case3

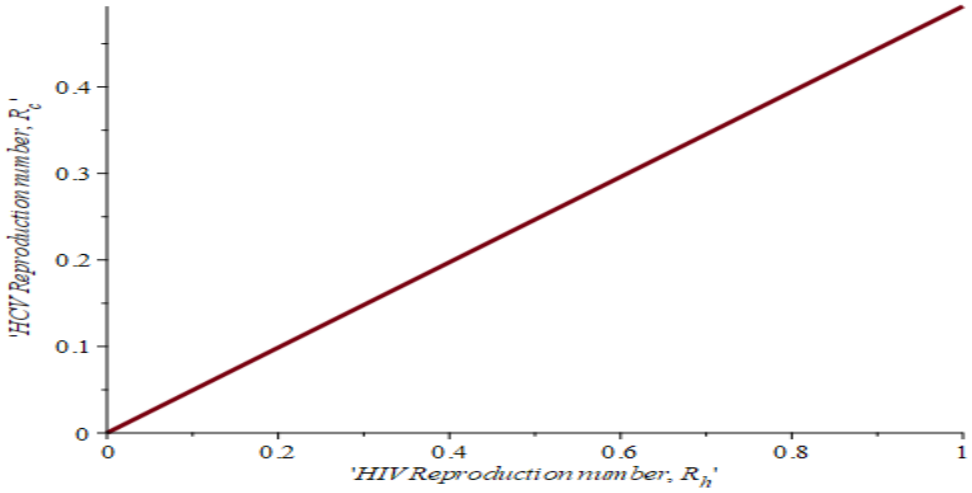

Figure 4.52: Impact of HIV reproduction number on HCV reproduction number for model case3

Figure 4.51-4.52 shows the linear contour plots of the impact of HCV on HIV and the impact of HIV on HCV. From the plots, it is evident that as HCV increases HIV also increases and vice versa. This simply means there's a need to reduce the HCV transmission rate since any slight increase in HCV lead to an increase in HIV.

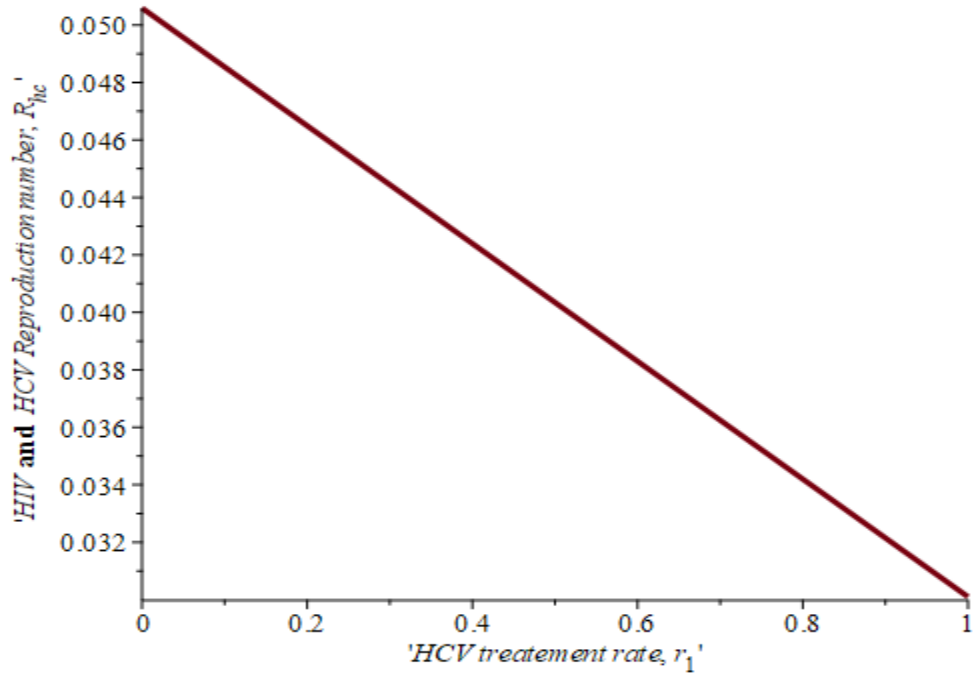

Figure 4.53: Impact of HCV treatment on HIV-HCV co-infection reproduction number for model case 3

Figure 4.53 gives the impact of treating HCV first on the HIV-HCV co-infection population. The linear contour plot shows that when 20% of the co-infected individual is treated for HCV the reproduction numberR_{ech} is 0.046 (4.6%), also if we treat 40% of the individual who are co-infected of their HCV first the R_{ech} reduces to 0.042 (4.2%). The plot depicts that if we treat more of the dually infected population with HCV first, the transmission rate of the co-infection will be reduced by 0.4% thereby lowering the danger of liver cancer and death due to HIV/AIDS or death due to HCV.

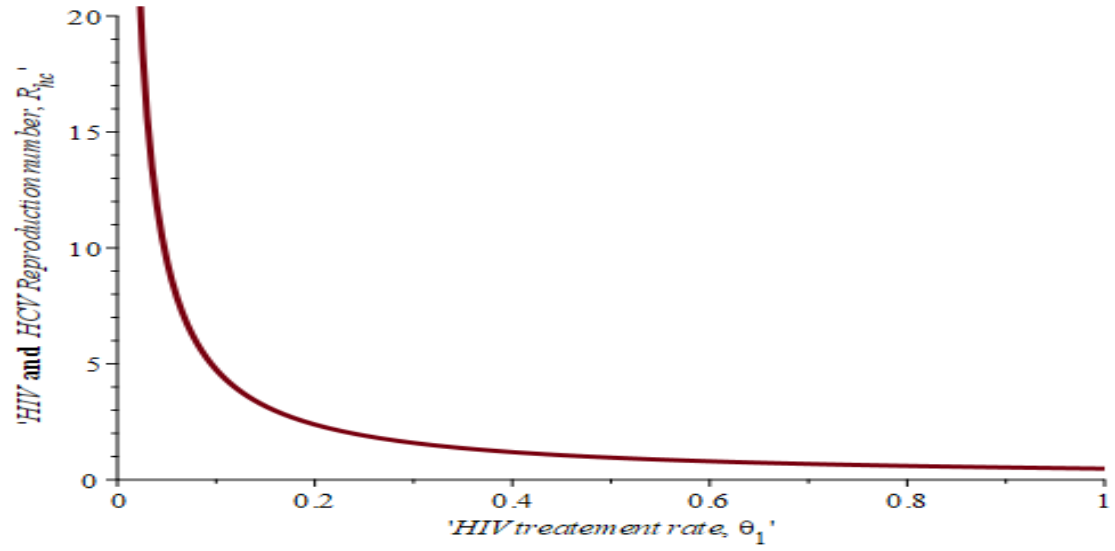

Figure 4.54: Impact of HIV treatment rate on HIV-HCV co-infection reproduction number for model case 3

Figure 4.54 depicts the impact of treating HIV first on the HIV-HCV co-infection population. According to the linear contour plot, when (0.60) 60% of the co-infected individual is treated for HIV the reproduction numberR_{ehc} is 0.906 (90.6%), also if we treat (0.8) 80% of the individual who are co-infected of their HIV first the R_{ehc} drops to 0.725 (72.5%). The plots (figure 4.54 and figure 4.55) show that treating more of the dually infected population with HCV first, the transmission rate of the co-infection more than treating HIV first in co-infected patients, thereby lowering the danger of liver cancer and death due to HIV/AIDS or death due to HCV.

4.4 Discussion of Findings

To solve the problem of HIV-HCV co-infection transmission and acquisition, three models were developed: the HIV model, the HCV model, and the co-infection model, all using a mathematical modelling approach and taking into account the vertical and horizontal transmission processes as

well as treatment availability for mono and dual infections.

The result obtained from the sensitivity indices means interventions should target and concentrate on reducing the values of the average number of sexual partners acquired per year, the number of defaulters lost to follow-up, and HIV transmission probability per sexual contact, since the increasing rate of progression from HIV to AIDS would imply fast progression to AIDS. Also, the effective use of condoms should be enforced as a precaution to reduce the transmission rate of HIV/AIDS as reported (Pinto and Carvalho, 2015; Rana and Sharma, 2020). The observation obtained in figure 4.2 agrees well with the findings of (Teng *et al.*, 2019) for population dynamics with a basic reproduction number of less than 1, and as such, the average contact infected number with an infectious person declines in magnitude. Figure 4.16 suggest that if the proportion of the population that fall out of treatment increase, the rate number of secondary infection that will be transmit will be on the high side, this supports the data fitting done by (Akudibillah *et al.*, 2019). The results in figure 4.20 align with the findings by the World Health Organization (WHO, 2020a), which says that with effective information and strict adherence to treatment, there is a tendency to have a reduction in the number of HIV/AIDS infected individuals.

Furthermore, this study found that children born to HIV-unaware mothers are recruited directly into the unaware population until they are tested at the age of 48 hours, at age 1-2 months, and again at age 3-6 months (Delia and Richard 2020). Early detection allows for prompt antiretroviral therapy, which lowers HIV viral load and thus slows virus transmission. It has been demonstrated that if infected-born children are prevented by HIV testing and treatment of pregnant women, the overall infective population will remain under control, reducing the AIDS population. It is also observed that, as more infected children are born, the number of people with AIDS goes up, while

the number of people who are being treated goes down.

Individuals who discontinue HIV treatment or engage in habits or lifestyles that reduce the potency or effects of treatment in the HIV class during treatment, which aggravates HIV progression and transmission processes, as well as early testing at the unaware HIV state of the virus and treatment at the aware state, help in better virus management. It has also been demonstrated that HCV acutely infected individuals spontaneously clear the virus, and treatment in the chronic infectious class aids in mitigating the risk of HCV-related liver cirrhosis. In this study, the importance of HIV and HCV testing and treatment, HCV treatment in HIV co-infected people, and strict adherence to treatment with effective condom use cannot be overstated because it is the foundation of reducing disease transmission. Strategies and control interventions are cost-effective, i.e., they reduce costs while increasing the number of recovered HCV people. It has been demonstrated that early detection and treatment of opportunistic or comorbid infections such as HCV may be the most effective way to reduce the threat of HIV progression to AIDS and liver cirrhosis in HCV. Furthermore, treating HCV first in people infected with HIV has been found to be the most effective way of reducing AIDS-related deaths caused by liver fibrosis or cirrhosis and increased viral load.

CHAPTER FIVE

5.0 SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

5.1 Summary

Using mathematical models, this study investigated the transmission and acquisition processes of the Human Immunodeficiency Virus, Hepatitis C virus, and co-infection of the two viruses, as well as the impact of condoms, counselling and testing, and treatment as control strategies. Vertical and horizontal transmission, which are the primary routes of disease transmission, were specifically examined using the basic reproduction number and the stability analysis. Furthermore, various intervention scenarios for HIV, HCV, and HIV-HCV co-infection were addressed and investigated.

The formulation, analysis, and methods of solutions for the HIV, HCV, and HIV-HCV co-infection models were discussed. Using established theorems, a class of ODE systems was formulated and analyzed. The positivity and boundedness of the solutions were investigated, which revealed that the solutions are bounded and well-posed in the various regions. Using the Lyapunov method, the disease-free and endemic equilibrium points were analyzed to be locally and globally asymptotically stable under certain conditions of the basic reproduction number. The behavior of the disease-free equilibrium was investigated using bifurcation analysis when the basic reproduction rate $R_o = 1$. Then, Portryagin's maximum principle was used to consider the formulation of the optimal control problem, the analysis of the optimal control problem, adjoint conditions, optimality conditions, and the optimality system for the HIV, HCV, and HIV-HCV co-infection models.

The numerical computation of the models under consideration was done. Using the basic reproduction number (R_o) $[R_o < 1 \; and \; R_o > 1]$. The necessary conditions for disease-free equilibrium to be asymptotically stable were established analytically and numerically. The possibility of disease eradication was demonstrated using parameters from published articles and some arbitrary values. The findings also demonstrated the effects of changing some sensitive parameters on the dynamics of different populations. Following that, the optimal control computation was highlighted to show the effects of control measures on the population. It was also determined that treating HCV first in co-infected individuals with HIV is the first step in reducing risk factors associated with HIV-HCV co-infection because treating HCV-infected individuals reduces the reproduction number of co-infection. It was also discovered that HCV reproduction affects HIV and vice versa. In order to maintain the increasing rate of HIV co-infection with HCV, it is necessary to reduce HCV, as this has an impact on HIV, which is associated with the same transmission rate, and if the two are low, the co-infection reproduction number R_{ech} will be low.

5.2 Conclusions

The following conclusions were drawn from this study:

1. By setting the various compartments to zero, the disease-free and endemic equilibria for the HIV, HCV, and HIV-HCV co-infection full model models were determined. All compartmental values for the disease-free equilibrium and the endemic equilibrium were obtained. It was discovered that the various models' disease-free and endemic equilibriums exist. This demonstrates that the disease is manageable in a variety of situations.

2. The basic reproduction number is calculated to investigate the spread of secondary infected

cases caused by primary infected individuals. The numerical solutions for $R_0 < 1$ were validated, and it was discovered that the average number of infected people in relation to infectious people decreases in magnitude. This influences the virus's transmission process.

3. The linearization of the various models determined the stability analysis. The eigenvalues of the linearized models were calculated using the Jacobian matrix of the models. According to the findings, the disease-free equilibrium is asymptotically stable for $R_0 < 1$. This means that solutions converge to and remain close to the equilibrium, and as a result, the solution is stable, which means that the disease will die out over time. Meanwhile, when $R_0 > 1$, the endemic equilibrium is asymptotically stable. This implies that disease control is urgently needed to avoid endemicity; a solid measure to mitigate virus spread should be encouraged.

4. The sensitivity analysis revealed that the testing, α and treatment rate of HIV θ, treatment rate r, and condom usage rate, ψ of HCV are the most sensitive parameters in the current study. This implies that more attention should be focused on these parameters to avoid a disease explosion that could lead to uncontrollable effects of HIV, Hepatitis C virus, and their co-infection in society.

5. The bifurcation results of the models were computed using the center manifold theory. The stable upper bifurcation and unstable lower bifurcation reveal that bifurcation transitions will occur over time. Since $a > 0$, then endemic equilibriums of the various models are locally asymptotically stable for the associated basic reproduction number greater than unity.

6. It was determined computationally that the models developed and the control measures imposed on them have a significant effect on reducing the transmission and acquisition of HIV, HCV, and their co-infection. So, it's safe to say that control strategies help reduce the danger that viruses pose to a population.

The study's objectives were met as the models were developed, tested, and analyzed qualitatively and quantitatively to show that condoms, testing, treatment, and efficient follow-up on people who are on treatment increase the recovery rate of people who are infected with HCV. This reduces the risk of increased viral load in people with HIV/AIDS who also have HCV, as well as the chance of liver cancer in HIV-HCV co-infected people.

5.3 Recommendations

This study's recommendations are as follows:

1. Before beginning treatment, individuals who exhibit symptoms of any of the diseases should be properly diagnosed. This is recommended so that one knows whether to treat HIV only, HCV only, or both.

2. The current study recommends that health workers and health policymakers take immediate action to reduce the progression rate ρ of HIV diagnosis and treatment, contact rate, c and transmission rate b_h.

3. As a follow-up to the second recommendation above, the most effective way to stop the spread of HIV is to condom use, strict adherence to treatment (ART), counseling and testing, treating pregnant women, not having more than one sexual partner, and so on should be encouraged.

4. To control the spread of HCV disease, a combination of the three controls: condom use, counseling and testing, and HCV treatment (direct-acting antiviral (DAA) tablets) is recommended.

5. While the combination of the four controls proves to be the most effective in interrupting the transmission of HIV-HCV disease, the combination of condom usage, counseling and testing, antiretroviral therapy (ART) for HIV/AIDS and direct-acting antiviral (DAA) tablets for HCV, treatment and prevention using both ART and condoms is also recommended for controlling the spread of HIV-HCV co-infection. This strategy is cost-effective compared to using all the controls and it has the same impact as using all four controls.

6. Finally, in dually infected individuals, treating HCV infection first is recommended because the increasing effect of HCV treatment rate leads to a reduction in co-infection reproduction number R_{ech} and also because increasing HCV reproduction number, R_{ec} leads to an increase in HIV reproduction number, R_{eh}.

5.4 Contributions to Knowledge

The findings of the present work and hence the contributions to knowledge are:

1. this study have validated that children born of unaware infected mothers are recruited into an unaware population who later progress to an HIV aware stage after testing within the first 2 days of life, at 1 to 2 months of age, and at 4 to 6 months of age. Possible solutions for reducing modes of HIV vertical transmission were also presented.
2. as a result of the latter contribution in 1, HIV disease can be cleared from the population

or go into extinction if $R_c < R_h <$. Our result also suggests that even if $R_h < 1$ the disease-free equilibrium E_0 can still co-exist with an endemic equilibrium. Hence, for total HIV disease eradication R_c is expected to be brought lower than a certain critical threshold R_c.

3. in model case 3, where both HIV and HCV co-exist, our result indicates that $R_{ec} < R_{eh} < R_{ech} < 1$ must be satisfied whereas previous studies held the claim that $R_h < R_c < 1$.
4. people who drop out of treatment because of their habits add to the number of HIV-positive people, which is a problem that needs to be fixed by a series of public awareness campaigns about the risks of not following treatment procedures and patterns.
5. the development of a mathematical model that incorporates horizontal and vertical transmission, the progression of HIV-infected people to the AIDS stage, and treatment at the early stage of HIV awareness to avoid increased viral loads. To the best of our knowledge, the co-existence of the two viruses with treatment readily available for both viruses, treatment dropouts, and those who engage in risk factors after HCV treatment in the population is a significant contribution to this work. The existence of the aforementioned parameters has been clinically demonstrated, and this has now been confirmed by some of the findings in this study. Some of our findings have established the existence of children born to unaware HIV-infected people and the possible intervention to curb them.

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APPENDICES

APPENDIX I: F_i and V_i for co-infectionReproduction Number

$F_i =$

$$\begin{pmatrix} c(-\psi\xi+1)b_h & 0 & 0 & c(-\psi\xi+1)b_h & 0 & 0 & c(-\psi\xi+1)b_h\kappa_1 & 0 & 0 & c(-\psi\xi+1)b_h\kappa_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & c(-\psi\xi+1)b_c & c(-\psi\xi+1)b_c & c(-\psi\xi+1)b_c\kappa_2 & 0 & 0 & c(-\psi\xi+1)b_c\kappa_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad (1)$$

V_i

$$= \begin{pmatrix} -\Lambda\varphi+k_1 & 0 & 0 & 0 & 0 & 0 & -\epsilon_1\omega\sigma_c & 0 & 0 & 0 & -r_2 & 0 & 0 & 0 \\ -\alpha_1 & k_2 & 0 & 0 & 0 & 0 & 0 & -\epsilon_1\omega\sigma_c & 0 & 0 & 0 & -r_3 & 0 & 0 \\ 0 & -\theta_1 & k_3 & -\theta_2 & 0 & 0 & 0 & 0 & -\epsilon_1\omega\sigma_c & 0 & 0 & 0 & -r_4 & 0 \\ -\rho_1 & 0 & -\upsilon_1 & k_4 & 0 & 0 & 0 & 0 & 0 & -\epsilon_1\omega\sigma_c & 0 & 0 & 0 & -r_5 \\ 0 & 0 & 0 & 0 & \left(\omega_0+\eta_0\right)\sigma_c+\mu & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \eta\sigma_c & k_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & k_6 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\alpha_2 & k_7 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\theta_3 & k_8 & -\theta_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\eta\epsilon_2\sigma_c & 0 & 0 & k_9 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\eta\epsilon_2\sigma_c & 0 & -\alpha_3 & k_{10} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\eta\epsilon_2\sigma_c & 0 & -\theta_5 & k_{11} & 0 & -\theta_6 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\rho_2 & 0 & -\upsilon_2 & 0 & 0 & 0 & k_{12} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\rho_3 & 0 & -\upsilon_3 & -\eta\epsilon_2\sigma_c & k_{13} \end{pmatrix} \quad (2)$$

APPENDIX II: Co-infection Local Stability at DFE Proof

$$\begin{bmatrix} -\mu-\lambda & b_1 & 0 & 0 & b_2 & b_3 & b_4 & b_5 & 0 & 0 & b_6 & 0 & 0 & 0 & 0 \\ 0 & \varphi\Lambda + c(-\psi\xi+1)b_h - k_1 - \lambda & 0 & 0 & b_7 & 0 & 0 & b_8 & 0 & 0 & b_9 & r_2 & 0 & 0 & 0 \\ 0 & \alpha_1 & -k_2-\lambda & 0 & 0 & 0 & 0 & 0 & \omega\varepsilon_1\sigma_c & 0 & 0 & 0 & r_3 & 0 & 0 \\ 0 & 0 & \theta_1 & -k_3-\lambda & \theta_2 & 0 & 0 & 0 & 0 & \omega\varepsilon_1\sigma_c & 0 & 0 & 0 & r_4 & 0 \\ 0 & \rho_1 & 0 & \upsilon_1 & -k_4-\lambda & 0 & 0 & 0 & 0 & 0 & \omega\varepsilon_1\sigma_c & 0 & 0 & 0 & r_5 \\ 0 & 0 & 0 & 0 & 0 & b_{10} & b_{11} & b_{12} & 0 & 0 & b_{13} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \eta_0\sigma_c & -k_5-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -k_6-\lambda & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha_2 & -k_7-\lambda & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \theta_3 & -k_8-\lambda & \theta_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta\varepsilon_2\sigma_c & 0 & 0 & -k_9-\lambda & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta\varepsilon_2\sigma_c & 0 & \alpha_3 & -k_{10}-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta\varepsilon_2\sigma_c & 0 & \theta_5 & -k_{11}-\lambda & 0 & \theta_6 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \rho_2 & 0 & \upsilon_2 & 0 & 0 & 0 & -k_{12}-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \rho_3 & 0 & \upsilon_3 & \eta\varepsilon_2\sigma_c & -k_{13}-\lambda \end{bmatrix} =$$

$$0 \qquad (3)$$

where

$$b_1 = -\varphi\Lambda - c(-\psi\xi+1)b_h;\ b_2 = -c(-\psi\xi+1)b_h;\ b_3 = \omega_0\sigma_c - c(-\psi\xi+1)b_c;\ b_4 = r_1 -$$

$$c(-\psi\xi+1)b_c;\ b_5 = -\frac{\left(\frac{c(-\psi\xi+1)b_h\kappa_1\mu}{\Lambda} + \frac{c(-\psi\xi+1)b_c\kappa_2\mu}{\Lambda}\right)\Lambda}{\mu};\ b_6 = c(-\psi\xi+1)b_h;\ b_7 = c(-\psi\xi +$$

$$1)b_h\kappa_1 + \omega\varepsilon_1\sigma_c;\ b_8 = c(-\psi\xi+1)b_h\kappa_1;\ b_9 = c(-\psi\xi+1)b_h\kappa_1;\ b_{10} = c(-\psi\xi+1)b_c -$$

$$(\omega_0+\eta_0)\sigma_c - \mu - \lambda;\ b_{11} = c(-\psi\xi+1)b_c;\ b_{12} = c(-\psi\xi+1)b_c\kappa_2;\ b_{13} = c(-\psi\xi+1)b_c\kappa_2$$

$$J(E_0) =$$

$$\begin{bmatrix} \varphi\Lambda + c(-\psi\xi+1)b_h - k_1 - \lambda & 0 & 0 & c(-\psi\xi+1)b_h & 0 & 0 \\ \alpha_1 & -k_2-\lambda & 0 & 0 & 0 & 0 \\ 0 & \theta_1 & -k_3-\lambda & \theta_2 & 0 & 0 \\ \rho_1 & 0 & \upsilon_1 & -k_4-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & c(-\psi\xi+1)b_c - (\omega_0+\eta_0)\sigma_c - \mu - \lambda & c(-\psi\xi+1)b_c \\ 0 & 0 & 0 & 0 & \eta\sigma_c & -k_5-\lambda \end{bmatrix} =$$

$$0 \qquad (4)$$

APPENDIX III: Co-infection Global Stability at DFE Proof

$$\begin{pmatrix} \frac{dH_U}{dt} \\ \frac{dH_A}{dt} \\ \frac{dH_T}{dt} \\ \frac{dA_A}{dt} \\ \frac{dI_C}{dt} \\ \frac{dC_C}{dt} \\ \frac{dH_{UI}}{dt} \\ \frac{dH_{AI}}{dt} \\ \frac{dH_{TI}}{dt} \\ \frac{dH_{UC}}{dt} \\ \frac{dH_{AC}}{dt} \\ \frac{dH_{TC}}{dt} \\ \frac{dA_{AI}}{dt} \\ \frac{dA_{AC}}{dt} \end{pmatrix} = (F - V) \begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \\ I_C \\ C_C \\ H_{UI} \\ H_{AI} \\ H_{TI} \\ H_{UC} \\ H_{AC} \\ H_{TC} \\ A_{AI} \\ A_{AC} \end{pmatrix} - \left(1 - \frac{S_h}{N_h}\right)\left(1 - \frac{S_c}{N_c}\right) F \begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \\ I_C \\ C_C \\ H_{UI} \\ H_{AI} \\ H_{TI} \\ H_{UC} \\ H_{AC} \\ H_{TC} \\ A_{AI} \\ A_{AC} \end{pmatrix}$$

F and V are defined in appendix I

Considering the disease-free $H_A = H_T = A_a = I_c = C_c = H_{uI} = H_{AI} = H_{TI} = H_{UC} = H_{AC} = H_{TC} = A_{AI} = A_{aC} = 0 \rightarrow (0,0,0,0,0,0,0,0,0,0,0,0,0,0)$ and $S_h \leq N_h$, $S_h \leq N_h$ as $t \rightarrow \infty$ in Γ_{ch}. Thus,

$$\begin{pmatrix} \frac{dH_U}{dt} \\ \frac{dH_A}{dt} \\ \frac{dH_T}{dt} \\ \frac{dA_A}{dt} \\ \frac{dI_C}{dt} \\ \frac{dC_C}{dt} \\ \frac{dH_{UI}}{dt} \\ \frac{dH_{AI}}{dt} \\ \frac{dH_{TI}}{dt} \\ \frac{dH_{UC}}{dt} \\ \frac{dH_{AC}}{dt} \\ \frac{dH_{TC}}{dt} \\ \frac{dA_{AI}}{dt} \\ \frac{dA_{AC}}{dt} \end{pmatrix} \leq (F), (V) \begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \\ I_C \\ C_C \\ H_{UI} \\ H_{AI} \\ H_{TI} \\ H_{UC} \\ H_{AC} \\ H_{TC} \\ A_{AI} \\ A_{AC} \end{pmatrix} \Longrightarrow \begin{pmatrix} \frac{dH_U}{dt} \\ \frac{dH_A}{dt} \\ \frac{dH_T}{dt} \\ \frac{dA_A}{dt} \\ \frac{dI_C}{dt} \\ \frac{dC_C}{dt} \\ \frac{dH_{UI}}{dt} \\ \frac{dH_{AI}}{dt} \\ \frac{dH_{TI}}{dt} \\ \frac{dH_{UC}}{dt} \\ \frac{dH_{AC}}{dt} \\ \frac{dH_{TC}}{dt} \\ \frac{dA_{AI}}{dt} \\ \frac{dA_{AC}}{dt} \end{pmatrix} \leq (F - V) \begin{pmatrix} H_U \\ H_A \\ H_T \\ A_A \\ I_C \\ C_C \\ H_{UI} \\ H_{AI} \\ H_{TI} \\ H_{UC} \\ H_{AC} \\ H_{TC} \\ A_{AI} \\ A_{AC} \end{pmatrix} \tag{5}$$

Then all of the $(F - V)$ matrix's eigenvalues have negative real parts, i.e.

$F - V =$

$$\begin{bmatrix} D_1 - k_1 & 0 & 0 & D_2 & 0 & 0 & D_3 & 0 & 0 & D_4 & r_2 & 0 & 0 & 0 \\ \alpha_1 & -k_2 & 0 & 0 & 0 & 0 & 0 & \omega\epsilon_1\sigma_c & 0 & 0 & 0 & r_3 & 0 & 0 \\ 0 & \theta_1 & -k_3 & \theta_2 & 0 & 0 & 0 & 0 & \omega\epsilon_1\sigma_c & 0 & 0 & 0 & r_4 & 0 \\ \rho_1 & 0 & \upsilon_1 & -k_4 & 0 & 0 & 0 & 0 & 0 & \omega\epsilon_1\sigma_c & 0 & 0 & 0 & r_5 \\ 0 & 0 & 0 & 0 & D_5 & D_6 & D_7 & 0 & 0 & D_7 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\eta_0\sigma_c & -k_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -k_6 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \alpha_2 & -k_7 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \theta_3 & -k_8 & \theta_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \eta\epsilon_2\sigma_c & 0 & 0 & -k_9 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta\epsilon_2\sigma_c & 0 & \alpha_3 & -k_{10} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta\epsilon_2\sigma_c & 0 & \theta_5 & -k_{11} & 0 & \theta_6 \\ 0 & 0 & 0 & 0 & 0 & 0 & \rho_2 & 0 & \upsilon_2 & 0 & 0 & 0 & -k_{12} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \rho_3 & 0 & \upsilon_3 & \eta\epsilon_2\sigma_c & -k_{13} \end{bmatrix} \tag{6}$$

Evaluating along the first column gives the characteristic equation

$$(\lambda + k_6)(\lambda + k_7)(\lambda + k_9)(\lambda + k_8)(\lambda + k_{10})(\lambda + k_{12})(\lambda^2 + (k_{13} + k_{11})\lambda + k_{13}k_{11} - \upsilon_3\theta_6)(\lambda^4 + (b_h c\psi\xi - \Lambda\varphi - b_h c + k_1 + k_2 + k_3 + k_4)\lambda^3 + (b_h c\psi\xi k_2 + b_h c\psi\xi k_3 + b_h c\psi\xi k_4 + b_h c\psi\xi\rho_1 - \Lambda\varphi k_2 - \Lambda\varphi k_3 - \Lambda\varphi k_4 - b_h c k_2 - b_h c k_3 - b_h c k_4 - b_h c\rho_1 + k_1 k_2 +$$

$k_1k_3 + k_1k_4 + k_2k_3 + k_2k_4 + k_3k_4 - \theta_2\upsilon_1)\lambda^2 + (b_hc\psi\xi k_2k_3 + b_hc\psi\xi k_2k_4 + b_hc\psi\xi k_2\rho_1 +$

$b_hc\psi\xi k_3k_4 + b_hc\psi\xi k_3\rho_1 - b_hc\psi\xi\theta_2\upsilon_1 - \Lambda\varphi k_2k_3 - \Lambda\varphi k_2k_4 - \Lambda\varphi k_3k_4 + \Lambda\varphi\theta_2\upsilon_1 -$

$b_hck_2k_3 - b_hck_2k_4 - b_hck_2\rho_1 - b_hck_3k_4 - b_hck_3\rho_1 + b_hc\theta_2\upsilon_1 + k_1k_2k_3 + k_1k_2k_4 +$

$k_1k_3k_4 - k_1\theta_2\upsilon_1 + k_2k_3k_4 - k_2\theta_2\upsilon_1)\lambda + b_hc\psi\xi\alpha_1\theta_1\upsilon_1 + b_hc\psi\xi k_2k_3k_4 + b_hc\psi\xi k_2k_3\rho_1 -$

$b_hc\psi\xi k_2\theta_2\upsilon_1 - \Lambda\varphi k_2k_3k_4 + \Lambda\varphi k_2\theta_2\upsilon_1 - \alpha_1cb_h\upsilon_1\theta_1 - b_hck_2k_3k_4 - b_hck_2k_3\rho_1 +$

$b_hck_2\theta_2\upsilon_1 + k_1k_2k_3k_4 - k_1k_2\theta_2\upsilon_1)(\lambda^2 + (b_cc\psi\xi - b_cc + \eta_0\sigma_c + \omega_0\sigma_c + \mu + k_5)\lambda -$

$b_cc\psi\xi\eta_0\sigma_c + b_cc\psi\xi k_5 + \eta_0\sigma_ccb_c - b_cck_5 + \eta_0k_5\sigma_c + k_5\omega_0\sigma_c + \mu k_5) = 0$ (7) Equation (7) has two negative roots by Descartes's rule of signs if

$[(\lambda + k_6)(\lambda + k_7)(\lambda + k_9)(\lambda + k_8)(\lambda + k_{10})(\lambda + k_{12})(\lambda^2 + (k_{13} + k_{11})\lambda + k_{13}k_{11} -$
$\upsilon_3\theta_6)(\lambda^4 + (b_hc\psi\xi - \Lambda\varphi - b_hc + k_1 + k_2 + k_3 + k_4)\lambda^3 + (b_hc\psi\xi k_2 + b_hc\psi\xi k_3 +$
$b_hc\psi\xi k_4 + b_hc\psi\xi\rho_1 - \Lambda\varphi k_2 - \Lambda\varphi k_3 - \Lambda\varphi k_4 - b_hck_2 - b_hck_3 - b_hck_4 - b_hc\rho_1 + k_1k_2 +$
$k_1k_3 + k_1k_4 + k_2k_3 + k_2k_4 + k_3k_4 - \theta_2\upsilon_1)\lambda^2 + (b_hc\psi\xi k_2k_3 + b_hc\psi\xi k_2k_4 + b_hc\psi\xi k_2\rho_1 +$
$b_hc\psi\xi k_3k_4 + b_hc\psi\xi k_3\rho_1 - b_hc\psi\xi\theta_2\upsilon_1 - \Lambda\varphi k_2k_3 - \Lambda\varphi k_2k_4 - \Lambda\varphi k_3k_4 + \Lambda\varphi\theta_2\upsilon_1 -$
$b_hck_2k_3 - b_hck_2k_4 - b_hck_2\rho_1 - b_hck_3k_4 - b_hck_3\rho_1 + b_hc\theta_2\upsilon_1 + k_1k_2k_3 + k_1k_2k_4 +$
$k_1k_3k_4 - k_1\theta_2\upsilon_1 + k_2k_3k_4 - k_2\theta_2\upsilon_1)\lambda + b_hc\psi\xi\alpha_1\theta_1\upsilon_1 + b_hc\psi\xi k_2k_3k_4 + b_hc\psi\xi k_2k_3\rho_1 -$
$b_hc\psi\xi k_2\theta_2\upsilon_1 - \Lambda\varphi k_2k_3k_4 + \Lambda\varphi k_2\theta_2\upsilon_1 - \alpha_1cb_h\upsilon_1\theta_1 - b_hck_2k_3k_4 - b_hck_2k_3\rho_1 +$
$b_hck_2\theta_2\upsilon_1 + k_1k_2k_3k_4 - k_1k_2\theta_2\upsilon_1)(\lambda^2 + (b_cc\psi\xi - b_cc + \eta_0\sigma_c + \omega_0\sigma_c + \mu + k_5)\lambda] <$
$(b_cc\psi\xi\eta_0\sigma_c + b_cc\psi\xi k_5 + \eta_0\sigma_ccb_c - b_cck_5 + \eta_0k_5\sigma_c + k_5\omega_0\sigma_c + \mu k_5)$ (8)

APPENDIX IV: Jacobian Matrix of Local Stability at Endemic Equilibrum

The resulting Jacobian matrix at $E_0{}^*$ is given as:

$$J = \begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} & a_{15} & a_{16} & a_{17} & a_{18} & a_{19} & a_{110} & a_{111} & a_{112} & a_{113} & a_{114} & a_{115} \\ a_{21} & a_{22} & a_{23} & a_{24} & a_{25} & a_{26} & a_{27} & a_{28} & a_{29} & a_{210} & a_{211} & a_{212} & a_{213} & a_{214} & a_{215} \\ a_{31} & a_{32} & a_{33} & a_{34} & a_{35} & a_{36} & a_{37} & a_{38} & a_{39} & a_{310} & a_{311} & a_{312} & a_{313} & a_{314} & a_{315} \\ a_{41} & a_{42} & a_{43} & a_{44} & a_{45} & a_{46} & a_{47} & a_{48} & a_{49} & a_{410} & a_{411} & a_{412} & a_{413} & a_{414} & a_{415} \\ a_{51} & a_{52} & a_{53} & a_{54} & a_{55} & a_{56} & a_{57} & a_{58} & a_{59} & a_{510} & a_{511} & a_{512} & a_{513} & a_{514} & a_{515} \\ a_{61} & a_{62} & a_{63} & a_{64} & a_{65} & a_{66} & a_{67} & a_{68} & a_{69} & a_{610} & a_{611} & a_{612} & a_{613} & a_{614} & a_{615} \\ a_{71} & a_{72} & a_{73} & a_{74} & a_{75} & a_{76} & a_{77} & a_{78} & a_{79} & a_{710} & a_{711} & a_{712} & a_{713} & a_{714} & a_{715} \\ a_{81} & a_{82} & a_{83} & a_{84} & a_{85} & a_{86} & a_{87} & a_{88} & a_{89} & a_{810} & a_{811} & a_{812} & a_{813} & a_{814} & a_{815} \\ a_{91} & a_{92} & a_{93} & a_{94} & a_{95} & a_{96} & a_{97} & a_{98} & a_{99} & a_{910} & a_{911} & a_{912} & a_{913} & a_{914} & a_{915} \\ a_{101} & a_{102} & a_{103} & a_{104} & a_{105} & a_{106} & a_{107} & a_{108} & a_{109} & a_{1010} & a_{1011} & a_{1012} & a_{1013} & a_{1014} & a_{1015} \\ a_{111} & a_{112} & a_{113} & a_{114} & a_{115} & a_{116} & a_{117} & a_{118} & a_{119} & a_{1110} & a_{1111} & a_{1112} & a_{1113} & a_{1114} & a_{1115} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta\epsilon_2\sigma_c & 0 & \alpha_3 & a_{1212} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \eta\epsilon_2\sigma_c & 0 & \theta_5 & a_{1313} & 0 & \theta_6 \\ a_{141} & a_{142} & a_{143} & a_{144} & a_{145} & a_{146} & a_{147} & a_{148} & a_{149} & a_{1410} & a_{1411} & a_{1412} & a_{1413} & a_{1414} & a_{1415} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \rho_3 & 0 & \upsilon_3 & \eta\epsilon_2\sigma_c & a_{1515} \end{bmatrix} \quad (9)$$

Considering the upper triangular matrix of the (above matrix), we have

$$|A(C_0{}^*) - \lambda I| = \begin{bmatrix} a_{11}-\lambda & a_{12} & a_{13} & a_{14} & a_{15} & a_{16} & a_{17} & a_{18} & a_{19} & a_{110} & a_{111} & a_{112} & a_{113} & a_{114} & a_{115} \\ 0 & a_{22}-\lambda & a_{23} & a_{24} & a_{25} & a_{26} & a_{27} & a_{28} & a_{29} & a_{210} & a_{211} & a_{212} & a_{213} & a_{214} & a_{215} \\ 0 & 0 & a_{33}-\lambda & a_{34} & a_{35} & a_{36} & a_{37} & a_{38} & a_{39} & a_{310} & a_{311} & a_{312} & a_{313} & a_{314} & a_{315} \\ 0 & 0 & 0 & a_{44-\lambda} & a_{45} & a_{46} & a_{47} & a_{48} & a_{49} & a_{410} & a_{411} & a_{412} & a_{413} & a_{414} & a_{415} \\ 0 & 0 & 0 & 0 & a_{55}-\lambda & a_{56} & a_{57} & a_{58} & a_{59} & a_{510} & a_{511} & a_{512} & a_{513} & a_{514} & a_{515} \\ 0 & 0 & 0 & 0 & 0 & a_{66}-\lambda & a_{67} & a_{68} & a_{69} & a_{610} & a_{611} & a_{612} & a_{613} & a_{614} & a_{615} \\ 0 & 0 & 0 & 0 & 0 & 0 & a_{77}-\lambda & a_{78} & a_{79} & a_{710} & a_{711} & a_{712} & a_{713} & a_{714} & a_{715} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{88}-\lambda & a_{89} & a_{810} & a_{811} & a_{812} & a_{813} & a_{814} & a_{815} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{99}-\lambda & a_{910} & a_{911} & a_{912} & a_{913} & a_{914} & a_{915} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{1010}-\lambda & a_{1011} & a_{1012} & a_{1013} & a_{1014} & a_{1015} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{1111}-\lambda & a_{1112} & a_{1113} & a_{1114} & a_{1115} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{1212}-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{1313}-\lambda & 0 & \theta_6 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{1414}-\lambda & a_{1415} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & a_{1515}-\lambda \end{bmatrix} =$$

$$0 \quad (10)$$

where

$$a_{11} = -\Big(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Big)x_1 -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \mu\ ,$$

$$a_{22} = \varphi\Lambda + \frac{c(-\psi\xi+1)b_h x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - k_1\ ,$$

$$a_{33} = \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - k_2\ ,$$

$$a_{44} = \frac{\delta_3 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\delta_3 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - k_3\ ,$$

$$a_{55} = \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - k_4\ ,$$

$$a_{66} = a_{66} = \frac{c(-\psi\xi+1)b_c x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - (\omega_0+\eta_0)\sigma_c +$$

$$\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \mu\ ,$$

$$a_{77} = \frac{\tau c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\tau c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - k_5\ ,$$

$$a_{88} = \frac{\delta_1 c(-\psi\xi+1)b_c\kappa_2 x_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\gamma c(-\psi\xi+1)b_h\kappa_1 x_6}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - k_6\ ,$$

$$a_{99} = -\frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - k_7\ ,$$

$$a_{1010} = -\frac{\delta_3 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - k_8\ ,$$

$$a_{1111} = \frac{\tau c(-\psi\xi+1)b_h\kappa_1 x_7}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\tau c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - k_9\ ,$$

$$a_{1212} = -k_{10}\ ,\ a_{1313} = -k_{11}$$

$$a_{1414} = -\frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - k_{12}\ ,\ a_{1515} = -k_{13}\ ,$$

$$a_{12} = -\varphi\Lambda - \Bigg(\frac{c(-\psi\xi+1)b_h}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg)x_1\ ,$$

$$a_{13} = -\Bigg(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg)x_1\ ,$$

$$a_{14} = -\Bigg(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg)x_1\ ,$$

$$a_{15} = -\Bigg(\frac{c(-\psi\xi+1)b_h}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+\mathrm{x}_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg)x_1\ ,$$

$$a_{15} = -\Bigg(\frac{c(-\psi\xi+1)b_h}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg)x_1\ ,$$

$$a_{17} = r_1 - \Big(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{c(-\psi\xi+1)b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Big)x_1 ,$$

$$a_{18} = -\Big(\frac{c(-\psi\xi+1)b_h\kappa_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+\mathrm{x}_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Big)x_1 ,$$

$$a_{19} = -\Big(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+\mathrm{x}_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Big)x_1 ,$$

$$a_{110} = -\Big(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Big)x_1 ,$$

$$a_{111} = -\Big(\frac{c(-\psi\xi+1)b_h\kappa_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Big)x_1 ,$$

$$a_{112} = -\left(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - \right.$$

$$\left.\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_1 ,$$

$$a_{113} = -\left(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(\mathrm{x}_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - \right.$$

$$\left.\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_1 ,$$

$$a_{114} = -\left(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - \right.$$

$$\left.\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_1 ,$$

$$a_{115} = -\left(-\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - \right.$$

$$\left.\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_1 ,$$

$$a_{23} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{24} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{25} = \frac{c(-\psi\xi+1)b_h x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{25} = \frac{c(-\psi\xi+1)b_h x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2},$$

$$a_{27} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\left(\frac{\delta_1 c(-\psi\xi+1)b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -\right.$$

$$\left.\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_2\,,$$

$$a_{28} = \frac{c(-\psi\xi+1)b_h\kappa_1 x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} + \omega\varepsilon_1\sigma_c -$$

$$\left(\frac{\delta_1 c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -\right.$$

$$\left.\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_2\,,$$

$$a_{29} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{210} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{211} = \frac{c(-\psi\xi+1)b_h\kappa_1 x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\left(\frac{\delta_1 c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -\right.$$

$$\left.\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_2\,,$$

$$a_{212} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} + r_2 +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{213} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{214} = -\frac{c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{215} = -\frac{2c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{2\delta_1 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{34} = \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{35} = \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\,,$$

$$a_{36} = -\left(\frac{\delta_2 c(-\psi\xi+1)b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_3 ,$$

$$a_{37} = -\left(\frac{\delta_2 c(-\psi\xi+1)b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_3 ,$$

$$a_{38} = -\left(\frac{\delta_2 c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_3 ,$$

$$a_{39} = \omega\varepsilon_1\sigma_c + \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{310} = \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{311} = -\left(\frac{\delta_2 c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_3 ,$$

$$a_{312} = \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{313} = r_3 + \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{314} = \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{315} = \frac{\delta_2 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} ,$$

$$a_{45} = \theta_2 + \frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2},$$

$$a_{46} = -\Bigg(\frac{\delta_3 c(-\psi\xi+1) b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right)}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg) x_4,$$

$$a_{47} = -\Bigg(\frac{\delta_3 c(-\psi\xi+1) b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right)}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg) x_4,$$

$$a_{48} = -\Bigg(\frac{\delta_3 c(-\psi\xi+1) b_c \kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right)}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg) x_4$$

$$a_{49} = \frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{410} = \omega\varepsilon_1\sigma_c + \frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{411} = -\Bigg(\frac{\delta_3 c(-\psi\xi+1) b_c \kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right)}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\Bigg) x_4$$

$$a_{412} = \frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{413} = \frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{414} = r_4 + \frac{\delta_3 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{415} = \frac{\delta_3 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{56} = -\left(\frac{\delta_4 c(-\psi\xi+1)b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_5$$

$$a_{57} = -\left(\frac{\delta_4 c(-\psi\xi+1)b_c}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_5$$

$$a_{58} = -\left(\frac{\delta_4 c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_5$$

$$a_{59} = \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{510} = \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{511} = \omega\varepsilon_1\sigma_c - \left(\frac{\delta_4 c(-\psi\xi+1)b_c\kappa_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_5$$

$$a_{512} = \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{513} = \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{514} = \frac{\delta_4 c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{515} = r_5 + \frac{\delta_4 c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{67} = \frac{c(-\psi\xi+1) b_c x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\gamma c(-\psi\xi+1) b_h \left(x_2+x_5+\kappa_1(x_8+x_{11})\right) x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{68} = \frac{c(-\psi\xi+1) b_c \kappa_2 x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\left(\frac{\gamma c(-\psi\xi+1) b_h \kappa_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -\right.$$

$$\left.\frac{\gamma c(-\psi\xi+1) b_h \left(x_2+x_5+\kappa_1(x_8+x_{11})\right)}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right) x_6$$

$$a_{69} = -\frac{c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\gamma c(-\psi\xi+1) b_h \left(x_2+x_5+\kappa_1(x_8+x_{11})\right) x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{610} = -\frac{c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} +$$

$$\frac{\gamma c(-\psi\xi+1) b_h \left(x_2+x_5+\kappa_1(x_8+x_{11})\right) x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{611} = \frac{c(-\psi\xi+1) b_c \kappa_2 x_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{c(-\psi\xi+1) b_c \left(x_6+x_7+\kappa_2(x_8+x_{11})\right) x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\left(\frac{\gamma c(-\psi\xi+1)b_h\kappa_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}}-\right.$$

$$\left.\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_6$$

$$a_{612}=-\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}+$$

$$\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{613}=-\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}+$$

$$\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{614}=-\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}+$$

$$\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{615}=-\frac{c(-\psi\xi+1)b_c(x_6+x_7+\kappa_2(x_8+x_{11}))x_1}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}+$$

$$\frac{\gamma c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{78}=-\left(\frac{\tau c(-\psi\xi+1)b_h\kappa_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}}-\right.$$

$$\left.\frac{\tau c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_7$$

$$a_{79}=\frac{\tau c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{710}=\frac{\tau c(-\psi\xi+1)b_h(x_2+x_5+\kappa_1(x_8+x_{11}))x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{711} = -\left(\frac{\tau c(-\psi\xi+1)b_h\kappa_1}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}\right)x_7$$

$$a_{712} = \frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{713} = \frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{714} = \frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{715} = \frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{89} = -\frac{\delta_1 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - \frac{\gamma c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{810} = -\frac{\delta_1 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} - \frac{\gamma c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{811} = \frac{\delta_1 c(-\psi\xi+1)b_c\kappa_2 x_2}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\delta_1 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} + \frac{\gamma c(-\psi\xi+1)b_h\kappa_1 x_6}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} - \frac{\gamma c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{812} = -\frac{\delta_1 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\gamma c(-\psi\xi+1) b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{813} = -\frac{\delta_1 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\gamma c(-\psi\xi+1) b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{814} = -\frac{\delta_1 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\gamma c(-\psi\xi+1) b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{815} = -\frac{\delta_1 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_2}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} -$$

$$\frac{\gamma c(-\psi\xi+1) b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_6}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{910} = -\frac{\delta_2 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{911} = \frac{\delta_2 c(-\psi\xi+1) b_c \kappa_2 x_3}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\delta_2 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{912} = -\frac{\delta_2 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{913} = -\frac{\delta_2 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{914} = -\frac{\delta_2 c(-\psi\xi+1) b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{915} = -\frac{\delta_2 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_3}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1011} = \frac{\delta_3 c(-\psi\xi+1)b_c\kappa_2 x_4}{x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15}} -$$

$$\frac{\delta_3 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2} + \theta_4$$

$$a_{1012} = -\frac{\delta_3 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1013} = -\frac{\delta_3 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1014} = -\frac{\delta_3 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1015} = -\frac{\delta_3 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_4}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1112} = -\frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1113} = -\frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1114} = -\frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1115} = -\frac{\tau c(-\psi\xi+1)b_h\left(x_2+x_5+\kappa_1(x_8+x_{11})\right)x_7}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$

$$a_{1415} = -\frac{\delta_4 c(-\psi\xi+1)b_c\left(x_6+x_7+\kappa_2(x_8+x_{11})\right)x_5}{(x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}+x_{12}+x_{13}+x_{14}+x_{15})^2}$$