Mathematical modeling and analysis of HIV/AIDS control measures

by

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Abstract

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In this thesis, we investigate the HIV/AIDS epidemic in a population which experiences a significant flow of immigrants. We derive and analyse a mathematical model that describes the dynamics of HIV infection among the immigrant youths and intervention that can minimize or prevent the spread of the disease in the population. In particular, we are interested in the effects of public-health education and of parental care.
We consider existing models of public-health education in HIV/AIDS epidemiology, and provide some new insights on these. In this regard we focus attention on the papers [b] and [c], expanding those researches by adding sensitivity analysis and optimal control problems with their solutions.
Our main emphasis will be on the effect of parental care on HIV/AIDS epidemiology. In this regard we introduce a new model. Firstly, we analyse the model without parental care and investigate its stability and sensitivity behaviour. We conduct both qualitative and quantitative analyses. It is observed that in the absence of infected youths, disease-free equilibrium is achievable and is asymptotically stable. Further, we use optimal control methods to determine the necessary conditions for the optimality of intervention, and for disease eradication or control. Using Pontryagin's Maximum Principle to check the effects of screening control and parental care on the spread of HIV/AIDS, we observe that parental care is more effective than screening control. However, the most efficient control strategy is in fact a combination of parental care

and screening control. The results form the central theme of this thesis, and are included in the manuscript [a] which is now being reviewed for publication. Finally, numerical simulations are performed to illustrate the analytical results.

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[a] Abiodun, G.J., Marcus, N., Witbooi, P., Okosun, K.: A model for control of HIV/AIDS with parental care. (Submitted for publication).

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Declaration

I declare that *Mathematical modeling and analysis of HIV/AIDS control measures* is my work, that it has not been submitted before for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

G.J Abiodun 11 May 2012

Signed.....

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Publications

[1] KO Okosun, OD Makinde, and Gbenga Jacob Abiodun. Transmission dynamics of HIV/AIDS with optimal control in the presence of carefree susceptible and treatment. in *BIOMAT: International Symposium on Mathematical and Computational Biology*: 2011, pp 131-152, A Chapter in BIOMAT book series, World Scientific Publishing Co. Pty. Ltd, 2012.

[2] Gbenga Jacob Abiodun, N Marcus, P Witbooi, KO Okosun. A model for control of HIV/AIDS with parental care. (Submitted for publication).

Contents

List of Tables

List of Figures

Chapter 1

General Introduction

It is estimated that HIV spreads at the rate of 7,000 people per day worldwide [83]. It has killed more than 30 million people in the last 30 years [83]. Over three million children under age 15 have been infected with HIV and 600 000 are newly infected annually. The majority of these children live in sub-Saharan Africa, where between 25-40% die before their fifth birthday [83]. Apart from inducing unbearable illness that kills people prematurely, HIV devastates families and communities. The epidemic continues to increase most rapidly in Africa and Asia, where antiretroviral therapy is not sufficiently available and health care is seriously inadequate. It also spreads among the youths and teenagers which thus poses an extraordinary risk to life expectancy. The disease strikes children directly through infection, creates orphans and places a heavy burden on young shoulders when family members fall ill. The most susceptible individuals at risk of acquiring this deadly disease are people having sexual contacts with HIV infected individuals, homosexual and bisexual men, intravenous drug abusers and persons transfused with contaminated blood [65].

1.1 HIV/AIDS biological background

Human Immunodeficiency Virus (HIV), the virus that causes the acquired immune deficiency syndrome (AIDS), transferred to human in Africa probably between 1884 and 1924 [39]. Human infection entered Haiti around 1966, and the United States around 1970 [81]. AIDS was first recognized among homosexual men in the United States in 1981 [36]. In that year through 1987, the

average life expectancy for people diagnosed with AIDS was 18 months while more than 38,000 cases of the diseases were reported from 85 countries [81].

The origin of AIDS was recently traced to West Africa. It was linked to the consumption of monkey meat in Cameroon or sexual activity with monkeys, but these theories have been proved wrong amongst Africans because this is not a normal practice in African countries. The current theories revolve around the idea that colonial horrors of mid-20th-century Africa allowed the virus to jump from chimpanzees to humans and become established in human populations around 1930. Hence, it is highly probable that this is where the disease originated since early cases of it have been traced back to colonial Africa in the rubber plantations [36].

HIV, which was initially called pneumocystis carinii pneumonia (PCP) [36] cannot grow or reproduce on its own but rather infect the cells of a living organism to make new copies. A virus is mainly known through its ability to infect target cells (infectivity) and by its antigenic signature (antigenicity), defined as both the capacity to induce an immune response and also its strength and type. Immunogenicity is the ability of antigens to elicit a response from cells of the immune system. Mutations during virus replication may therefore release infective or non-infective viruses, of the same or of different antigenicity. There are two major types of HIV: HIV-1 and HIV-2. Both types are transmitted by sexual contact, through blood, and from mother to child, and they both lead to AIDS. HIV-2 type is concentrated in West Africa and is rarely found elsewhere while HIV-1 is worldwide the predominant virus and people generally refer to it as HIV. For HIV-1, the ratio of infectious to non-infectious particles is estimated to range from 1:1 to 1:60 000, depending on the type of cell infected and the viral strain. Whether the virus is infective or not, over 800 mutations affecting HIV-1 antigenicity were identified in it's envelop gene alone. By encoding its own replication enzymes, the virus has control over its replication fidelity and thereby challenges heavily the immune system, due to the huge burden imposed by the number of infective virions produced and their antigenic diversity. This burden is even worse when the virus targets part of the immune system, as is the case for HIV-1. In addition, the immune cell proliferation induced by the viral attack will provide HIV-1 virions with new targets, engaging the cell-virus dynamics in an exponentially soaring extension regime. It continuously attacks the T-cells in the human immune system until the system can no longer fight off any other infections. HIV-1 is related to viruses found in chimpanzees and gorillas living in west-

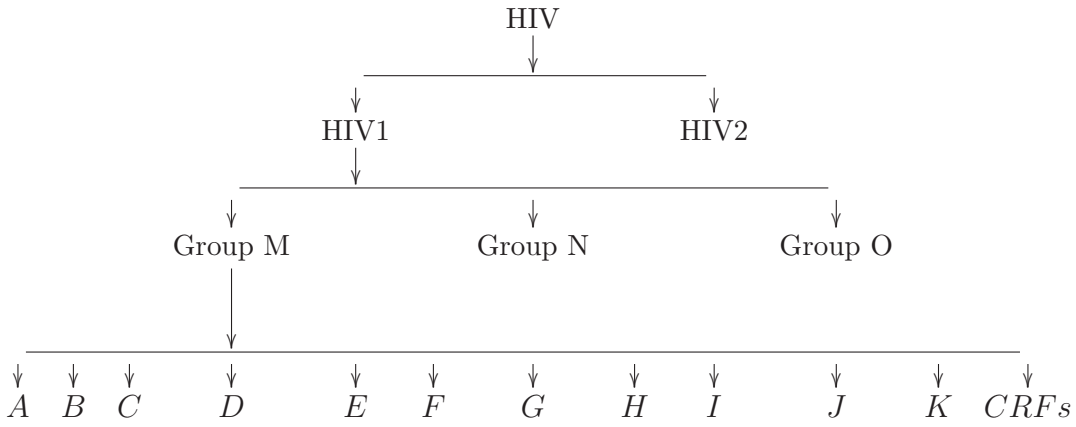


Figure 1.1: Classification of HIV into Various Groups

ern Africa. Its strains can be classified into four groups: group M (the major group), group O (the outliers group) and two new groups, N and P. The M group is subdivided further into subtypes A, B, C, D, F, G, H, J, K, and CRFs (circulating recombinant forms).

- Subtype A is common in West Africa [36].
- Subtype B is the dominant form in Europe, America, Japan, Thailand, and Australia [36].
- Subtype C is the dominant form in Southern Africa, India, and Nepal [36].
- Subtype D is generally only seen in Eastern and Central Africa [36].
- Subtype E has never been identified as a non recombinant, only recombined with subtype A [36].
- Subtype F has been found in Central Africa, South America and Eastern Europe [36].
- Subtype G have been found in Africa and Central Europe [36].
- Subtype H is limited to Central Africa [36].
- Subtype J is primarily found in North, Central and West Africa, and the Caribbean [33].

- Subtype K is limited to the Democratic Republic of Congo and Cameroon [53].

Symptoms and prevention of HIV/AIDS

HIV infection or AIDS cannot easily be diagnosed based on symptoms alone. Its symptoms are very similar to the symptoms of other illnesses. Once the immune system is sufficiently weakened by HIV, such infections will develop and produce any of a wide range of symptoms. So the only way to be sure if a person is infected or not is through HIV test.
HIV can be transmitted in three main ways:

- Mother-to-child transmission (MTCT): This is when an HIV-infected woman passes the virus to her baby during pregnancy, labour and delivery, or breastfeeding. Nine out of ten children infected with HIV were infected through their mother either during pregnancy, labour and delivery or breastfeeding [85]. MTCT is relatively rare in well developed and high-income countries with preventive measures. This shows that with funding, trained staff and resources, the infections and deaths of many thousands of children could be avoided. MTCT can also be prevented by:

  - Preventing HIV infection among prospective parents.
  - Avoiding unwanted pregnancies among HIV positive women.
  - Integration of HIV care, treatment and support for women found to be positive and their families.

- Transmission through blood: This involves passing of unscreened blood from a donor to the recipient. This can occur in medical settings especially in the less privileged countries where the use of contaminated injections and unscreened blood transfusion are common practices. Between 1987 to 1991 in Romania, record has it that over 10,000 babies and children were infected with HIV as a result of unsafe medical practices [45]. The following preventions can be followed:

  - A nationally coordinated blood transfusion service.
  - Voluntary unpaid donors.

  - All donated blood must be tested.
  - Using of blood efficiently and appropriately.
  - Ensuring of a safe transfusion practice.
  - Having a quality systems check throughout the blood transfusion process.

- Sexual transmission: It is not having sex, but rather having unprotected sex, which places young people at serious risk of HIV infection. Sexual transmission does not account for a high proportion of child infections but in some countries children are sexually active at an early age. This is potentially conducive to the sexual spread of HIV among children, especially in areas where condom use is low and HIV prevalence is high. In sub-Saharan Africa 16 percent of young females (aged 15-19) and 12 percent of young males reported having sex before they were 15 in 2007 [38, 39]. In Lesotho, these figures are 16 percent and 30 percent, respectively; in Kenya, 15 percent and 31 percent [40]. Someone can eliminate or reduce their risk of becoming infected with HIV during sex by choosing to:
  - Abstain from sex or delay first sex.
  - Be faithful to one partner or have fewer partners.
  - Condomise, which means using male condoms or female condoms consistently and correctly.

Children, HIV and AIDS

Over 1,000 children are newly infected with HIV every day, and of these more than half will die as a result of AIDS because of a lack of access to HIV treatment [89]. At the end of 2010, there were 3.4 million children living with HIV around the world [89]. In addition to this, millions more children every year are indirectly affected by the epidemic as a result of the death and suffering caused in their families and communities. Record also has it that over 390,000 children became newly infected with HIV in 2010 [84]. It is also in record that 1.8 million people who died of AIDS during 2010, one in seven were children. Every hour, around 30 children die as a result of AIDS [89]. Most children living with HIV/AIDS are from sub-Saharan Africa where AIDS is known to have its greatest toll

in the world [89].

Children affected by HIV/AIDS
Children orphaned by AIDS are at greater risk of abuse, exploitation, discrimination, developmental problems and illness than those orphaned by other causes. Other children are also affected: increasing numbers are living with sick family members, or in households that are struggling because they have taken in orphans. Here are some of the ways HIV/AIDS affects children either on their parent or on themselves:

Physical and sexual abuse : Children without parental or family protection are more vulnerable to physical and sexual abuse, which increases their risk to HIV infection. Absence of parental protection and care, combined with HIV infection, contributes significantly to the increase in deaths of young children in the countries most affected by HIV/AIDS.

Poor nutrition: Families struck by HIV/AIDS may have less money available for nutritious food. Poor childhood nutrition results in developmental problems and poor school performance.

Taking on adult responsibilities: As parents and other family members fall ill, children increasingly take over care of the sick, care of younger siblings, household chores and income generation. The eldest child may take on the role of head of the household.

Child labour: Children may have to work excessively to supplement the household income, reduced when ill adults cannot work and savings are spent on medical treatment. Children who cannot find work may be forced into early marriage, prostitution, and crime or begging on the streets.

Psychological stress: Children who watch their parents suffer and die, undergo severe emotional distress. The psychological impact of witnessing a parent dying of AIDS can be greater than for children whose parents die from more sudden causes. With AIDS, there may be long periods of stress, suffering and uncertainty before the parent dies. In poor communities, effective pain or symptom relief to ease the parent's suffering is often unavailable. Worries about future survival can add to a child's already high stress levels. Ongoing emotional distress can lead to problems such as depression and aggressive behaviour.

Loss of parenting: Growing up under stress without adequate parental guidance and support, and poorly supervised by relatives and welfare organizations, children orphaned by AIDS are at higher risk of developing

antisocial behaviour (such as criminal activity and drug abuse) and failing to become productive members of society.

Societal discrimination and stigma: People in the community may discriminate against children who have HIV, who have family members with HIV, or who have been orphaned by HIV/AIDS. This puts them at higher risk of abuse and social exclusion, and they may be denied basic needs such as education and housing. Orphans taken in by a new family may be expected to work harder than the other children, and may be the last to receive benefits such as having their school fees paid. In some communities, families will not take in orphans, because of the stigma of caring for non-related children, particularly those associated with AIDS. The stigma still often attached to HIV/AIDS makes it harder for children to deal with the illness and death of their parents.

Growing up in impoverished conditions: HIV/AIDS has put great pressure on the traditional extended family system; the ability of poor communities to support children orphaned by AIDS is increasingly strained, particularly in countries lacking adequate social welfare services. With the increase of mortality among adults, the burden of caring for children is often taken up by grandparents, who may find it hard to cope physically and economically. The result is that many children orphaned by AIDS grow up in impoverished conditions. Some will become homeless and be forced to live on the streets.

Negative impact on education: Children, especially girls, may drop out of school to care for ill parents, work, or tend the household. Orphans may leave school because of discrimination or emotional distress, or because they cannot afford school fees. Early school-leavers have an increased risk of HIV infection in that they are less likely to gain the skills needed to avoid unsafe sex, and will become economically vulnerable and open to sexual exploitation. School performance is affected by the psychological and physical stress of living with HIV/AIDS. Education is also negatively impacted by teachers lost to the disease: AIDS-related deaths among South African teachers rose by over 40% in 2000 and 2001.

Loss of inheritance: Sometimes parents die without making financial provisions for their children, or with unsettled financial debts. In some cases, wills are disregarded by relatives or customary law, with resulting loss of inheritance for the children. Sometimes children lose the house they were living in.

1.2 Research aims and objectives

The main goal of this study is to investigate the impact of parental care on HIV/AIDS among youths. We introduce a new model and determine the optimal strategies for rolling out the intervention using Pontryagin's Maximum Principle. Both analytical and numerical studies of the model will be conducted to obtain necessary information that could be useful towards reducing the spread of HIV/AIDS.
We also intend to expand some studies on public-health [73] and carefree susceptibles [75] by adding sensitivities analysis and optimal control problems with their solutions.

1.3 Layout of the thesis

The thesis is organized as follows: In Chapter 1, we described the biological background of HIV/AIDS, as well as research aims and objectives. Chapter 2 is devoted to a literature review on mathematical modelling of HIV/AIDS and applications of optimal control methods in epidemiological models. Chapter 3 presents the preliminary background of epidemiological modelling as well as a background on ordinary differential equations and optimal control theory. In Chapter 4, we analyze a model with presence of carefree susceptibles with treatment. In addition to paper [75], we perform the sensitivity analysis of the model parameters. In Chapter 5, we analyze an HIV/AIDS model with public-health campaigns and infective withdrawal. Also in addition to paper [73], we perform the sensitivity analysis of the model parameters. In Chapter 6, we develop and examine a new HIV/AIDS model without parental care. The existence and endemic equilibria is also presented. In Chapter 7, we further our studies on parental care. We apply optimal control methods to determine the most effective control of HIV/AIDS among youths between screening control method and parental care. Numerical results and discussions is offered. In Chapter 8, we continue our analysis and additions on paper [73]. We discuss the optimal control analysis of public-health campaigns and infective withdrawal. Numerical results and discussion is thus presented. Chapter 9 gives a concluding summary of the whole study.

Chapter 2

Literature Review

Mathematical models of transmission dynamics of HIV play a significant role to improve our understanding on epidemiological patterns for diseases control. There is no established vaccine yet for HIV/AIDS and it is not likely that any highly effective one will soon be available despite all the vigorous studies on vaccination and treatment of the disease [71]. However, mathematical models have been comprehensively used as a means of informing control strategies, or at least their impact, since they provide short and long term prediction of HIV and AIDS incidence. From the initial models of May and Anderson [5, 6, 61] several modifications of the modelling structure have been presented. Some of these issues have also been addressed by Arazoza, Lounes [8] and Moghadas and Gumel [64]. In particular, Anderson et al. [62] presented a simple HIV transmission model to help clarify the effects of various factors on the overall pattern of AIDS epidemic while Hyman et al. [46] assessed the impact of variations in infectiousness considering some different levels of virus between individuals during the chronic phase of infection. In the year 2004, Greenhalgh [28] assessed the impact of condom use on the sexual transmission of HIV and AIDS amongst a homogeneously mixing male homosexual population. In the same year Piqueira et al. [76] presented a model for HIV transmission in homosexual populations by taking into account different attitudes, blood screening and effects of social networks. Hsieh and Chen [41] structured a model for a community of two classes of commercial sex workers and two classes of sexually active male customers with different levels of sexual activity. Naresh and Tripathi [70] analysed the spread of HIV infection in a population in the presence of tuberculosis in 2006. A year later, Naresh et al. [3] worked on modelling the

effect of screening of unaware infectives on the spread of HIV infection, continuing on studies by Del Valle et al. [19] on the effects of education in a set-up with vaccination and treatment on HIV transmission in homosexuals with heterogeneity. Del Valle [19], in his studies, followed the concepts of Blower and Maclean [63] that partly effective vaccines should be accompanied by educational campaigns. HIV/AIDS models with a delay due to the incubation period of the disease have been studied in [16] of Cai et al. and other papers. An investigation on the potential effects and benefits of educational campaigns on HIV/AIDS transmission dynamics in a sexually active population with no other intervention, is undertaken in [65]. Mukandavire et al. [66] also investigate the potential effects and benefits of educational campaigns on HIV/AIDS transmission dynamics in a sexually active population where no other intervention is available in [65]. Another study was done by Nyabadza et al. [73] on HIV/AIDS model with public-health information campaigns and individual withdrawal (i.e abstinence). In this paper, they investigated the reduction in infection by checking the sexual behaviour change through public-health information campaigns and withdrawal of individuals with AIDS from sexual activity. Their results showed that an increase in effective public-health information campaigns, and individual AIDS who withdraw from sexual activities, reduces the spread of HIV/AIDS. In addition to [73], this thesis will also consider the sensitivity analysis of the parameters used and also establish optimal strategies for the control of the disease, in order to check the most effective control between public-health information campaigns and withdrawal of individuals with AIDS from sexual activity.

Williams and Anderson [92] studied a mathematical model of the transmission dynamics of the HIV-1 in England and Wales. The model studies the transmission within and between different sexual activity classes; the needle sharing classes in the case of intravenous drug users and within and between different risk groups such as male homosexuals, intravenous drug users and heterosexuals. The parameters that the above authors used were based on published data. They also noticed the importance of mixing patterns to future trends and concluded that future trends are uncertain within the heterosexual population. Blower and Porco [12] developed and used mathematical models to evaluate vaccine programs for controlling two subtypes of HIV, both for developing countries where more than one subtype is present and for other countries where only one subtype is present but other subtypes may invade. They formulated a model of the basic transmission dynamics of the two HIV subtypes

and then extended this model to also check the effects of a prophylactic vaccine that provides a degree of protection against infection by one subtype and vaccine-induced cross-immunity against infection by the second subtype. Using these models, they assessed the likely impact of using a prophylactic vaccine when one subtype of HIV is endemic and a second subtype is introduced into the community. Hsieh and Wang [43] calculated the basic reproduction number for an HIV epidemic model incorporating direct and indirect commercial sex, as well as behaviour change by the female commercial sex workers (CSWs) and their male customers in response to the propagation of the disease in the community.

However, the authors are not aware of mathematical models in the literature, which includes the effect of parental care, its optimal control and cost effectiveness. This thesis is an attempt towards filling this gap.

Ever since the development of optimal control theory, see Pontryagin et al. [77], it has been successfully used in decision making in various applications. A very handy reference on application of optimal control theory to epidemiology is the book of Lenhart and Workman [55]. There are numerous studies on epidemiological models where optimal control methods were applied. For instance, Wickwire [90] applied optimal control to a mathematical model on pest and infectious diseases control. Okosun and Makinde [58] studied the impact of chemo-theraphy on the malaria disease using optimal control. The paper [75] by Okosun, Makinde and Abiodun, on transmission dynamics of HIV/AIDS with optimal control in the presence of carefree susceptibles and treatment, investigates the effectiveness of HIV/AIDS preventive and treatment measures. It considers a mathematical model for the transmission dynamics of the disease that includes treatment of HIV individuals, treatment of AIDS, and enlightenment campaign and recruitment rate of carefree susceptibles in reducing the spread of HIV/AIDS. It also derives the necessary conditions for the optimal control of the disease. This thesis also contain an extension of [75] by carrying out the sensitivity analysis of the reproductive number (R_0). Regarding HIV itself, much work has already been done on optimal management strategies. The optimal control approaches on drug therapy in HIV treatment was studied by Joshi [50] and Adams et al. [2], this theme or variations of it has enjoyed further attention in the work [32] of Garira et al., in [51] of Karrakchou et al. and in [10] by Banks et al. In respect to this, application of optimal control theory to

epidemiology is an important tool to test the efficacy of various policies and control.
Okosun et al. [94] analyzed an optimal control method with SIS epidemic model to investigate the impact of infected immigrant in an avail influenza transmission dynamics. Adams et al. [2] analyzed the optimal control approaches on dynamics of multidrug therapy for HIV. Zaman et al. [95] studied a general SIR epidemic model, applied stability analysis to the equilibrium solutions and the used optimal control to determine the optimal vaccination strategies to reduce the impact of the disease. Xiefei et al. [93] used optimal control methods to study the outbreak of SARS using Pontryagin's Maximum Principle and genetic algorithm. Wickwire [90] applied optimal control to mathematical model on pest and infectious diseases control. Wiemer [91] studied Schistosomiasis using optimal control methods. In our thesis the control variables are more of a social nature, and therefore it is completely different from the aforementioned theme.
It has been pointed out that parental care has substantial effect on the spread of AIDS among the youths. Parental care means bringing up a child in a decent manner, providing for their moral, material, financial needs and giving them quality education. Parental care also involves providing children with sex education and introducing them to some health educational campaign where they can learn about transmission of different diseases and how they can be protected. Research clearly shows that a child who lacks adequate parental instruction stands at risk of recalcitrance [22]. The same study also reveals that out of 94,000 cases of child delinquent behaviour, about 80% stems from children in a household with poor parental care and counselling. In general, a child without adequate and sustained parental care, instruction or counselling is insecure and confused. Such children may slowly or rapidly grow into drug addiction, prostitution, vandalism and violent crime, as well as other social vices.

In this study, our objective is to show how parental care could reduce the spread of HIV/AIDS among the youths. We propose and analyze a nonlinear mathematical model to study the effect of parental care among the youth with a variable size structure on epidemiological considerations. We also determine the optimal levels of intensity of parental care for the disease control using Pontryagin's Maximum Principle. Both the analytical and numerical studies of the model are conducted to obtain necessary information that could be useful towards reducing the spread of the disease.

Chapter 3

Preliminary Background

In this chapter we discuss some useful mathematical background material, used throughout our study. We define concepts such as existence and uniqueness of a solution, Routh-Hurwitz criteria, Hartman-Grobman theorem, Lyapunov functions, etc., and give some basic results. Our main references on such basics are Okosun [74], Birkhoff [11], Guanrong [29], Lenhart [55, 56], Emanuel [24].

3.1 Well-posedness for ordinary differential equations

As stated in [11], the differential equation

$$\frac{d\mathbf{x}}{dt} = \mathbf{X}(\mathbf{x}, t), \tag{3.1}$$

is said to be well-posed if its solution solution exists, unique, and continously depends on its initial values. The following theorems show that if $\mathbf{X}$ satisfies the Lipschitz condition (3.1), then the differential equation (3.1) defines a well-posed initial value problem.

Definition 3.1.1 ([11], **Lipschitz condition**).
A family of vector fields $\mathbf{X}(\mathbf{x}, t)$ satisfies a *Lipschitz condition* in a region $\Re$ of $(\mathbf{x}, t)$ - space if and only if, for some so-called *Lipschitz constant* L,

$$|\mathbf{X}(\mathbf{x}, t) - \mathbf{X}(\mathbf{y}, t)| \leq L|\mathbf{x} - \mathbf{y}| \text{ if } (\mathbf{x}, t) \text{ and } (\mathbf{y}, t) \in \Re. \tag{3.2}$$

Theorem 3.1.2 ([11], **Uniqueness Theorem**).
If the vector fields $\mathbf{X}(\mathbf{x}, t)$ *satisfy a Lipschitz condition (3.1) in a domain* $\Re$, *there is at most one solution* $\mathbf{x}(t)$ *of the vector differential equation (3.1) that satisfies a given initial condition* $\mathbf{x}(t) = \mathbf{c}$ *in* $\Re$.

Theorem 3.1.3 ([11], **Continuity Theorem 1**).
Let $\mathbf{x}(t)$ *and* $\mathbf{y}(t)$ *be any two solutions of the vector differential equation (3.1), where* $\mathbf{X}(\mathbf{x}, t)$ *is continuous and satisfies the Lipschitz condition (3.1). Then*

$$|\mathbf{x}(a+h) - \mathbf{y}(a+h)| \leq e^{L|h|}|\mathbf{x}(a) - \mathbf{y}(a)| \tag{3.3}$$

Theorem 3.1.4 ([11], **Continuity Theorem 2**).
Let $\mathbf{x}(t)$ *and* $\mathbf{y}(t)$ *satisfy the differential equations*

$$\frac{dx}{dt} = \mathbf{X}(\mathbf{x}, t), \tag{3.4}$$

$$\frac{dy}{dt} = \mathbf{Y}(\mathbf{y}, t),$$

respectively, on $a \leq t \leq b$. *Further, let the functions* $\mathbf{X}$ *and* $\mathbf{Y}$ *be defined and continuous in a common domain* D, *and let*

$$|\mathbf{X}(\mathbf{z}, t) - \mathbf{Y}(\mathbf{z}, t)| \leq \epsilon, \;\; a \leq t \leq b, \;\; \mathbf{z} \in D. \tag{3.5}$$

Finally, let $\mathbf{X}(\mathbf{x}, t)$ *satisfy the Lipschitz condition (3.1). Then*

$$|(\mathbf{x}(t)) - (\mathbf{y}(t))| \leq \mathbf{x}(a) - \mathbf{y}(a)|e^{L|t-a|} + \frac{\epsilon}{L}(e^{L|t-a|} - 1). \tag{3.6}$$

3.2 Stability for ordinary differential equations

In this section, we present results which will be used to prove the local stability for systems of ordinary differential equations. Hence the following definitions and theorems will be used to determine the local stability of the disease free equilibrium of a system of ordinary differential equations.

Definition 3.2.1 ([74], **The basic reproductive number**).
The basic reproductive number is used to measure the ability of the disease to reproduce, and is denoted by R_0. This is defined as the expected number of secondary cases reproduced by one infected individual in his/her entire infectious period. When $R_0 < 1$, each infected individual can produce an average of less than one new infected individual during his entire period of infectiousness. In this case the disease will not persist in the population and may be eradicated. But in a situation where $R_0 > 1$ implies that each infected individuals during the entire period of infectiousness can produce more than one new infected individual. This is a strong indication that the disease can persist and invade the population.

Definition 3.2.2 ([74], **The next generation method**).
The so-called next generation method introduced by van den Driessche et al. [88] and Diekmann et al. [20] is a general method for deriving R_0 in cases where one or more classes of infectives are involved. Suppose we have n disease compartments and m non-disease compartments, and let $x \in \mathbb{R}^n$ and $y \in \mathbb{R}^m$ be the sizes of these compartments. Also, denote the rate of secondary infection increase of the i^{th} disease compartments by F_i. However V_i is the rate of disease progression, death and recovery decrease the i^{th} compartment, the compartmental model can then be written in the form:

$$\begin{aligned} \frac{dx_i}{dt} &= F_i(x,y) - V_i(x,y), \quad i = 1, ..., n, \\ \frac{dy_i}{dt} &= g_j(x,y), \quad j = 1, ..., m. \end{aligned} \tag{3.7}$$

The calculation of the basic reproduction number is based on the linearization of the ordinary differential equations (ODE) model about a disease-free equilibrium, while the following assumptions ensure the existence and well-posedness of a model.

1. Assume $F_i(0,y) = 0$ and $V_i(0,y) = 0$ for all $y \geq 0$ and $i = 1, ..., n$. All new infections are secondary arising from infected hosts.

2. $F_i(0,y) \geq 0$ for all non-negative x and y and $i = 1, ..., n$. Then function F represent new infections and cannot be negative.

3. $V_i(0, y) \leq 0$ whenever $x_i = 0, i = 1, ..., n$. Each component, V_i represents a net outflow from compartment i and must be negative (inflow only) whenever the compartment is non- empty.

4. Assume $\sum_{i=1}^{n} V_i(x, y) \geq 0$ for all non-negative x and y. The sum represents the total outflow from all infected compartments. Terms in the model leading to increases in $\sum_{i=1}^{n} x_i$ are assumed to represent secondary infections and therefore belong in F.

5. Assume the disease-free system $\frac{dy}{dt} = g(0, y)$ has a unique equilibrium that is asymptotically stable. That is, all solutions with initial conditions of the form $(0, y)$ approach a point $(0, y_0)$ as $t \to \infty$. This point is referred to as the disease-free equilibrium.

Assuming that F_i and V_i meet above conditions, we can form the next generation matrix (operator) FV^{-1} from matrices of partial derivatives of F_i and V_i particularly

$$F = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right] \quad \text{and} \quad V = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right] \tag{3.8}$$

where $i, j = 1, ..., m$ and where x_0 is the disease-free equilibrium. The R_0 is given by the spectral radius (dominant eigenvalue) of the matrix FV^{-1}.

3.2.1 Routh-Hurwitz criteria

The Routh-Hurwitz stability criterion is a necessary and sufficient condition to establish the stability of a single-input, single-output (SISO), linear time invariant (LTI) control system. The criterion establishes a systematic way to show that the linearized equations of motion of a system have only stable solutions. Consider the characteristic equation

$$\Omega^n + a_1\Omega^{n-1} + a_2\Omega^{n-2} + ... + a_{n-1}\Omega + a_n = 0, \tag{3.9}$$

determining the n eigenvalues Ω of a real $n \times n$ square matrix A. Then the eigenvalues Ω all have negative real parts if

$$H_1 > 0, H_2 > 0, H_3 > 0, ...H_n > 0,$$

where H_n are the following determinants:

$$H_1 = |a_1|,$$

$$H_2 = \begin{vmatrix} a_1 & 1 \\ a_3 & a_2 \end{vmatrix},$$

$$H_2 = \begin{vmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{vmatrix},$$

$$H_n = \begin{vmatrix} a_1 & 1 & \dots & 0 \\ a_3 & a_2 & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ a_{2n-1} & a_{2n-2} & \dots & a_n \end{vmatrix}.$$

The steady state is stable (that is, $\mathrm{Re}(\Omega) < 0$) for all λ if and only if $H_j \geq 0$ for all $j = 1, 2, 3, ..., n$.
The criterion can be performed using either polynomial divisions or determinant calculus.

3.2.2 Hartman-Grobman Theorem

Definition 3.2.3 ([11], **Hyperbolic Fixed Point**).
A hyperbolic fixed point for a system of differential equation is a point at which the eigenvalues of the Jacobian for the system evaluated at that point all have nonzero real parts.

Theorem 3.2.4 ([74], **Hartman-Grobman Theorem**).
Let $f : \mathbb{R}^n \to \mathbb{R}^n$ be a smooth map with a hyperbolic fixed point p. Let A denote the linearization of f at point p. Then there exists a neighbourhood U of p and a homeomorphism

$$h : U \to \mathbb{R}^n$$

such that

$$f_U = h^{-1} \circ A \circ h$$

that is, in the neighbourhood U of p, f is topologically conjugate to its linearization.

The theorem explains the local behaviour of dynamical systems in the neighbourhood of a hyperbolic equilibrium point.

3.2.3 Lyapunov functions and stability

In this Section, we (ab)use the "dot" notation. The reason for this is that this abuse is so widespread that it is better to adopt it.
Suppose we are given an ODE

$$\dot{u} = f(u) \tag{3.10}$$

and differentiable function

$$V : N \to \mathbb{R}, \quad x \mapsto V(x) \tag{3.11}$$

where $N \subseteq \mathbb{R}^n$. Denoting by $t \mapsto u(t)$ a solution of (3.11) and using the chain rule we obtain

$$\frac{d}{dt}V(u(t)) = \sum_{k=1}^{n} \partial_k V(u(t)) \frac{du_k(t)}{dt} = \nabla V(u(t)).f(u(t)), \tag{3.12}$$

where

$$\partial_k V(x) := \frac{\partial V(x_1, ..., x_n)}{\partial x_k} \tag{3.13}$$

$$\nabla V(x) := (\partial_1 V(x), ..., \partial_n V(x))^T \tag{3.14}$$

for $x = (x_1, ..., x_n)^T \in \mathbb{R}^n$.

Due to the above calculation, the following notation is often used

$$\dot{V}(x) = \nabla V(x).f(x), \tag{3.15}$$

despite V not being a function of time and the "dotted" V not being exactly a time derivative. This notation comes for the fact that we are "dotting" the composite of V with u, $V(u(t))$, with respect to time and the rigorous notation should be $V(u))$ or $V \circ u$. Since this is a bit more cumbersome, we stick to "dot" notation $\dot{V}$.
Hence the following technical results, summarises the idea behind Lyapunov functions.

Lemma 3.2.5 ([29], **Lyapunov barrier**).
Let $V : N \to \mathbb{R}$, be continuously differentiable, where $N \subseteq \mathbb{R}^m$, is a non-empty open and bounded set, with $\dot{V}(x) \leq 0$ for all $x \in N$,, and let $m = \min_{x \in \delta N} V(x)$. Then, for any $u_0 \in N$ such that $V(u_0) < m$, the set $C(u_0) = \{u \in N : V(u) \leq V(u_0)\}$ has the property that $\Gamma^+(u_0) \subseteq C \subseteq N$.

Proof. Choose $u_0 \in N$ such that $V(u_0) < m$. Since $u(t)$ is continuous, be either $u_0 \in N$ for all $t \geq 0$ or there exist $t_1 > 0$ such that $u_0 \in N$ for $0 \leq t < t_1$ and $u(t_1) \in \partial N$. However in the latter case, as $\dot{V} \leq 0$ for all $u \in N$,

$$V(u(t_1)) = V(u_0) + \int_0^{t_1} \dot{V}(u(t))dt \leq V(u_0) < m, \tag{3.16}$$

which contradicts $u(t_1) \in \partial N$, since $m = \min_{u \in \partial N} V(u)$. Therefore $u(t) \in C$ for all $t \geq 0$, i.e., $\Gamma^+(u_0) \subseteq C(u_0)$.

Definition 3.2.6 ([29], **(Sign) definite functions**).
A function $F : N \to \mathbb{R}$ is *positive definite* at $u^* \in \mathrm{N}$ *if*
(i) $\mathrm{F}(\mathrm{u}^*) = 0$
(ii) $F(u) > 0$ for all $u \in N$ with $u \neq u^*$
F is *negative definite* if $-F$ is positive definite.

Definition 3.2.7 ([29], **Lyapunov functions**).
A continuous differentiable function $V : N \to \mathbb{R}$, where $N \subseteq \mathbb{R}^m$, is a *Lyapunov function* for $\dot{u} = f(u)$ at $u^* \in N$ if
(i) $V(u)$ is positive definite at u^*, and
(ii) $\dot{V}(u) \leq 0$ for all $u \in N$.
If in addition, $\dot{V}(u)$ is negative definite at u^*, then V is a *strict Lyapunov function*.

Theorem 3.2.8 ([29], **Lyapunov's first stability theorem (Lyapunov stability condition)**).
Suppose that u^* is a fixed point of $\dot{u} = f(x)$. Suppose that for some open set $N \subseteq \mathbb{R}^m$, containing u^* there exists $V : N \to \mathbb{R}$, such that V is Lyapunov at u^*. Then u^* is Lyapunov-stable.

Proof. Let $B(u^*, \epsilon)$ be the (closed) ball of radius ϵ centered at u^*,

$$B(u^*, \epsilon) := \{u : \|u - u^*\| \leq \epsilon\},$$

and choose $\epsilon > 0$ sufficiently small that $B(u^*, \epsilon) \subseteq N$. To prove Lyapunov stability we need to find $\delta > 0$ such that if $u_0 \in B(u^*, \delta)$ then $\Gamma^+(u_0) \subset B(u^*, \epsilon)$.
Note that as V is a Lyapunov function at u^* defined on N and $B(u^*, \epsilon) \subseteq N$ it follows that V is a Lyapunov function at u^* defined on $B(u^*, \epsilon)$. Let

$$m = \min_{u \in \partial B(u^*, \epsilon)} V(u),$$

where $\partial B(u^*, \epsilon)$ is the boundary of $B(u^*, \epsilon)$. Since a continuous function on a compact (closed and bounded) set achieves its infimum, there exists $y \in \partial B(u^*, \epsilon)$ such that $V(y) = m$. Moreover, since $V(u) > 0$ throughout $B(u^*, \epsilon) | \{u^*\}$, it follows that $m > 0$.
As V is continuous and $V(u^*) = 0$ there exists $\delta > 0$ such that $V(u) < m$ for all $u \in B(u^*, \delta)$.
Applying Lyapunov Barrier Lemma above to the set $N := B(u^*, \epsilon)$ and any point $u_0 \in B(u^*, \delta)$. It gives $\Gamma^+(u_0) \subseteq B(u^*, \epsilon)$ as required. □

Theorem 3.2.9 ([29], **Lyapunov's second stability theorem (Lyapunov asymptotic stability condition)**).
Suppose there exist a Lyapunov function and let u^* be a fixed point of $\dot{u} = f(u)$ and suppose that for some open set $N \subset \mathbb{R}^m$, containing u^*, there exists $V : N \to \mathbb{R}$, such that V is strict Lyapunov at u^*. Then u^* is asymptotically stable.

Proof. Since a strict Lyapunov function is a Lyapunov function, Lyapunov's first stability theorem implies that u^* is Lyapunov-stable and it remains only to prove quasi-asymptotic stability (q.a.s.).
Define ϵ and δ as in the proof of Lyapunov's first stability theorem. Thus if $u_0 \in B(u^*, \delta)$ then $\Gamma^+(u_0) \subseteq B(u^*, \epsilon)$. Pick any such $u_0 \in B(u^*, \delta)$.
Since $\dot{V}(u(t)) \leq 0$ it follows that $V(u(t))$ is non-increasing in t and as V is bounded below by 0 it follows that $\lim_{t\to\infty} V(u(t)) = c \geq 0$ exists. We shall show that $c = 0$.
As $\Gamma^+(u_0)$ is bounded, $\omega(u_0)$ is non-empty. Consider any $x \in \omega(u_0)$. Then since there exist $t_k \to \infty$ such that $S(t_k)u_0 \to x$ as $k \to \infty$, by continuity of V,

$$V(x) = \lim_{k\to\infty} V(S(t_k)u_0) = c.$$

But since $\omega(u_0)$ is forward invariant, if $x \in \omega(u_0)$ then $S(t)x \in \omega(u_0)$ for all $t \geq 0$, and so

$$V(S(t)x) = c \quad \forall t \geq 0.$$

Thus $\dot{V}(x) = 0$ for all $x \in \omega(u_0)$. But $\dot{V}(u) \neq 0$ for $u \neq u^*$, and thus $x = u^*$. So $\omega(u_0) = \{u^*\}$. As V is positive-definite at $u^*, V(u^*) = 0$, i.e. $c = 0$. Therefore $u(t) \to u^*$ as $t \to \infty$, showing that u^* is q.a.s. □

3.3 Compartmental Modelling

In order to model the progress of an epidemic in a large population, comprising many different individuals in various fields, we must reduce or subdivide the population diversity to a few key characteristics which are relevant to the infection under consideration. These subdivisions of the population are called compartments. The classes usually under consideration are primarily:

- Susceptible Class (S): A collection of individual in a population are classified as susceptibles if they are not infected but are at risk of being infected.

- Exposed class (E): These are individuals who have been infected with the disease pathogen, but are not able to infect others. They may still be in the incubating stage, and do not have immunity. This class is also known as the latent class.

- Infected class (I): This is a collection of individuals who are infected and are infectious.

- Recovered/removed class (R): These are individuals who recover and acquire temporary or permanent immunity and may not contract or transmit the disease, either because they are no longer infectious and are immuned or because they have been vaccinated.

- Other classes: Different diseases require different compartments and some of such are not listed here.

Compartmental models have provided valuable insights into epidemiology of many infectious diseases including HIV/AIDS. Diseases that confer immunity have a different compartmental structure from diseases without immunity. For diseases which confer immunity, the SIR terminology is used, describing the passage of individuals from susceptible class (S) to the infective (I) and then to the removed/recovered class (R). The term SIS describes a disease with no immunity, indicating the movement of individuals from susceptible class to infective and then back to susceptible class. Other possibilities include the SEIR and the SEIR models with an exposed period, a stage of being infected and becoming infective after a period of time, and SIRS models with temporary immunity on recovery from infection.
Some other classes may be added to increase accuracy of the model. Specifically a class V of vaccinated individuals. The sizes of each at the time t are represented b $S(t), E(t), I(t), R(t)$ respectively, $N(t)$ denotes the total population size, that is, $S(t) + E(t) + I(t) + R(t) = N(t)$.
The transmission of diseases may be through horizontal incidence, from infected to susceptible and vertical transmission, for example from mother to children. The probability per unit time at which a susceptible member

of the population are infected is called *force of infection* and generally seen as a function of total number of infective individuals. The number of individuals that become infected in any given period of time is called *incidence*. It is often referred to as incidence rate, which is the incidence per unit time. *Prevalence* is the proportion of the population that is infected.

3.3.1 The basic SIR model

The basic compartmental models to describe the transmission of communicable diseases are contained in a sequence of three papers of Kermack and McKendrick [62, 63]. The simplest models they proposed are also of the form below with the following assumptions:

βN : average infective individual making appropriate contact sufficient to transmit infection per unit time.
$\frac{S}{N}$: probabilities of contact between infective with a susceptible individual
γ : fraction of infectives recovered per time.

The model is given below:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI, \\ \frac{dI}{dt} &= -\beta SI - \gamma I, \\ \frac{dR}{dt} &= -\gamma I. \end{aligned} \tag{3.17}$$

In this model, once I is known, R can be determined, so we may want to consider the S and I equation only.

$$\begin{aligned} \frac{dI}{dt} &= \frac{(\beta S - \gamma)I}{-\beta SI}, \\ &= -1 + \frac{\gamma}{\beta S}. \end{aligned} \tag{3.18}$$

At this point we can easily solve for I by integrating both sides:

$$I = -S + \frac{\gamma}{\beta} \log S + c. \tag{3.19}$$

3.3.2 Mass action (density dependent)

This describes a factor that influences individuals in a population to a degree that varies in response to the crowd of the population. It can also be described as the probability of transmission in a given time period a function of the number of infectious individuals in a given area. In this case the contact rate depends on the size of the total host population. This type of incidence has been used in modelling several infectious diseases including HIV/AIDS. The typical SIR model for a mass action (density dependent) transmission is given by the model due to Kermack and McKendrick, see [53, 54].

3.3.3 Standard incidence (frequence depedent)

This is the probability of transmission in a given time period is a function of the prevalence of infection in the population. The contact rate is assumed to be constant, that is, it depends on the proportion of susceptibles and infected within the population, not the total population size that affects the level of interactions. HIV/AIDS and other infectious diseases has been studied using this form of incidence, see [19, 23, 33, 36]. The typical SIR model for a standard (frequency dependent) transmission is given by (3.18).

3.3.4 More complex SIR models

Kermack and McKendrick proposed another SIR model that includes births in the susceptible class and deaths from all classes with the rate proportional to each class

$$\frac{dS}{dt} = -\beta SI + \mu(K - S), \tag{3.20}$$

$$\frac{dI}{dt} = \beta SI - \gamma I - \mu I,$$

$$\frac{dR}{dt} = \gamma I - \mu R,$$

where the total population size, N is defined as the total sum of the population in the classes. $N(t) = S(t)+I(t)+R(t)$ with the assumptions that there is no diseases induced death. Hethcote in 1976 [8], proposed a more general model

$$\begin{aligned} \frac{dS}{dt} &= \mu K - \beta SI - \mu S, \\ \frac{dI}{dt} &= \beta SI - (\gamma + \mu + \alpha)I, \\ \frac{dR}{dt} &= \gamma I - \mu R, \end{aligned} \tag{3.21}$$

where α is the disease induced death fraction; γ rate of recovery with acquired immunity, natural death rate μ and birth rate μK is assumed constant. Ignoring the R class of the system (3.21), the system is reduced to

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI + \mu(K - S), \\ \frac{dI}{dt} &= \beta SI - \gamma I - \mu I, \end{aligned} \tag{3.22}$$

The first step is to study the steady rate, the equilibrium points is obtained by setting the right hand of the system (3.23) to zero.

$$
\begin{aligned}
-\beta SI + \mu(K - S) &= 0, \\
\beta SI - \gamma I - \mu I &= 0.
\end{aligned}
\tag{3.23}
$$

The diseases free equilibrium (DFE) which describes the state where no infection is present in the population is obtained when $I^* = 0$, hence $S^* = K$. The endemic equilibrium, where infection persists at fixed level is obtained when $I^* \neq 0$, hence $S^* = \frac{\mu(\beta K - (\gamma+\mu+\alpha))}{\beta(\gamma+\mu+\alpha)}$, $I^* = \frac{\gamma+\mu+\alpha}{\beta}$. The eigenvalues of the Jacobian evaluated at these points will determine their linear stability. Therefore, linearizing the system (3.9) to study the local stability of the fixed point, the Jacobian matrix is obtained as

$$
J = \begin{bmatrix} -\mu - \beta I & -\beta S \\ \beta I & \beta S - (\gamma + \mu + \alpha) \end{bmatrix},
$$

The Jacobian matrix is given at DFE by

$$
\begin{bmatrix} -\mu & -\beta K \\ 0 & \beta K - (\gamma + \mu + \alpha) \end{bmatrix}.
$$

From the above matrix, the DFE of the system will be stable if $\beta K < (\gamma + \mu + \alpha)$. The Jacobian matrix evaluated at the endemic equilibrium is

$$
\begin{bmatrix} \frac{-\mu\beta K}{\beta(\gamma+\mu+\alpha)} & -(\gamma + \mu + \alpha) \\ \frac{\mu(\beta K - (\gamma+\mu+\alpha))}{\beta(\gamma+\mu+\alpha)} & 0 \end{bmatrix}.
$$

It is obvious from this matrix that the trace is negative while the determinant will be positive if $\beta K - (\gamma + \mu + \alpha) > 0$

The basic reproduction number R_0 is hence given as $\frac{\beta K}{\beta(\gamma+\mu+\alpha)}$.

If $R_0 < 1$, the disease-free equilibrium is stable and the endemic equilibrium does not exist.

If $R_0 > 1$, the disease-free equilibrium is unstable and the endemic equilibrium does exist and asymptotically stable.

3.4 Optimal control method

An optimal control is an extension of the calculus of variations and optimization method for deriving control policies. It deals with the problem of finding a control law for a given system such that a certain optimality criterion is achieved [24]. Optimal control theory is fundamentally the work of Lev Pontryagin and his collaborators in the Soviet Union in the early 1960s. This method has been powerful mathematical technique derived from the calculus of variation and is very suitable in decision making regarding composite biological situations. The behaviour of a dynamical system is described by the state variables(s). A control problem includes a cost functional that is a function of state and control variables.[55, 56].
The assumption is that there is a way to control the state variable x, by acting upon it with a suitable control. Thus the dynamics of the system (state x) depends on the control u. The ultimate goal is to adjust control u to minimize or maximize a given objective functional $J(u(t), x(t), t)$, that attains the desired goal and the required cost to achieving it. The optimal solution is the obtained when the most desired goal is achieved with least cost. The functional depends on the control and the state variables. There are different ways to calculate the optimal control for specific model. For example, Pontryagin's Maximum Principle allows the calculation of the optimal control for an ordinary differential equation model system with given constraints.

Definition 3.4.1 ([55], **Piecewise Continuous Functions**).
Let $I \subseteq \mathbb{R}$ be an interval (finite or infinite). We say a finite-valued function $u : I \to \mathbb{R}$ is piecewise continuous if it is continuous at each $t \in I$, with the possible exception of at most a finite number of t, and if u is equal to either its left or right limit at every $t \in I$.

Suppose $u : I \to \mathbb{R}$ is piecewise continuous. Let $g : \mathbb{R}^3 \to \mathbb{R}$ be continuous in three variables. Then, by the solution x of the differential equation

$$x^{'}(t) = g(t, x(t), u(t)) \tag{3.24}$$

it is meant a continuous function $x : I \to \mathbb{R}$ which is differentiable, with $x^{'}$ satisfying the above expression, wherever u is continuous. Similarly, if $I = [a, b]$, then x satisfies

$$x(t) = x(a) + \int_a^t g(s, x(s), u(s))ds.$$

An initial condition for $x(a)$ will be specified normally.

Definition 3.4.2 ([55], **Piecewise Differentiable Functions**).
Let $x : I \to \mathbb{R}$ be continuous on I and differentiable at all but finitely points of I. Further suppose that $x^{'}$ is continuous whenever it is defined. Then, we say x is piecewise differentiable.

Definition 3.4.3 ([55], **Continuous Differentiable Functions**).
Let $k : I \to \mathbb{R}$. We say k is continuously differentiable if $k^{'}$ exists and is continuous on I.

Definition 3.4.4 ([55], **Concave Functions**).
A function $k(t)$ is said to be concave on $[a, b]$ if

$$ak(t_1) + (1 - \alpha)k(t_2) \leq k(\alpha t_1 + (1 - \alpha)t_2$$

for all $0 \leq \alpha \leq 1$ and for all $a \leq t_1, t_2 \leq b$.

Definition 3.4.5 ([55], **Convex Functions**).
A function $k(t)$ is said to be convex on $[a, b]$ if

$$ak(t_1) + (1 - \alpha)k(t_2) \geq k(\alpha t_1 + (1 - \alpha)t_2$$

for all $0 \leq \alpha \leq 1$ and for all $a \leq t_1, t_2 \leq b$.

Theorem 3.4.6 ([55], **Mean Value Theorem**).
Let k be continuous on $[a, b]$ and differentiable on (a, b). Then, there is some $x_0 \in (a, b)$ such that $k(b) - k(a) = k^{'}(x_0)(b - a)$.

We use $u(t)$ for the control and $x(t)$ for the state variables in our basic optimal control problem for ordinary differential equation. The state variable satisfies a differential equation and depends on the control variable:

$$x^{'} = g(t, x(t), u(t)).$$

The solution to the differential changes as the control function changes. Our basic control problem consists of finding a piecewise continuous control $u(t)$ and the related state variable $x(t)$ to maximize the objective function

$$\max_u \int_{t_0}^{t_1} f(t, x(t), u(t))dt$$

$$\begin{aligned} \text{subject to} \quad x'(t) &= g(t, x(t), u(t)) \\ x(t_0) &= x_0 \text{ and } x(t_1) \text{ unrestricted.} \end{aligned} \tag{3.25}$$

Such a maximizing control is known as optimal control. Important characteristics in an optimal control problem are:

- Observability:-It helps to deduce system information from control input and observe output.
- Controllability: - control is use to steer a system from one position to another.
- Stabilization:- implementing controls to force stability.

3.4.1 Pontryagin's Maximum Principle

This is a powerful method for the computation of optimal controls, which has the crucial advantage that it does not require prior evaluation of the infimal cost function. The principle says that we can solve the optimization problem $J(u(t), x(t), t)$ using the Hamiltonian function H over one period. That is, the principle converts the maximization/minimization of the objective functional, J, coupled with the state variable into maximization/minimization point wise the Hamiltonian with respect to the control.
We continue with the set-up of the section but assume that b, c and C are differentiable in t and x with continuous derivatives, and the stopping set D is a hyper plane, thus $D = y + \sum$ for some $y \in \mathbb{R}^d$ and some vector subspace $\sum$ of $\mathbb{R}^d$. We define for $\lambda \in \mathbb{R}^d$ the *Hamiltonian*

$$H(t, x, u, \lambda) = \lambda^T b(t, x, u) - c(t, x, u).$$

Pontryagin's maximum principle states that, if $(x_t; u_t)_{t \leq \tau}$ is optimal, then there exist adjoint path$(\lambda)_{t \leq \tau}$ in $\mathbb{R}^d$ and $(\mu)_{t \leq \tau}$ in $\mathbb{R}$ with the following properties: for all $t \leq \tau$,

1. $H(t, x_t, u, \lambda_t) + \mu_t$ has maximum value 0, achieved at $u = u_t$,
2. $\dot{\lambda_t^T} = -\lambda_t^T \nabla b(t, x_t, u_t) + \nabla c(t, x_t, u_t)$,
3. $\dot{\mu_t} = -\lambda_t^T \dot{b}(t, x_t, u_t) + \dot{c}(t, x_t, u_t)$,
4. $\dot{x_t} = b(t, x_t, u_t)$. Moreover the following *transversality conditions hold*;
5. $(\lambda_t^T + \nabla C(\tau, x_\tau))\rho = 0$
   and, in the time-unconstrained case,
6. $\dot{C}(\tau, x_\tau) = 0$.

Note that, in the time-unconstrained case, if b, c and C are time-independent, then $\mu_t = 0$ for all t.
The Hamiltonian serves as a way of remembering the first four statements, which could be expressed alternatively as

$$(i)\ 0 = \partial H/\partial u, \quad (ii)\ \dot{\lambda} = -\partial H/\partial x, \quad (iii)\ \dot{\mu} = -\partial H/\partial t, \quad (iv)\ \dot{x} = \partial H/\partial \lambda.$$

Theorem 3.4.7 ([55])**.**
Suppose $u^*(t)$ and $x^*(t)$ are optimal for problem (3.26), then there exists a piecewise differentiable adjoint variable $\lambda(t)$, such that

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t))$$

for all controls u at each time t, where the Hamiltonian H is

$$H = f(t, x(t), u(t)) + \lambda(t) g(t, x(t), u(t)),$$

and

$$\frac{d\lambda(t)}{dt} = -\frac{\partial H(t, x^*(t), u^*(t), \lambda(t))}{\partial x},$$

$$\lambda(t_1) = 0.$$

Theorem 3.4.8 ([55]).
Suppose $f(t,x,u)$ and $g(t,x,u)$ are both continuous differentiable functions in their three arguments and concave in u. Suppose u^* is an optimal control for problem (3.26) with associated state u^*, and a piecewise differentiable function with $\lambda(t) \geq 0$ for all $t_0 \leq t \leq t_1$

$$0 = H_u(t, x^*(t), u(t), \lambda(t)).$$

Then for all controls u and each $t_0 \leq t \leq t_1$, we have

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t)).$$

Proof. Let us fix a control u and point in time $t_0 \leq t \leq t_1$. Then

$$H(t, x^*(t), u^*(t), \lambda(t))$$

$$= [f(t, x^*(t), u^*(t) + \lambda(t) g(t, x^*(t), u^*(t))] - [f(t, x^*(t), u(t) + \lambda(t) g(t, x^*(t), u(t))]$$

$$= [f(t, x^*(t), u^*(t) - f(t, x^*(t), u(t))] + \lambda[g(t, x^*(t), u^*(t) - g(t, x^*(t), u(t))]$$

$$\geq (u^*(t) - u(t)) f_u(t, x^*(t), u^*(t)) + \lambda(t)(u^*(t) - u(t)) g_u(t, x^*(t), u^*(t)).$$

Applying tangent line property to f and g, and because $\lambda(t) \geq 0$, we have

$$(u^*(t) - u(t)) H_u(t, x^*(t), u^*(t)) = 0. \qquad \square$$

Chapter 4

Transmission dynamics of HIV/AIDS in the presence of carefree susceptibles and treatment

In this chapter, we discuss the model proposed by Okosun et al. [75] and expand on it. They addressed the effectiveness of HIV/AIDS preventive and intervention measures, comprising the treatment of HIV individuals, enlightenment campaign in reducing the spread of the disease subject to the inflow of carefree susceptibles. They also considered a mathematical model for the transmission dynamics of the disease including these measures and conditions. They first considered the autonomous case, and calculated the basic reproduction number and investigated the existence and stability of equilibria. The model is found to exhibit backward bifurcation implying that for the disease to be eradicated, the basic reproductive number must be below a critical value less than one. In the time dependent control case, they used Pontryagin's Maximum Principle to derive necessary conditions for the optimal control of the disease. Finally, numerical simulations are performed to illustrate the analytical results. By way of expansion on [75], we present a sensitivity analysis of the parameters and notice the most sensitive parameters are the probability of contact careful susceptibles and infectives.

4.1 Model description

Carefree in our context means highly risky behaviour by individuals due to ignorance or just not being responsible. The model that we consider here is a slight modification of the model for HIV/AIDS transmission considered in [75, 66, 51]. It is neither a generalization of these ones, nor is it a special case of them. It is a standard model of HIV/AIDS in which we incorporated four time dependent control measures simultaneously:
(i) enlightenment campaign, (ii) treatment of HIV individuals, (iii) treatment of AIDS individuals and (iv) recruitment of carefree susceptibles. The model sub-divides the total population at time t, denoted by $N_h(t)$, into the following sub-populations of carefree susceptible individuals ($S_1(t)$), careful susceptible individuals ($S_2(t)$), infectious individuals ($I(t)$), individuals on treatment class ($T(t)$) and that of AIDS suffered $A(t)$. Thus we have

$$N_h(t) = S_1(t) + S_2(t) + I(t) + T(t) + A(t).$$

The susceptibles are individuals that have not contracted the infection but may be infected through the sexual contacts. The carefree susceptible are individuals who are not enlightened or well informed about the disease dynamics. The constants β_i $(i = 1, 2, 3, 4, 5, 6)$ are the probabilities of transmission of susceptible individuals supposed to have different values for different kinds of susceptibles i.e. carefree susceptible individuals, carefree susceptibles with infectious individuals (not under treatment) and with individuals under treatment, careful susceptible individuals, careful susceptible with infectious individuals and with individuals on treatment. Carefree susceptibles are recruited at a rate $(1 - \pi)$, where π are the proportion of individuals assumed to be careful. When carefree individuals are enlightened and their attitude changed they move to the careful susceptible class at a rate θ. Infectious individuals are treated at a rate σ and the rate at which the infectious individuals without treatment progress to AIDS is δ while $\rho\delta$ is the rate of progression into AIDS by treatment. Here, ρ is the modification parameter due to treatment. The term $\gamma(t)$ measures the rate at which AIDS individuals are treated in each time period, and μ is the natural mortality rate unrelated to HIV/AIDS. We assume also that the AIDS class A is sexually active and so they can transmit the disease. Here c_i $(i = 1, 2, 3, 4, 5, 6)$ are the number of sexual partners by individuals in each of the six subclasses of susceptibles. We consider a special case of [75] taking $\alpha = 0$ and we regard the state variables as normalized. This means $S_1(t) + S_2(t) + I(t) + T(t) + A(t) = 1$. The resulting system of equations is shown below:

$$\begin{cases} \frac{dS_1}{dt} = (1-\pi) - \lambda_1 - \theta S_1 - \mu S_1 \\ \frac{dS_2}{dt} = \pi - \lambda_2 + \theta S_1 - \mu S_2 \\ \frac{dI}{dt} = \lambda_1 + \lambda_2 - \sigma I - \delta I - \mu I \\ \frac{dT}{dt} = \sigma I + \gamma A - (\rho\delta + \mu)T \\ \frac{dA}{dt} = \delta I + \rho\delta T - (\gamma + \mu)A. \end{cases} \tag{4.1}$$

where

$\lambda_1 = \beta_1 c_1 I S_1 - \beta_3 c_3 T S_1 - \beta_5 c_5 A S_1,$

$\lambda_2 = \beta_2 c_2 I S_2 - \beta_4 c_4 T S_2 - \beta_6 c_6 A S_2.$

4.2 Stability of the disease-free equilibrium

The disease-free equilibrium (DFE) of the HIV/AIDS model (4.1) is given by

$$E_0 = \left(\frac{1-\pi}{\theta+\mu}, \frac{\mu\pi + \theta}{\mu(\theta+\mu)}, 0, 0, 0 \right).$$

The basic reproduction number of the model in the presence of carefree susceptibles (4.1), is given by

$R_{0\pi} = \frac{\Lambda_3 + ((1-\pi)\,\mu\,c_1\,\beta_1 + (\theta+\pi\,\mu)\,c_2\,\beta_2)\,\Lambda_1 + ((1-\pi)\,\mu\,c_3\,\beta_3 + (\theta+\pi\,\mu)\,c_4\,\beta_4)\,\Lambda_2}{\mu\,(\theta+\mu)\,(\mu\,(\gamma+\mu+\delta\,\rho))\,(\delta+\mu+\sigma)},$

where

$\Lambda_1 = \mu\,(\gamma + \mu + \rho\delta)\,,$

$\Lambda_2 = \gamma\delta + (\gamma + \mu)\,\sigma,$

$\Lambda_3 = (\delta\,(\mu + \rho\delta) + \rho\delta\sigma)\,((1-\pi)\,\mu\,c_5\,\beta_5 + (\theta + \pi\,\mu)\,c_6\,\beta_6)\,.$

The DFE is locally asymptotically stable if $R_{0\pi} < 1$ and unstable if $R_{0\pi} > 1$. All of the above is clarified in the paper [75].

4.3 Existence of endemic equilibrium

This section is an exercise in computational exploration. Calculating the endemic equilibrium point, we obtain,

$$\begin{cases} S_1^* = \frac{(1-\pi)}{\theta+\mu+\beta_1 c_1 I^*+\beta_3 c_3 T^*+\beta_5 c_5 A^*}, \\ S_2^* = \frac{\pi+\theta S_1^*}{\beta_2 c_2 I^*+\beta_4 c_4 T+\beta_6 c_6 A^*+\mu}, \\ I^* = \frac{\beta_3 c_3 T^* S_1^*+\beta_4 c_4 T^* S_2^*+\beta_5 c_5 A^*+\beta_6 c_6 A^*}{\sigma+\delta+\mu-\beta_1 c_1 S_1^*-\beta_2 c_2 S_2^*}, \\ T^* = \frac{\sigma I^*+\gamma A^*}{\rho\delta+\mu}, \\ A^* = \frac{\delta I^*+\rho\delta T^*}{\gamma+\mu}. \end{cases} \tag{4.2}$$

The endemic value of I^* satisfies the following polynomial

$$P(I^*) = A(I^*)^2 + B(I^*) + C = 0, \tag{4.3}$$

where

$A = (\delta+\mu+\sigma)((\mu(\gamma+\mu)+\delta\mu\rho)\beta_1 c_1 + (\gamma\delta+(\gamma+\mu)\sigma)\beta_3 c_3)$
$+ \delta(\mu+\rho(\delta+\sigma))c_5\beta_5((\mu(\gamma+\mu)+\delta\mu\rho)\beta_2 c_2$
$+ (\gamma\delta+(\gamma+\mu)\sigma)\beta_4 c_4 + \delta(\mu+\rho(\delta+\sigma))c_6\beta_6),$

$B = \mu(\theta+\mu)(\mu(\gamma+\mu)+(\delta\mu\rho)(\delta+\mu+\sigma)^2(R_0-R),$

$C = (\mu(\gamma+\mu)+\delta\mu\rho)^2(1-R_{0\pi}).$

$R_0 = \frac{D+\delta\,\mu\,\rho+(\gamma+\mu)\,(\mu\,c_1\,\beta_1+(\theta+\mu)\,c_2\,\beta_2)+(\gamma\,\delta+(\gamma+\mu)\,\sigma)\,(\mu\,c_3\,\beta_3+(\theta+\mu)\,c_4\,\beta_4)}{\mu\,(\theta+\mu)\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)},$

where $D = (\mu+\rho\ (\delta+\sigma))\ (\delta\,c_5\,\beta_5+\delta\ (\theta+\mu)\ c_6\,\beta_6)\,.$

$R_0 > 1$ if and only if

$$\beta_6 > \beta_6^+ := \frac{\mu(\delta+\mu+\sigma)\Omega - \Omega_1 c_1\beta_1 + \Omega c_2\beta_2 + \Omega_2(\mu c_3\beta_3 + (\theta+\mu)c_4\beta_4 + \delta(\mu+\rho(\delta+\sigma))c_5\beta_5)}{c_6\delta(\theta+\mu)(\mu+\rho(\delta+\sigma))},$$

where

$$\begin{cases} \Omega = (\theta+\mu)(\mu(\gamma+\mu)+\delta\mu\rho), \\ \Omega_1 = (\mu(\gamma+\mu)+\delta\mu\rho), \\ \Omega_2 = (\gamma\delta+(\gamma+\mu)\sigma). \end{cases} \tag{4.4}$$

4.4 Sensitivity analysis of model parameters

We carry out sensitivity analysis to investigate the model robustness to parameter values. This will help us to know the parameters that have high impact on the disease's transmission, that is, on the reproductive number R_0. To carry out this analysis, we use the normalised forward sensitivity index of a variable to a parameter approach, described in [74]. This is known as the ratio of the relative change in the variable to the relative change in the parameter. Another way to derive sensitivity index is by using partial derivatives when the variable is a differentiable function of the parameter.

Definition 4.4.1. The normalised forward sensitivity index of a variable, m, that depends differentiable on a parameter, n, is defined as:

$$\Upsilon_n^m = \frac{\partial m}{\partial n} \times \frac{n}{m}.$$

Sensitivity analysis of R_0

We derive the sensitivity of R_0 to each of the parameters described in Table (4.1). The sensitivity indices are shown below:

$$\frac{\partial R_0}{\partial c_1} \times \frac{c_1}{R_0} = \frac{(\gamma+\mu)\,\beta_1}{(\theta+\mu)\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial c_2} \times \frac{c_2}{R_0} = \frac{(\gamma+\mu)\,\beta_2}{\mu\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial c_3} \times \frac{c_3}{R_0} = \frac{(\gamma\,\delta+(\gamma+\mu)\,\sigma)\,\beta_3}{(\theta+\mu)\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial c_4} \times \frac{c_4}{R_0} = \frac{(\gamma\,\delta+(\gamma+\mu)\,\sigma)\,\beta_4}{\mu\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial c_5} \times \frac{c_5}{R_0} = \frac{\delta\,(\mu+\rho\,(\delta+\sigma))\,\beta_5}{\mu\,(\theta+\mu)\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial c_6} \times \frac{c_6}{R_0} = \frac{\delta\,(\mu+\rho\,(\delta+\sigma))\,\beta_6}{\mu\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial \beta_1} \times \frac{\beta_1}{R_0} = \frac{(\gamma+\mu)\,c_1}{(\theta+\mu)\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial \beta_2} \times \frac{\beta_2}{R_0} = \frac{(\gamma+\mu)\,c_2}{\mu\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial \beta_3} \times \frac{\beta_3}{R_0} = \frac{(\gamma\,\delta+(\gamma+\mu)\,\sigma)\,c_3}{(\theta+\mu)\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial \beta_4} \times \frac{\beta_4}{R_0} = \frac{(\gamma\,\delta+(\gamma+\mu)\,\sigma)\,c_4}{\mu\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial \beta_5} \times \frac{\beta_5}{R_0} = \frac{\delta\,(\mu+\rho\,(\delta+\sigma))\,c_5}{\mu\,(\theta+\mu)\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial \beta_6} \times \frac{\beta_6}{R_0} = \frac{\delta\,(\mu+\rho\,(\delta+\sigma))\,c_6}{\mu\,(\mu\,(\gamma+\mu)+\delta\,\mu\,\rho)\,(\delta+\mu+\sigma)}$$

where $F = (-(\gamma\,\mu\,c_3\,\beta_3) - \gamma\,(\theta+\mu)\,c_4\,\beta_4 - (\mu+\delta\,\rho)\,(c_5\,\beta_5 + (\theta+\mu)\,c_6\,\beta_6))$.

In Table 4.1., we listed some values of parameters and calculated the sensitivity of R_0 to such parameters. In the Table the parameters are arranged from the most sensitive to the least. The most sensitive parameter here is the probability of careful susceptible contact with infectives (β_2) with +7.783, followed by the number of sexual partners with infectives (c_1) with +5.665. Other important parameters is the rate at which AIDS individuals are treated (γ) with +4.281. The least of the sensitivity parameters is the natural mortality related to HIV/AIDS (μ) with -0.0186.
The sensitivity index of R_0 with respect to the probability of careful susceptible contact with infectives (β_2) with +7.763, implying that decreasing (or increasing) β_2 by 10% decreases (or increases) R_0 by 77.63%. The same applies to the number of sexual partners with infectives (c_1), a decreasing (or

increasing) of c_1 by 10% decreases (or increases) R_0 by 56.65%. Similarly increasing (or decreasing) the sensitivity parameters is the natural mortality related to HIV/AIDS (μ) by 10%, increases (or decreases) the R_0 by approximately 0.186%.
For all the parameters, the sign of the sensitivity indices of R_0 agrees with intuitive expectation whether R_0 increases or decreases when the parameters increases.

Table 4.1: Sensitivity indices of R_0 in "carefree" model

Parameter	Parameter values	Ref	Sensitivity
β_2	0.15	[3]	+7.763
c_1	4	[65]	+5.665
γ	0.5	[75]	+4.281
ρ	0.02	[3]	-3.4634
c_2	4	[65]	+2.898
β_4	0.015	[75]	+2.833
β_1	0.34	[3]	+1.672
δ	0.1	[3]	-1.2323
β_3	0.015	[75]	+0.807
μ	0.02	[3]	-0.0186

In the next chapter, we do more analysis on the transmission dynamics of HIV/AIDS model with public-health information campaigns and individual withdrawal [73] where we check the sensitivity of each parameter used and performs optimal control strategies.

Chapter 5

HIV/AIDS model with public-health campaigns and infective withdrawal

In this chapter we consider the model proposed by Nyabadza et al. see [73]. In contribution to this paper, we analyse the sensitivity of the parameters and optimal control strategies to know the effect of public-health campaigns programmes and voluntary withdrawal of infectives individual on the spread of HIV/AIDS.
It is a general knowledge that most infections occur when an uninfected individual comes sexually in contact with infected individual. *Contact rate* is the numbers of contact made per unit time between individuals that result in infection. Such contact determines the rate of transmission of the disease. In other words, contact rate determines the *transmission probability* which is the probability of a new infection.

5.1 Model description

Considering a sexually active population of size $N(t)$ at time t. We subdivide the population into the following subclasses (compartments): susceptibles $S(t)$, asymptomatic infectives $I_1(t)$ (infectious individuals who are yet to show symptoms of the disease), symptomatic infectives $I_2(t)$ (infectious individuals who show symptoms of the disease) and full blown individuals AIDS $A(t)$. We assume that the mode of transmission is via heterosexual contacts. Then the

following equation holds.

$$N(t) = S(t) + I_1(t) + I_2(t) + A(t).$$

We also assume that each susceptible individual is equally likely to be infected by an infectious individual.

The recruitment rate of susceptible individuals is given by μb and μ is the per capital background mortality. The transfer rate from the asymptomatic compartment to the symptomatic compartment is σ and the removal rate of the symptomatic infectives as they develop to AIDS is given by ρ. The disease's death rate is given by δ. Thus we have the following system.

$$\begin{cases} \frac{dS}{dt} = \mu b - \mu S - \lambda(\mathbf{I}, A)S, \\ \frac{dI_1}{dt} = \lambda(\mathbf{I}, A)S - (\mu + \sigma)I_1, \\ \frac{dI_2}{dt} = \sigma I_1 - (\mu + \rho)I_2, \\ \frac{dA}{dt} = \rho I_2 - (\mu + \delta)A, \end{cases} \tag{5.1}$$

where

$$\lambda(\mathbf{I}, A) = \frac{c\beta\{I_1 + \eta_1 I_2 + \eta_2(1-q)A\}}{1 + \alpha\{I_1 + \eta_1 I_2 + \eta_2(1-q)A\}},$$

η_1 and η_2 measure the relativity of I_2 and A when compared to I_1, and $\mathbf{I} = (I_1, I_2)$.

The constants c and β are mean number of sexual partners per given time and probability of infection respectively while q represent the proportion of individuals who voluntarily withdraw from sexual activities as a result of knowing their HIV infection status or the disease, implying $(1 - q)$ engage in sexual activities. We quantify α as the effectiveness of information as it spreads in preventing HIV transmission in an environment with public-health HIV/AIDS information campaigns.

Note that all parameters are positive and the initial conditions of the system (5.1) is given as

$$S(0) = S_0 > 0, \quad I_1(0) = I_{10} > 0, \quad I_2(0) = I_{20} > 0, \quad A(0) = A_0 > 0.$$

The proposed contact rate is set to depend on the number of infectived individuals in the population. It is determined by $\lambda(\mathbf{I}, A)$ which is of the form $\frac{c\beta g(\mathbf{I},A)}{\varphi(\mathbf{I},A)}$, where $g(\mathbf{I}, A) = I_1 + \eta_1 I_2 + \eta_2(1-q)A$ and $\varphi(\mathbf{I}, A) = 1 + \alpha g(\mathbf{I}, A)$. Obviously, if $\alpha = 0$, then $\varphi(\mathbf{I}, A) = 1$. The assumption here that the rate of HIV transmission in the community is basically determined by the amount of HIV/AIDS public health information available in the community. It is important to note that $\frac{c\beta g(\mathbf{I},A)}{\varphi(\mathbf{I},A)}$ tends to a close approximation of the term $c\beta g(\mathbf{I}, A)$. The incident function thus reduces to a mass action incidence function in this case. However, $\frac{c\beta g(\mathbf{I},A)}{\varphi(\mathbf{I},A)}$ approaches the constant $\frac{c\beta}{\alpha}$ for a very large values of I_1, I_2 and A. It is also important to note that $\lambda(\mathbf{I}, A)$ is an increasing function of η_1 and η_2 and decreasing function of q since $\lambda'(\mathbf{I}, A) = \frac{c\beta}{(1+\alpha\{I_1+\eta_1 I_2+\eta_2(1-q)A\})^2}$.

In our study here, we will consider and set infectives withdrawal (q) and public-health campaigns (α) as main controls of the transmission of HIV/AIDS. Note that when $\alpha = 0$, that is when there is no public-health campaigns, then we have

$$\lambda(\mathbf{I}, A) = c\beta\{I_1 + \eta_1 I_2 + \eta_2(1-q)A\}.$$

When $q = 0$, that is, when there is no voluntary withdrawal of infectives, then

$$\lambda(\mathbf{I}, A) = \frac{c\beta\{I_1 + \eta_1 I_2 + \eta_2 A\}}{1 + \alpha\{I_1 + \eta_1 I_2 + \eta_2 A\}}.$$

Similarly,

$$\lambda(\mathbf{I}, A) = c\beta\{I_1 + \eta_1 I_2 + \eta_2 A\}.$$

when there is no public-health campaigns and no infective withdrawal, that is, when $\alpha = q = 0$.
More analysis and optimal control strategies of these two controls will be established in Chapter 8 of this thesis.

5.2 Stability of the disease-free equilibrium

From the system equation (5.1), we can easily check that the disease-free equilibrium is given by

$$E_0 = (b, 0, 0, 0).$$

Theorem 5.2.1. *The basic reproductive number R_0 of model (5.1) is given by*

$$R_0 = \frac{\beta bc}{\mu + \sigma}\left[1 + \frac{\eta_1 \sigma}{\rho + \mu} + \frac{\eta_2 \rho \sigma (1-q)}{(\rho + \mu)(\delta + \mu)}\right].$$

Outline of proof (a detailed proof is given in [73]). Following van den Driessche and Watmough [88], the basic reproductive number R_0 of model (5.1) is calculated by using the next generation matrix. It is given by

$$R_0 = r(FV^{-1}),$$

where $r(.)$ denotes the spectral radius, with

$$F = \begin{pmatrix} c\beta b & c\beta b\eta_1 & c(1-q)\beta b\eta_2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \mu + \sigma & 0 & 0 \\ -\sigma & \mu + \rho & 0 \\ 0 & -\rho & \mu + \delta \end{pmatrix}.$$

The numerical value of R_0 can be routinely calculated as asserted. □

Theorem 5.2.2 ([73], p 3)**.**
The disease-free equilibrium of system (5.1) is locally asymptotically stable whenever $R_0 < 1$ and unstable otherwise.

The number R_0 can be expressed as

$$R_0 = b\{R_{I_1} + \frac{\sigma}{\mu + \sigma} R_{I_2} + \frac{\rho\sigma(1-q)}{(\rho + \mu)(\delta + \mu)} R_A\},$$

where

$$R_{I_1} = \frac{\beta c}{\mu + \sigma}, \quad R_{I_2} = \frac{\eta_1 \beta c}{\mu + \rho} \quad \text{and} \quad R_A = \frac{\eta_2 \beta c}{\mu + \delta}.$$

The latter three numbers represent the contribution of the asymptomatic, symptomatic and AIDS compartments to the overall model reproduction number R_0 respectively. The proportion of asymptomatic individuals who become symptomatic and individuals who develop to full-blown AIDS are given by $\frac{\sigma}{\sigma+\mu}$ and $(\frac{\rho}{\rho+\sigma})(\frac{\sigma}{\sigma+\mu})$ respectively.

5.3 Steady states and stability analysis

Existence and uniqueness of the endemic equilibrium
There is an endemic equilibrium point (S^*, I_1^*, I_2^*, A^*) satisfying the following identities:

$$I_2^* = \frac{\sigma}{\mu + \rho} I_1^*, \tag{5.2}$$

$$A^* = \frac{\sigma\rho}{(\mu + \rho)(\mu + \delta)} I_1^*, \tag{5.3}$$

$$\lambda^*(\mathbf{I}, A) = \frac{c\beta\Gamma I_1^*}{1 + \alpha\Gamma I_1^*}, \tag{5.4}$$

where

$$\Gamma = 1 + \frac{\eta_1\sigma}{\mu + \rho} + \frac{\eta_2\rho\sigma(1-q)}{(\mu + \rho)(\mu + \delta)}.$$

Substituting $\lambda^*(\mathbf{I}, A)$ in the second equation of (5.1), we have $I_1^* = 0$, and

$$S^* = \frac{(\sigma + \mu)(1 + \alpha\Gamma I_1^*)}{c\beta\Gamma}. \tag{5.5}$$

Adding the first two equations of (5.1), we obtain

$$\mu b - \mu S^* - (\sigma + \mu) I_1^* = 0.$$

Substituting for S^* in the equation above, we find I_1^* as

$$I_1^* = \frac{\mu(R_0 - 1)}{\alpha\mu + c\beta\Gamma}.$$

Note from the above equation that I_1^* has only one positive solution if $R_0 > 1$ and no other positive solution when $R_0 < 1$. We now substitute I_1^* into equations (5.2) to (5.5) above to get the endemic equilibrium point $E_1 = (S^*, I_1^*, I_2^*, A^*) \in \Omega$.

$$\begin{cases} S^* = \frac{(\mu+\sigma)(\alpha\mu+c\beta\Gamma+\alpha\mu(R_0-1))}{c\beta\Gamma(\alpha\mu+c\beta\Gamma)}, \\ I_1^* = \frac{\mu(R_0-1)}{\alpha\mu+c\beta\Gamma}, \\ I_2^* = \frac{\alpha\mu(R_0-1)}{(\mu+\rho)(c\beta\Gamma+\alpha\mu)}, \\ A^* = \frac{\mu\sigma\rho(R_0-1)}{(\mu+\rho)(\alpha\mu+c\beta\Gamma)(\delta+\mu)}. \end{cases} \tag{5.6}$$

We now consider the following theorem on the existence of the endemic equilibrium.

Theorem 5.3.1 ([73], p 4)**.**
If $R_0 > 1$, the system (5.1) has a unique endemic equilibrium given by E_1 in Ω.

Remark. If $R_0 = 1$, the endemic equilibrium E_1 reduces to the disease free equilibrium E_0. Hence the potential of the spread of any infection in a population depends on the reproduction number.

Local stability of the endemic equilibrium

The local stability of the endemic equilibrium point E_1 is decided by considering the sign of the eigenvalues of the Jacobian matrix of the system (5.1). The Jacobian matrix of the system is given as

$$J^{E_1} = \begin{pmatrix} -(\mu+\Delta_1) & -\Delta_1 & -\eta_1\Delta_1 & -(1-q)\eta_1\Delta_1 \\ \Delta_1 & \Delta_1-(\mu+\sigma) & \eta_1\Delta_1 & -(1-q)\eta_1\Delta_1 \\ 0 & \sigma & -(\mu+\sigma) & 0 \\ 0 & -\rho & 0 & -(\mu+\delta) \end{pmatrix}.$$

where

$$\Delta_1 = \frac{c\beta g(\mathbf{I}^*, A^*)}{\varphi(\mathbf{I}^*, A^*)} \quad \text{and} \quad \Delta_1 = \frac{c\beta S^*}{\varphi(\mathbf{I}^*, A^*)} \left(1 - \frac{\alpha g(\mathbf{I}^*, A^*)}{\varphi \mathbf{I}^*, A^*)}\right).$$

Also note that $0 < \frac{\alpha g(\mathbf{I}^*, A^*)}{\varphi \mathbf{I}^*, A^*)} < 1$, showing that Δ_1, Δ_2 are both positive. Hence the characteristic equation of J^{E_1} is given by

$$P(\chi) = \chi^4 + \bar{a}_3\chi^3 + \bar{a}_2\chi^2 + \bar{a}_1\chi + \bar{a}_0\chi = 0, \tag{5.7}$$

where

$$\begin{aligned}
\bar{a}_3 &= (\mu + \sigma) + (\mu + \rho) + (2\mu + \delta) + (\Delta_1 - \Delta_2), \\
\bar{a}_2 &= (\Delta_1 - \Delta_2)(3\mu + \delta + \rho) + \sigma(\Delta_1 - \Delta_2\eta_1) + (2\mu + \rho + \sigma)(3\mu + \delta) + \mu\delta + \rho\sigma, \\
\bar{a}_1 &= (\Delta_1 - \Delta_2)[(2\mu + \delta)(\mu + \rho) + \mu(\mu + \delta)] \\
&\quad + \sigma(2\mu + \delta)(\Delta_1 - \Delta_2\eta_1) + \rho\sigma\{\Delta_1 - \Delta_2(1 - q)\eta_2 + z, \\
\bar{a}_0 &= (\mu + \sigma)(\mu + \delta)(\mu + \rho)(\mu + \Delta_1)[\tfrac{\mu\Delta_2\Gamma}{(\mu+\delta)(\mu+\eta_1)} - 1].
\end{aligned} \tag{5.8}$$

where

$$z = \mu^2[3(\rho + \sigma + \delta)] + 2\mu\rho(\sigma + \delta) + \delta\sigma(2\mu + \rho).$$

If $\bar{a}_3 > 0, \bar{a}_3\bar{a}_2 - \bar{a}_1 > 0$ and $\bar{a}_1[\bar{a}_3\bar{a}_2 - \bar{a}_1] - \bar{a}_3^2\bar{a}_0 > 0$, then the polynomial (5.7) has roots with negative parts. Hence the following result holds:

Theorem 5.3.2 ([73], p 5)**.**
If $R_0 > 1$, the endemic equilibrium E_1 is locally asymptotically stable.

5.4 Sensitivity analysis of model parameters and state variables

We also carry out sensitivity analysis with the same purpose of investigating the model robustness to parameter values. Also helps in making recommendation more credible and understandable. This analysis helps in identifying the

parameters that have high impact on the reproductive number (R_0). To carry out this analysis, we use the normalised forward sensitivity index of a variable to a parameter approach as described in [74].

Sensitivity analysis of R_0

We derive the sensitivity of R_0 to each of the parameters described in Table (4.1). The sensitivity indices is shown below,

$$\frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = \frac{bc}{\mu+\sigma}[1 + \frac{\eta_1\sigma}{\rho+\mu} + \frac{\eta_2\rho\sigma(1-q)}{(\rho+\mu)(\delta+\mu)}]$$

$$\frac{\partial R_0}{\partial c} \times \frac{c}{R_0} = \frac{\beta b}{\mu+\sigma}[1 + \frac{\eta_1\sigma}{\rho+\mu} + \frac{\eta_2\rho\sigma(1-q)}{(\rho+\mu)(\delta+\mu)}]$$

$$\frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = \frac{b\,c\,\beta\left((q-1)\,\rho\,\sigma\left(3\,\mu^2+\rho\,\sigma+2\,\mu\,(\rho+\sigma)+\delta\,(2\,\mu+\rho+\sigma)\right)\eta_2-1-\sigma\,(2\,\mu+\rho+\sigma)\,\eta_1\right)}{(\mu+\sigma)^2(\mu+\rho)^2(\delta+\mu)^2\,(\mu+\rho)^2}$$

$$\frac{\partial R_0}{\partial \sigma} \times \frac{\sigma}{R_0} = \frac{b\,c\,\beta\,((-\delta-\mu)\,(\mu+\rho)+\mu\,(\delta+\mu)\,\eta_1-(q-1)\,\mu\,\rho\,\eta_2)}{(\delta+\mu)\,(\mu+\rho)\,(\mu+\sigma)^2}$$

$$\frac{\partial R_0}{\partial \rho} \times \frac{\rho}{R_0} = -\left(\frac{b\,c\,\beta\,\sigma\,((\delta+\mu)\,\eta_1+(q-1)\,\mu\,\eta_2)}{(\delta+\mu)\,(\mu+\rho)^2\,(\mu+\sigma)}\right)$$

$$\frac{\partial R_0}{\partial q} \times \frac{q}{R_0} = -\left(\frac{b\,c\,\beta\,\rho\,\sigma\,\eta_2}{(\delta+\mu)\,(\mu+\rho)\,(\mu+\sigma)}\right)$$

$$\frac{\partial R_0}{\partial \delta} \times \frac{\delta}{R_0} = -\left(\frac{b\,c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2}{(\delta+\mu)^2\,(\mu+\rho)\,(\mu+\sigma)}\right)$$

$$\frac{\partial R_0}{\partial \eta_1} \times \frac{\eta_1}{R_0} = \frac{b\,c\,\beta\,\sigma}{(\mu+\rho)\,(\mu+\sigma)}$$

$$\frac{\partial R_0}{\partial \eta_2} \times \frac{\eta_2}{R_0} = -\left(\frac{b\,c\,(q-1)\,\beta\,\rho\,\sigma}{(\delta+\mu)\,(\mu+\rho)\,(\mu+\sigma)}\right).$$

Similarly, the parameters are also arranged from the most sensitive to the least. The most sensitive parameter here is the partner acquisition rate (c) and probability of transmission (β), followed by the natural death rate of individual (μ) with -0.0369433. Other important parameters include the rate of developing to AIDS (ρ) with -0.0224872. The least of the sensitivity parameters is the proportion of withdrawals by AIDS cases (q).
The sensitivity index of R_0 with respect to the partner acquisition rate (c) is 3.5715, implying that decreasing (or increasing) c by 10% decreases (or increases) R_0 by 35.7%. Same applicable to probability of transmission (β), a

decreasing (or increasing) β by 10% decreases (or increases) R_0 by 35.7%. Similarly increasing (or decreasing) the rate of developing to AIDS (ρ) by 10%, increases (or decreases) the R_0 by approximately 0.37%.
For all the parameters, the sign of the sensitivity indices of R_0 agrees with intuitive expectation whether R_0 increases or decreases when the parameters increases. The parameter values as from [73] is shown on Table (8.1).

Table 5.1: Sensitivity indices of R_0 in education model

Parameter description	Parameter	Sensitivity
Partner acquisition rate	c	+3.5715
Probability of transmission	β	+3.5715
Natural death rate	μ	-0.0369433
Rate of developing AIDS	ρ	-0.0224872
Rate of becoming symptomatic	σ	-0.00321246
Enhancement factor	η_1	0.00202385
Proportion of withdrawals by AIDS	q	-0.000674617

Sensitivity analysis of state variables

Here, we derive the sensitivity of the state variables to each of the parameters described in Table (5.1). The sensitivity indices is shown below,

$$\frac{\partial S^*}{\partial \alpha} \times \frac{\alpha}{S^*} = -\left(\frac{\mu\,(\delta+\mu)\,(\mu+\rho)\,((\delta+\mu)\,(\mu+\rho)\,(-(b\,c\,\beta)+\mu+\sigma)+b\,c\,\beta\,\sigma\,((-\delta-\mu)\,\eta_1+(-1+q)\,\rho\,\eta_2))}{((\delta+\mu)\,(c\,\beta+\alpha\,\mu)\,(\mu+\rho)-c\,(-1+q)\,\beta\,\rho\,\sigma+c\,\beta\,((\delta+\mu)\,\sigma\,\eta_1+\eta_2))^2}\right) \tag{5.9}$$

$$
\begin{cases}
\frac{\partial I_1^*}{\partial \mu} \times \frac{\mu}{I_1^*} = \frac{\beta\,\mu\,(\delta+\mu)\,(\mu+\rho)\,(\mu+b\,\alpha\,\mu+\sigma)\,((\delta+\mu)\,(\mu+\rho+\sigma\,\eta_1)-(-1+q)\,\rho\,\sigma\,\eta_2)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial I_1^*}{\partial \delta} \times \frac{\delta}{I_1^*} = \frac{c\,(-1+q)\,\beta\,\mu\,\rho\,(\mu+\rho)\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)\,\eta_2}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial I_1^*}{\partial \eta_2} \times \frac{\eta_2}{I_1^*} = -\left(\frac{c\,(-1+q)\,\beta\,\mu\,(\delta+\mu)\,\rho\,(\mu+\rho)\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2}\right) \\
\frac{\partial I_1^*}{\partial \eta_1} \times \frac{\eta_1}{I_1^*} = \frac{c\,\beta\,\mu\,(\delta+\mu)^2\,(\mu+\rho)\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial I_1^*}{\partial \beta} \times \frac{\beta}{I_1^*} = \frac{c\,\mu\,(\delta+\mu)\,(\mu+\rho)\,(\mu+b\,\alpha\,\mu+\sigma)\,((\delta+\mu)\,(\mu+\rho+\sigma\,\eta_1)-(-1+q)\,\rho\,\sigma\,\eta_2)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial I_1^*}{\partial \rho} \times \frac{\rho}{I_1^*} = -\left(\frac{c\,\beta\,\mu\,(\delta+\mu)\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)\,((\delta+\mu)\,\eta_1+(-1+q)\,\mu\,\eta_2)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2}\right)
\end{cases}
\tag{5.10}
$$

$$
\begin{cases}
\frac{\partial I_2^*}{\partial c} \times \frac{c}{I_2^*} = \frac{\beta\,\mu\,(\delta+\mu)\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)\,((\delta+\mu)\,(\mu+\rho+\sigma\,\eta_1)-(-1+q)\,\rho\,\sigma\,\eta_2)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial I_2^*}{\partial \alpha} \times \frac{\alpha}{I_2^*} = \frac{\mu^2\,(\delta+\mu)\,\sigma\,((\delta+\mu)\,(\mu+\rho)\,(-(b\,c\,\beta)+\mu+\sigma)+b\,c\,\beta\,\sigma\,((-\delta-\mu)\,\eta_1+(-1+q)\,\rho\,\eta_2))}{(\mu+\sigma)\,((\delta+\mu)\,(c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,((\delta+\mu)\,\eta_1-(-1+q)\,\rho\,\eta_2))^2} \\
\frac{\partial I_2^*}{\partial q} \times \frac{q}{I_2^*} = -\left(\frac{c\,\beta\,\mu\,(\delta+\mu)\,\rho\,\sigma^2\,(\mu+b\,\alpha\,\mu+\sigma)\,\eta_2}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2}\right) \\
\frac{\partial I_2^*}{\partial \delta} \times \frac{\delta}{I_2^*} = \frac{c\,(-1+q)\,\beta\,\mu\,\rho\,\sigma^2\,(\mu+b\,\alpha\,\mu+\sigma)\,\eta_2}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial I_2^*}{\partial \eta_1} \times \frac{\eta_1}{I_2^*} = \frac{c\,\beta\,\mu\,(\delta+\mu)^2\,\sigma^2\,(\mu+b\,\alpha\,\mu+\sigma)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial I_2^*}{\partial \eta_2} \times \frac{\eta_2}{I_2^*} = -\left(\frac{c\,(-1+q)\,\beta\,\mu\,(\delta+\mu)\,\rho\,\sigma^2\,(\mu+b\,\alpha\,\mu+\sigma)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2}\right) \\
\frac{\partial I_2^*}{\partial \beta} \times \frac{\beta}{I_2^*} = \frac{c\,\mu\,(\delta+\mu)\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)\,((\delta+\mu)\,(\mu+\rho+\sigma\,\eta_1)-(-1+q)\,\rho\,\sigma\,\eta_2)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2}
\end{cases}
\tag{5.11}
$$

$$
\begin{cases}
\frac{\partial A^*}{\partial c} \times \frac{c}{A^*} = \frac{\beta\,\mu\,\rho\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)\,((\delta+\mu)\,(\mu+\rho+\sigma\,\eta_1)-(-1+q)\,\rho\,\sigma\,\eta_2)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial A^*}{\partial \alpha} \times \frac{\alpha}{A^*} = \frac{\mu^2\,\rho\,\sigma\,((\delta+\mu)\,(\mu+\rho)\,(-(b\,c\,\beta)+\mu+\sigma)+b\,c\,\beta\,\sigma\,((-\delta-\mu)\,\eta_1+(-1+q)\,\rho\,\eta_2))}{(\mu+\sigma)\,((\delta+\mu)\,(c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,((\delta+\mu)\,\eta_1-(-1+q)\,\rho\,\eta_2))^2} \\
\frac{\partial A^*}{\partial \beta} \times \frac{\beta}{A^*} = \frac{c\,\mu\,\rho\,\sigma\,(\mu+b\,\alpha\,\mu+\sigma)\,((\delta+\mu)\,(\mu+\rho+\sigma\,\eta_1)-(-1+q)\,\rho\,\sigma\,\eta_2)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial A^*}{\partial q} \times \frac{q}{A^*} = -\left(\frac{c\,\beta\,\mu\,\rho^2\,\sigma^2\,(\mu+b\,\alpha\,\mu+\sigma)\,\eta_2}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2}\right) \\
\frac{\partial A^*}{\partial \eta_1} \times \frac{\eta_1}{A^*} = \frac{c\,\beta\,\mu\,(\delta+\mu)\,\rho\,\sigma^2\,(\mu+b\,\alpha\,\mu+\sigma)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2} \\
\frac{\partial A^*}{\partial \eta_2} \times \frac{\eta_2}{A^*} = -\left(\frac{c\,(-1+q)\,\beta\,\mu\,\rho^2\,\sigma^2\,(\mu+b\,\alpha\,\mu+\sigma)}{(\mu+\sigma)\,((\delta+\mu)\,((c\,\beta+\alpha\,\mu)\,(\mu+\rho)+c\,\beta\,\sigma\,\eta_1)-c\,(-1+q)\,\beta\,\rho\,\sigma\,\eta_2)^2}\right).
\end{cases}
\tag{5.12}
$$

Table 5.2., row one shows that probability of transmission (β) is most sensitive on AIDS individual (A^*) with 6.18892 and least sensitive on asymptomatic infectives (I_1^*) with 1.85668. This implies that increasing (or decreasing) (β) by 10% will increase (or decrease) (A^*) by 61.8892% and (I_1^*) by 18.5668%. Similarly in row two of the same Table, an increase (or decrease) in partner acquisition rate (c) by 10% increases (or decreases) S^* by 0.129083%, I_1^* by 0.00105212%, I_2^* by 0.00210423% and A^* by 0.000350706%, but we note that c is most sensitive on S^* and least sensitive on A^*. We can easily check for other parameters following this trend.

Table 5.2: Sensitivity indices of state variables to model parameters on education

	S^*	I_1^*	I_2^*	A^*
β	-2.27794	1.85668	3.71335	6.18892
c	-0.0129083	0.000105212	0.000210423	0.0000350706
σ	0.335107	0.000439967	$-0.1.11085$	-1.85141
ρ	0.483908	-0.00116902	0.222164	-1.85195
q	-0.0166226	-0.0000350706	-0.0000701411	-0.0000116902
μ	-1.980673	-0.00556235	0.222076	0.462704
δ	0.255362	0	0	0.92578
α	-0.696143	0.999715	1.99943	0.333238
b	0.0462204	0.000018212	0.0000364239	0.00000607065
η_1	0.0483784	0.000105212	0.000210423	0.0000350706
η_2	-0.0459651	0	0	0

Chapter 6

HIV/AIDS model with screening control and parental care

This chapter together with Chapter 7 are original contributions of this thesis and the essence of the two chapters have been submitted for publication see [1].
In this chapter, we present and develop a model for HIV transmission. We then analyze the stability and also carry out the sensitivity analysis of the parameters used, reproductive number (R_0) as well as for the state variables.

6.1 Model description and analysis

We propose a model which is depicted in the flow diagram of Fig. 6.1. The total population at time t, denoted by $N(t)$ is sub-divided into sub-population of susceptible individuals ($S(t)$), individuals newly infected with HIV ($I(t)$), individuals with HIV but not yet developed to AIDS ($H(t)$), and individuals with AIDS ($A(t)$). The population size is $N(t)$ and

$$N(t) = S(t) + I(t) + H(t) + A(t).$$

The natural death rate is μ. Susceptible individuals are recruited at a rate $(1 - \rho u_1)\mu N$ where ρ is the proportion of infectious youths where $u_1 \in [0, 1]$ are screening control efforts on immigrant youths (a quarantine se). The susceptible acquire HIV by any blood contact with infectious youths at a rate

$$(1 - u_2)\frac{S}{N}(\beta_1 c_1 I + \beta_2 c_2 H + \beta_3 c_3 A)$$

where u_2 accounts for parental care and $\beta_1, \beta_2, \beta_3$ are transmission probabilities. The progression rate from newly infected individuals to HIV is γ and that of HIV to AIDS is σ. The number of partners with newly infected individuals, individuals having HIV, and individuals having AIDS are c_1, c_2 and c_3 respectively.
To make a significant model to be close to the real life phenomenon, we assume that all other classes of individuals except susceptible are infectious and that the number of infectious individuals, that is, $I(t) + H(t) + A(t)$, are less than that of susceptible, $S(t)$. We further assume that parental care involves all efforts and activities taken by parents to prevent their children from contracting HIV. The resulting system of equations is shown below.

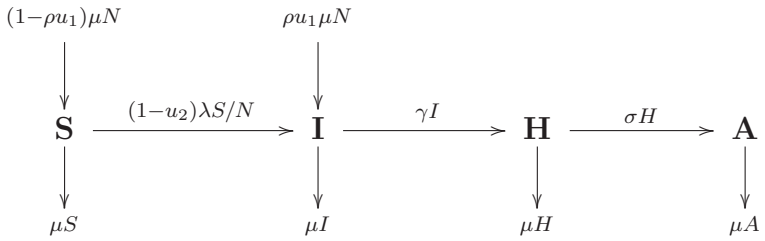
$$\begin{cases} \frac{dS}{dt} = (1-\rho u_1)\,\mu N \; - \frac{S\,(1-u_2)\,(\,I\,c_1\,\beta_1 + H\,c_2\,\beta_2 + A\,c_3\,\beta_3)}{N} - \mu S \\ \frac{dI}{dt} = \rho u_1 \mu N \; + \frac{S\,(1-u_2)\,(\,I\,c_1\,\beta_1 + H\,c_2\,\beta_2 + A\,c_3\,\beta_3)}{N} - \; (\gamma+\mu)\,I \\ \frac{dH}{dt} = \gamma I - (\mu+\sigma)\,H \\ \frac{dA}{dt} = \sigma H - \mu A. \end{cases} \tag{6.1}$$

Normalizing the model, we introduce the following variables

$s = (S/N)$, $i = (I/N)$, $h = (H/N)$, $a = (A/N)$.

Then the system becomes;

$$\begin{cases} \frac{ds}{dt} = (1-\rho u_1)\,\mu \; - s\;(1-u_2)\;(\,i\,c_1\,\beta_1 + h\,c_2\,\beta_2 + a\,c_3\,\beta_3) - \mu s \\ \frac{di}{dt} = \rho u_1 \mu \; + s\;(1-u_2)\;(\,i\,c_1\,\beta_1 + h\,c_2\,\beta_2 + a\,c_3\,\beta_3) - \; (\gamma+\mu)\,i \\ \frac{dh}{dt} = \gamma i - (\mu+\sigma)\,h \\ \frac{da}{dt} = \sigma h - \mu a. \end{cases} \tag{6.2}$$



Flow diagram for HIV/AIDS transmission

6.2 Model without parental care/control

When there is lack of parental care/control among the youths, i.e., for $u_2 = 0$, the above model becomes;

$$\begin{cases} \frac{ds}{dt} = (1 - \rho u_1)\,\mu - s\,\lambda - \mu s, \\ \frac{di}{dt} = \rho u_1 \mu + s\,\lambda - (\gamma + \mu)\,i, \\ \frac{dh}{dt} = \gamma i - (\mu + \sigma)\,h, \\ \frac{da}{dt} = \sigma h - \mu a, \end{cases} \tag{6.3}$$

where

$\lambda = (\, i\, c_1\, \beta_1 + h\, c_2\, \beta_2 + a\, c_3\, \beta_3)\,.$

6.3 Stability of the disease-free equilibrium

In the absence of infected and infectious youths entering the population, that is when $\rho = 0$, we establish the stability of the *disease free equilibrium* (DFE), $E_0 = (1, 0, 0, 0)$.

Theorem 6.3.1. *The basic reproductive number R_0 of model (6.3) is given by*

$$R_0 = \frac{\mu\ ((\mu + \sigma)\ c_1\, \beta_1 + \gamma\, c_2\, \beta_2) + \gamma\, \sigma\, c_3\, \beta_3}{\mu\ (\gamma + \mu)\ (\mu + \sigma)}\ .$$

Proof. Following van den Driessche and Watmough [88], the basic reproductive number R_0 of model (6.3) is calculated by using the next generation matrix. It is given by

$$R_0 = r(FV^{-1}),$$

where $r(.)$ denotes the spectral radius, with

$$F = \begin{pmatrix} \beta_1 c_1 & \beta_2 c_2 & \beta_3 c_3 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$V^{-1} = \begin{pmatrix} \frac{1}{\mu} & 0 & 0 \\ \frac{\gamma(1+\mu)}{\mu\,(\gamma+\mu)\,(\mu+\sigma)} & \frac{1}{\mu+\sigma} & 0 \\ \frac{\gamma\,\sigma}{\mu\,(\gamma+\mu)\,(\mu+\sigma)} & \frac{\gamma\,\sigma+\mu\,\sigma}{\mu\,(\gamma+\mu)\,(\mu+\sigma)} & \frac{1}{\mu} \end{pmatrix}.$$

The numerical value of R_0 can be routinely calculated as asserted. □

Remark. If $R_0 < 1$, system (6.3) has a unique equilibrium point, the DFE, which can be shown to be locally asymptotically stable. If $R_0 > 1$, the DFE becomes unstable and we show in the sequel that the system has a different steady state.

6.4 Steady states and stability analysis

Existence of endemic equilibrium

In search of an endemic equilibrium point, we arrive at the following point E_1.

$$\begin{cases} S^* = \frac{\mu\,(1-\rho\,u_1)}{\lambda+\mu}, \\ I^* = \frac{\lambda\,\mu+\mu^2\,\rho\,u_1}{(\gamma+\mu)\,(\lambda+\mu)}, \\ H^* = \frac{\gamma\,\left(\lambda\,\mu+\mu^2\,\rho\,u_1\right)}{(\gamma+\mu)\,(\lambda+\mu)\,(\sigma+\mu)}, \\ A^* = \frac{\gamma\,\sigma\,(\lambda+\mu\,\rho\,u_1)}{(\gamma+\mu)\,(\lambda+\mu)\,(\mu+\sigma)} \end{cases} \tag{6.4}$$

The number λ is as defined earlier, in the system of equations (6.3). At the same time, λ is a root of the following polynomial

$$W_1\lambda^{*2} + W_2\lambda^* + W_3 = 0; \tag{6.5}$$

with,

$$\begin{aligned} W_1 &= \mu\,(\gamma+\mu)\,(\mu+\sigma)\,, \\ W_2 &= \mu^2\,((\mu+\sigma)\,(\gamma+\mu-c_1\,\beta_1) - \gamma\,c_2\,\beta_2) - \gamma\,\mu\,\sigma\,c_3\,\beta_3, \\ W_3 &= -\mu^2\,\rho\,u_1\,((\mu+\sigma)\,c_1\,\beta_1 + \gamma\,c_2\,\beta_2)\,\mu + \gamma\,\sigma\,c_3\,\beta_3. \end{aligned} \tag{6.6}$$

Let us write $-W_2 = \omega$. For the case $\rho = 0$, the quadratic equation (6.5) has a root $\lambda = 0$ which corresponds to the disease-free equilibrium and another root

$$\lambda = \frac{\gamma\,\mu\,\sigma\,c_3\,\beta_3 - \left(\mu^2((\mu+\sigma)\,(\gamma+\mu-c_1\,\beta_1) - \gamma\,c_2\,\beta_2)\right)}{\mu\,(\gamma+\mu)\,(\mu+\sigma)} \tag{6.7}$$

which is positive if and only if $-W_2 > 0$, i.e., if $\omega > 0$. At the same time we note that a negative value of λ will result in a point E_1 which is non-feasible.

If $\rho > 0$ the quadratic equation has one positive root and one negative root. By definition of λ we have $\lambda \geq 0$, and therefore we discard the negative root. The positive root is given as

$$\lambda^* = \frac{-W_2 + \sqrt{{W_2}^2 - 4\,W_1\,W_3}}{2\,W_1}$$

that is,

$$\lambda^* = \frac{-W_2+\sqrt{4\,\mu^2\,(\gamma+\mu)\,\rho\mu\,(\mu+\sigma)\,u_1\,(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)+{W_2}^2}}{2\,\mu\,(\gamma+\mu)\,(\mu+\sigma)}. \tag{6.8}$$

The unique endemic equilibrium therefore has its S - value given as

$$\begin{cases} S^* = \frac{\mu\,(1-\rho\,u_1)}{\lambda^*+\mu}, \\ \\ \lambda^* = \frac{-W_2+\sqrt{4\,\mu^2\,(\gamma+\mu)\,\rho\mu\,(\mu+\sigma)\,u_1\,(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)+{W_2}^2}}{2\,\mu\,(\gamma+\mu)\,(\mu+\sigma)}. \end{cases} \tag{6.9}$$

Now we observe that;

$$\lim_{\rho\to 0}\lambda^* = \frac{\omega+|\omega|}{2W_1} = \begin{cases} 0 & (\omega<0), \\ \frac{\omega}{W_1} & (\omega>0). \end{cases}$$

Recall from Theorem 6.3.1. that

$$R_0 = \frac{\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3}{\mu\,(\gamma+\mu)\,(\mu+\sigma)}. \tag{6.10}$$

We note that $\lim_{\rho\to 0}\lambda^* = 0$ if $R_0 < 1$, and

$\lim_{\rho\to 0}\lambda^* > 0$ if $R_0 > 1$.

For ρ sufficiently close to zero, we use the binomial approximation $(1+x)^{1/2} = 1+(x/2)$, see [14]. Hence, from (6.10) we obtain

$$W_1\lambda^* = \omega + |\omega|\left[1+\frac{2\,\mu^2\,(\gamma+\mu)\,\rho\,(\mu+\sigma)\,u_1\,\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)W_2}{\omega^2}\right]. \tag{6.11}$$

If $R_0 > 1$, so that $\omega > 0$, this gives

$$\lambda^* \approx \frac{\omega}{W_1} + \frac{\mu^2\,(\gamma+\mu)\,\rho\,(\mu+\sigma)\,u_1\,\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)}{\omega}. \tag{6.12}$$

If $R_0 < 1$, so that $\omega < 0$, this gives

$$\lambda^* \approx \frac{\omega}{W_1} + \frac{\mu^2\,(\gamma+\mu)\,\rho\,(\mu+\sigma)\,u_1\,\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)}{|\omega|}. \tag{6.13}$$

This shows that for ρ close to zero, the model has a threshold $R_0 = 1$. For $\rho > 0$, the disease remains endemic, so system (6.2) has one endemic equilibrium point for all parameter values for which the disease will always persist in

the population. For $R_0 < 1$, we find that as ρ tends to zero, then the endemic equilibrium tends to disease-free equilibrium. Otherwise if $R_0 > 1$ as $\rho \geq 0$, then the model has a unique endemic equilibrium.

6.5 Sensitivity analysis

The simplest form of sensitivity analysis is to simply vary one value in a model by a given amount, and examine the impact that the change has on the model's results. Similarly like in previous chapters, we also perform the sensitivity analysis to check the model robustness to parameter values. This helps in knowing the parameters that have high impact on the diseases transmission and also helps in checking for errors in our model. Here, we also use the normalised forward sensitivity index of a variable to a parameter approach, described in [56], to carry out the analysis.

Sensitivity analysis of R_0

We derive the sensitivity of R_0 to each of the parameters described in Table (6.1). The sensitivity indices are shown below,

$$\frac{\partial R_0}{\partial c_1} \times \frac{c_1}{R_0} = \frac{\mu\,(\mu+\sigma)\,c_1\,\beta_1}{\mu\,(\mu+\sigma)\,c_1\,\beta_1+\gamma\,\mu\,c_2\,\beta_2+\gamma\,\sigma\,c_3\,\beta_3}$$

$$\frac{\partial R_0}{\partial \beta_1} \times \frac{\beta_1}{R_0} = \frac{\mu\,(\mu+\sigma)\,c_1\,\beta_1}{\mu\,(\mu+\sigma)\,c_1\,\beta_1+\gamma\,\mu\,c_2\,\beta_2+\gamma\,\sigma\,c_3\,\beta_3}$$

$$\frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = -\left(\frac{\gamma\,\mu\,((\mu+\sigma)\,c_1\,\beta_1-\mu\,c_2\,\beta_2-\sigma\,c_3\,\beta_3)}{(\gamma+\mu)\,(\mu\,(\mu+\sigma)\,c_1\,\beta_1+\gamma\,\mu\,c_2\,\beta_2+\gamma\,\sigma\,c_3\,\beta_3)}\right)$$

$$\frac{\partial R_0}{\partial \beta_2} \times \frac{\beta_2}{R_0} = \frac{\gamma\,\mu\,c_2\,\beta_2}{\mu\,(\mu+\sigma)\,c_1\,\beta_1+\gamma\,\mu\,c_2\,\beta_2+\gamma\,\sigma\,c_3\,\beta_3}$$

$$\frac{\partial R_0}{\partial \beta_3} \times \frac{\beta_3}{R_0} = \frac{\gamma\,\sigma\,c_3\,\beta_3}{\mu\,(\mu+\sigma)\,c_1\,\beta_1+\gamma\,\mu\,c_2\,\beta_2+\gamma\,\sigma\,c_3\,\beta_3}$$

$$\frac{\partial R_0}{\partial c_2} \times \frac{c_2}{R_0} = \frac{\gamma\,\mu\,c_2\,\beta_2}{\mu\,(\mu+\sigma)\,c_1\,\beta_1+\gamma\,\mu\,c_2\,\beta_2+\gamma\,\sigma\,c_3\,\beta_3}$$

$$\frac{\partial R_0}{\partial c_3} \times \frac{c_3}{R_0} = \frac{\gamma\,\sigma\,c_3\,\beta_3}{\mu\,(\mu+\sigma)\,c_1\,\beta_1+\gamma\,\mu\,c_2\,\beta_2+\gamma\,\sigma\,c_3\,\beta_3}$$

The parameters are arranged from the most sensitive to the least in Table (6.1). The most sensitive parameter here is the number of partners with AIDS

Table 6.1: Sensitivity indices of R_0 in parental care model

Parameter	Parameter description	Sensitivity
c_3	Number of partners with AIDS individual	+0.769
β_3	Transmission probability of getting AIDS	+0.769
μ	Natural death rate of individual	-0.6956
γ	Progression rate from susceptibles to infected	-0.1688
c_1	Num. of partners with infected individual	+0.133
β_1	Transmission probability of getting infected	+0.133
σ	Progression rate from HIV to AIDS	-0.0546
c_2	Number of partners with HIV individual	+0.019
β_2	Transmission probability of getting HIV	+0.019

individuals (c_3), followed by transmission probability of getting AIDS (β_3). Other important parameter is natural death rate of individual (μ). The least of the sensitivity parameters is the progression rate from HIV to AIDS (σ). The sensitivity indices of R_0 with respect to the transmission probability of getting AIDS (β_3) is +0.769, implying that decreasing (or increasing) the β_3 by 10% decreases (or increases) R_0 by 7.69%. Similarly increasing (or decreasing) the natural death rate (μ) by 10%, increases (or decreases) the R_0 by 6.96%.

In other words HIV/AIDS infected youths/teenagers having minimal or no partners to have blood contact with tends to reduce the transmission, otherwise increases it.
For all the parameters, the sign of the sensitivity indices of R_0 agrees with intuitive expectation whether R_0 increases or decreases when the parameters

increases.

Sensitivity analysis of state variables

Here, we derive the sensitivity of the state variables to each of the parameters described in Table (6.2). The sensitivity indices are shown below.

$$
\begin{cases}
\frac{\partial S^*}{\partial \sigma} \times \frac{\sigma}{S^*} = -\frac{\gamma\,\mu\,(\gamma+\mu)\,(-1+\rho\,u_1)\,(\mu\,c_2\,\beta_2-\mu\,c_3\,\beta_3)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3 a)^2} \\
\frac{\partial S^*}{\partial \rho} \times \frac{\rho}{S^*} = -\frac{\mu\,(\gamma+\mu)\,(\mu+\sigma)\,u_1}{\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3} \\
\frac{\partial S^*}{\partial u_1} \times \frac{u_1}{S^*} = -\frac{\mu\,(\gamma+\mu)\,\rho\,(\mu+\sigma)}{\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3} \\
\frac{\partial S^*}{\partial c_1} \times \frac{c_1}{S^*} = \frac{\mu^2\,(\gamma+\mu)\,(\mu+\sigma)^2\,(-1+\rho\,u_1)\,\beta_1}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial S^*}{\partial c_2} \times \frac{c_2}{S^*} = \frac{\gamma\,\mu^2\,(\gamma+\mu)\,(\mu+\sigma)\,(-1+\rho\,u_1)\,\beta_2}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial S^*}{\partial c_3} \times \frac{c_3}{S^*} = \frac{\gamma\,\mu\,(\gamma+\mu)\,\sigma\,(\mu+\sigma)\,(-1+\rho\,u_1)\,\beta_3}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial S^*}{\partial \beta_1} \times \frac{\beta_1}{S^*} = \frac{\mu^2\,(\gamma+\mu)\,(\mu+\sigma)^2\,c_1\,(-1+\rho\,u_1)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial S^*}{\partial \beta_2} \times \frac{\beta_2}{S^*} = \frac{\gamma\,\mu^2\,(\gamma+\mu)\,(\mu+\sigma)\,c_2\,(-1+\rho\,u_1)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial S^*}{\partial \beta_3} \times \frac{\beta_3}{S^*} = \frac{\gamma\,\mu\,(\gamma+\mu)\,\sigma\,(\mu+\sigma)\,c_3\,(-1+\rho\,u_1)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2}
\end{cases}
\tag{6.14}
$$

$$
\begin{cases}
\frac{\partial I^*}{\partial \sigma} \times \frac{\sigma}{I^*} = \frac{\gamma\,\mu^2\,(-1+\rho\,u_1)\,(\mu\,c_2\,\beta_2-\mu\,c_3\,\beta_3)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial I^*}{\partial \beta_1} \times \frac{\beta_1}{I^*} = -\frac{\mu^3\,(\mu+\sigma)^2\,c_1\,(-1+\rho\,u_1)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial I^*}{\partial \beta_2} \times \frac{\beta_2}{I^*} = -\frac{\gamma\,\mu^3\,(\mu+\sigma)\,c_2\,(-1+\rho\,u_1)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial I^*}{\partial \beta_3} \times \frac{\beta_3}{I^*} = -\frac{\gamma\,\mu^2\,\sigma\,(\mu+\sigma)\,c_3\,(-1+\rho\,u_1)}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial I^*}{\partial c_1} \times \frac{c_1}{I^*} = -\frac{\mu^3\,(\mu+\sigma)^2\,(-1+\rho\,u_1)\,\beta_1}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial I^*}{\partial c_2} \times \frac{c_2}{I^*} = -\frac{\gamma\,\mu^3\,(\mu+\sigma)\,(-1+\rho\,u_1)\,\beta_2}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial I^*}{\partial c_3} \times \frac{c_3}{I^*} = -\frac{\gamma\,\mu^2\,\sigma\,(\mu+\sigma)\,(-1+\rho\,u_1)\,\beta_3}{(\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3)^2} \\
\frac{\partial I^*}{\partial \rho} \times \frac{\rho}{I^*} = \frac{\mu^2\,(\mu+\sigma)\,u_1}{\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3} \\
\frac{\partial I^*}{\partial u_1} \times \frac{u_1}{I^*} = \frac{\mu^2\,\rho\,(\mu+\sigma)}{\mu\,((\mu+\sigma)\,c_1\,\beta_1+\gamma\,c_2\,\beta_2)+\gamma\,\sigma\,c_3\,\beta_3}
\end{cases}
\tag{6.15}
$$

$$
\begin{cases}
\frac{\partial H^*}{\partial \rho} \times \frac{\rho}{H^*} = \frac{\mu^2 u_1}{\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3} \\
\frac{\partial H^*}{\partial \gamma} \times \frac{\gamma}{H^*} = \mu \left(\frac{\mu}{(\gamma+\mu)^2 (\mu+\sigma)} + \frac{\mu\left((-\mu)(\mu+\sigma) c_1 \beta_1+\rho u_1\left((-\mu) c_2 \beta_2-\sigma c_3 \beta_3\right)\right)}{\left(\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3\right)^2} \right) \\
\frac{\partial H^*}{\partial u_1} \times \frac{u_1}{H^*} = \frac{\mu^2 \rho}{\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3} \\
\frac{\partial H^*}{\partial \beta_1} \times \frac{\beta_1}{H^*} = \frac{\mu^3 (\mu+\sigma) c_1 (\gamma-\rho u_1)}{\left(\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3\right)^2} \\
\frac{\partial H^*}{\partial \beta_2} \times \frac{\beta_2}{H^*} = \frac{\gamma \mu^3 c_2 (\gamma-\rho u_1)}{\left(\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3\right)^2} \\
\frac{\partial H^*}{\partial \beta_3} \times \frac{\beta_3}{H^*} = \frac{\gamma \mu^2 \sigma c_3 (\gamma-\rho u_1)}{\left(\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3\right)^2} \\
\frac{\partial H^*}{\partial c_1} \times \frac{c_1}{H^*} = \frac{\mu^3 (\mu+\sigma) (\gamma-\rho u_1) \beta_1}{\left(\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3\right)^2} \\
\frac{\partial H^*}{\partial c_2} \times \frac{c_2}{H^*} = \frac{\gamma \mu^3 (\gamma-\rho u_1) \beta_2}{\left(\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3\right)^2} \\
\frac{\partial H^*}{\partial c_3} \times \frac{c_3}{H^*} = \frac{\gamma \mu^2 \sigma (\gamma-\rho u_1) \beta_3}{\left(\mu\left((\mu+\sigma) c_1 \beta_1+\gamma c_2 \beta_2\right)+\gamma \sigma c_3 \beta_3\right)^2}
\end{cases}
\tag{6.16}
$$

$$
\begin{cases}
\frac{\partial A^*}{\partial \rho} \times \frac{\rho}{A^*} = \frac{\mu\, u_1}{\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3} \\
\frac{\partial A^*}{\partial u_1} \times \frac{u_1}{A^*} = \frac{\mu\, \rho}{\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3} \\
\frac{\partial A^*}{\partial \beta_1} \times \frac{\beta_1}{A^*} = \frac{\mu^2\, (\mu+\sigma)\, c_1\, (\gamma\, \sigma - \rho\, u_1)}{\left(\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3\right)^2} \\
\frac{\partial A^*}{\partial \beta_2} \times \frac{\beta_2}{A^*} = \frac{\gamma\, \mu^2\, c_2\, (\gamma\, \sigma - \rho\, u_1)}{\left(\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3\right)^2} \\
\frac{\partial A^*}{\partial \beta_3} \times \frac{\beta_3}{A^*} = \frac{\gamma\, \mu\, \sigma\, c_3\, (\gamma\, \sigma - \rho\, u_1)}{\left(\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3\right)^2} \\
\frac{\partial A^*}{\partial c_1} \times \frac{c_1}{A^*} = \frac{\mu^2\, (\mu+\sigma)\, (\gamma\, \sigma - \rho\, u_1)\, \beta_1}{\left(\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3\right)^2} \\
\frac{\partial A^*}{\partial c_2} \times \frac{c_2}{A^*} = \frac{\gamma\, \mu^2\, (\gamma\, \sigma - \rho\, u_1)\, \beta_2}{\left(\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3\right)^2} \\
\frac{\partial A^*}{\partial c_3} \times \frac{c_3}{A^*} = \frac{\gamma\, \mu\, \sigma\, (\gamma\, \sigma - \rho\, u_1)\, \beta_3}{\left(\mu\left((\mu+\sigma)\, c_1\, \beta_1 + \gamma\, c_2\, \beta_2\right) + \gamma\, \sigma\, c_3\, \beta_3\right)^2}.
\end{cases}
\tag{6.17}
$$

From Table 6.2., we notice in row two that the natural death rate (μ) is most sensitive on AIDS individual (A^*) with 6.61061, and least sensitive on susceptibles individual (S^*) with 1.54053. If we thus increase or decrease μ by 10%, then S^* increases or decreases by 15.6653%, I^* by 42.9449%, H^* by 49.5083% and A^* by 66.1061%. Other parameters can be assessed further.

In the next chapter we proceed to study the optimal control and analysis of our model, considering the important model parameters. Into the model we include time dependent control measures for preventive interventions such as parental control/care and any other control on youths. Then we apply the optimal control method using Pontryagin's Maximum Principle to determine the necessary conditions for the control of HIV/AIDS.

Table 6.2: Sensitivity indices of state variables to model parameters on parental care

	S^*	I^*	H^*	A^*
ρ	-0.02807363	-0.0259964	-0.025820357	1.25717
μ	1.54053	4.29449	4.95083	6.61061
γ	0.001135	-0.0751882	-0.000237529	-2.73045
σ	0.0000738101	-0.000000128	-0.0996473	-3.17104
u_1	-0.000115202	0.0000002	0.000009198	0.071287
β_1	-0.000880152	0.000001528	-0.000001175653	-0.0254013
β_2	-0.0002525392	0.00000043843	-0.000000504	-0.0072883
β_3	-0.144308	0.000250534	-0.000287998	-4.16474
c_1	-0.00000748	0.0000000129884	-0.0000001493	-0.000215911
c_2	-0.00000588	0.00000001	-0.00000001159	-0.000167631
c_3	-0.000542234	0.000000914555	-0.00000108	-0.01533178

Chapter 7

Optimal control analysis of screening control and parental care

We proceed to the study of the optimal control of our model of Chapter 6 and its analysis considering the important model parameters. We include into the model time dependent control measures for preventive interventions such as parental control/care and any other control on youths. Then we apply the optimal control method using Pontryagin's Maximum Principle to determine the necessary conditions for the control of HIV/AIDS.

7.1 The control problem and solution

In order to investigate the optimal level of parental effort that would be needed to control the disease, we propose an objective function J below, which is to be minimized:

$$J = \int_0^\tau [Q_0 H + Q_1 I + Q_2 A + Q_3 u_1^2 + Q_4 u_2^2] dt, \tag{7.1}$$

for some $\tau > 0$. Here Q_1, Q_2, Q_3, Q_4 are positive weights, and we choose quadratic cost on the controls which is similar to other literature on epidemic controls see [2, 50, 74, 55]. With the given objective function $J(u_1, u_2)$, our goal is to minimize the number of infected youths and teenagers $I(t)$, being balance

against minimizing the cost of control $u_1(t), u_2(t)$. We choose an optimal control $u_1^*(t), u_2^*(t)$ such that

$$J(u_1^*, u_2^*) = \min\{J(u_1, u_2) | u_1, u_2 \in U\}, \tag{7.2}$$

where $U = \{(u_1, u_2)$ such that (u_1, u_2) are measurable, with $0 \leq u_1 \leq u_2 \leq 1\}$. The necessary conditions that optimal control must satisfy come from the Pontryagin's Maximum Principle [77]. This principle converts (6.2) and (7.2) into a problem of minimizing point wise a Hamiltonian $\mathcal{H}$, with respect to u_1 and u_2. The Hamiltonian is:

$$\begin{aligned}
&\mathcal{H} = Q_0 H + Q_1 I + Q_2 A + Q_3 u_1^2 + Q_4 u_2^2 \\
&+\eta_S[(1-\rho u_1)\,\mu\, - s\,(1-u_2)\,(\,i\,c_1\,\beta_1 + h\,c_2\,\beta_2 + a\,c_3\,\beta_3) - \mu s] \\
&+\eta_I[\rho u_1 \mu\, + s\,(1-u_2)\,(\,i\,c_1\,\beta_1 + h\,c_2\,\beta_2 + a\,c_3\,\beta_3) -\,(\gamma+\mu)\,i] \\
&+\eta_H[\gamma i - (\mu+\sigma)\,h] \\
&+\eta_A[\sigma h - \mu a],
\end{aligned} \tag{7.3}$$

where η_S, η_I, η_H and η_A are the adjoint variables. Applying Pontryagin's Maximum Principle and the existence result for the optimal control from [25], we obtain

Proposition 7.1.1. *For the optimal control (u_1^*, u_2^*) that minimizes $J(u_1, u_2)$, the adjoint variables η_S, η_I, η_H and η_A satisfy the following odes*

$$\begin{aligned}
-\tfrac{d\eta_S}{dt} &= (-1+u_2)\,(i\,c_1\,\beta_1 + h\,c_2\,\beta_2 + a\,c_3\,\beta_3)\,(\eta_i - \eta_s) + \mu\,\eta_s, \\
-\tfrac{d\eta_I}{dt} &= -Q_1 + s\,c_1\,(-1+u_2)\,\beta_1\,(-\eta_1 + \eta_2) - \gamma\,\eta_h + (\gamma+\mu)\,\eta_i, \\
-\tfrac{d\eta_H}{dt} &= -\,(\sigma\,\eta_a) + (\mu+\sigma)\,\eta_h + s\,c_2\,(-1+u_2)\,\beta_2\,(\eta_i - \eta_s)\,, \\
-\tfrac{d\eta_A}{dt} &= -Q_2 + \mu\,\eta_a + s\,c_3\,(-1+u_2)\,\beta_3\,(\eta_i - \eta_s)\,,
\end{aligned} \tag{7.4}$$

with transversality conditions

$$\eta_s(\tau) = \eta_i(\tau) = \eta_h(\tau) = \eta_a(\tau) = 0. \tag{7.5}$$

The optimal controls take the form :

$$
\begin{aligned}
u_1^* &= \max\{0,\ \min(1, \tfrac{\mu\,\rho\,\eta_i+\mu\,\rho\,\eta_s}{2\,Q_3})\} \\
u_2^* &= \max\{0,\ \min(1, \tfrac{s\,(i\,c_1\,\beta_1+h\,c_2\,\beta_2+a\,c_3\,\beta_3)\,\eta_i-s\,(i\,c_1\,\beta_1+h\,c_2\,\beta_2+a\,c_3\,\beta_3)\,\eta_s}{2\,Q_4})\}.
\end{aligned} \tag{7.6}
$$

Proof. Fleming et al. [25] gives the existence of an optimal control due to the convexity of the integrand of J with respect to u_1, u_2, a priori boundedness of the state solutions, and the Lipschitz property of the state system with respect to the variables. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control.

$$
\begin{aligned}
-\tfrac{d\eta_S}{dt} &= \tfrac{\partial \mathcal{H}}{\partial S} = (-1+u_2)\ (i\,c_1\,\beta_1 + h\,c_2\,\beta_2 + a\,c_3\,\beta_3)\ (\eta_i - \eta_s) + \mu\,\eta_s, \\
-\tfrac{d\eta_I}{dt} &= \tfrac{\partial \mathcal{H}}{\partial I} = -Q_1 + s\,c_1\ (-1+u_2)\ \beta_1\ (-\eta_1+\eta_2) - \gamma\,\eta_h + (\gamma+\mu)\ \eta_i, \\
-\tfrac{d\eta_H}{dt} &= \tfrac{\partial \mathcal{H}}{\partial H} = -\,(\sigma\,\eta_a) + (\mu+\sigma)\ \eta_h + s\,c_2\ (-1+u_2)\ \beta_2\ (\eta_i - \eta_s)\,, \\
-\tfrac{d\eta_A}{dt} &= \tfrac{\partial \mathcal{H}}{\partial A} = -Q_2 + \mu\,\eta_a + s\,c_3\ (-1+u_2)\ \beta_3\ (\eta_i - \eta_s)\,.
\end{aligned} \tag{7.7}
$$

By standard control arguments involving the bounds on the controls, we conclude

$$
u_1^* = \begin{cases} 0 & \text{if } \zeta_1^* \le 0, \\ \zeta_1^* & \text{if } 0 < \zeta_1^* < 1 \\ 1 & \text{if } \zeta_1^* \ge 1 \end{cases}
$$

$$
u_2^* = \begin{cases} 0 & \text{if } \zeta_2^* \le 0, \\ \zeta_2^* & \text{if } 0 < \zeta_2^* < 1 \\ 1 & \text{if } \zeta_2^* \ge 1 \end{cases}
$$

where

$$
\begin{aligned}
\zeta_1^* &= \tfrac{\mu\,\rho\,\eta_i+\mu\,\rho\,\eta_s}{2\,Q_3}, \\
\zeta_2^* &= \tfrac{s\,(i\,c_1\,\beta_1+h\,c_2\,\beta_2+a\,c_3\,\beta_3)\,\eta_i-s\,(i\,c_1\,\beta_1+h\,c_2\,\beta_2+a\,c_3\,\beta_3)\,\eta_s}{2\,Q_4}.
\end{aligned} \tag{7.8}
$$

Due to the boundedness of the state system, adjoint system and the resulting Lipschitz structure of the ODEs, we obtain the uniqueness of the optimal control for small τ. Uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of (7.1) and (7.2) with characterization (7.3). □

7.2 Numerical results and discussion

In this section we present some numerical solutions to the control problem. An iterative scheme is used for solving the optimality system. Using a fourth order Runge-Kutta scheme, we start off with a guess for the control over the simulated time, and solve for the state variables in a forward way. Because of the transversality conditions (7.5), the co-state variables are solved by a backward scheme using the current iterations solutions of the state equation. Then the controls are updated by using a convex combination of the previous controls and the value from the characterizations (7.6). This process is repeated and iteration stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iterations, see [55].

We examine our deterministic model and study the effects of screening control (u_1) and parental care (u_2) on each of the classes. We also investigate numerically the effect of the following optimal control strategies on the spread of HIV/AIDS among the youths.

- Strategy A: Optimal use of screening control (u_1) and parental care (u_2) on individuals.
- Strategy B: The use of only screening control (u_1) on individuals.
- Strategy C: The use of only parental care (u_2) on individuals.

We assume that the weight factor Q_4, associated with control u_2 is greater than Q_3 which is associated with u_1. This assumption is based on the fact that the cost associated with u_1 will include the cost of screening and surveillance, while those associated with u_2 will include the cost of education, hospitalization, medical test and so on. We have chosen the same set of weight factor $Q_1 = 920$, $Q_2 = 25$, $Q_3 = 80$ initial variables $S(0) = 700$, $I(0) = 100$, $H(0) = 10$, $A(0) = 0$ to illustrate the effect of different optimal control strategies on the spread of HIV/AIDS among the youths. Thus, we have considered the spread of HIV/AIDS in an endemic population.

Table 7.1: Parameters values used in simulating parental care model

Parameter	Parameter description	Estimated value	References
c_3	Num. of partners with AIDS indiv.	1	Estimate
β_3	Trans. prob. of getting AIDS	$0 \leq \beta_3 \leq 1$	[65]
μ	Natural death rate of individual	0.03	[16, 65]
γ	Prog. rate from S to I	0.18	[65]
c_1	Num. of partners with infected indiv.	4	Estimate
β_1	Trans. prob. of getting infected	$0 \leq \beta_1 \leq 1$	[65]
σ	Prog. rate from HIV to AIDS	0.05	[65]
c_2	Num. of partners with HIV indiv.	3	Estimate
β_2	Trans. prob. of getting HIV	$0 \leq \beta_2 \leq 1$	[65]

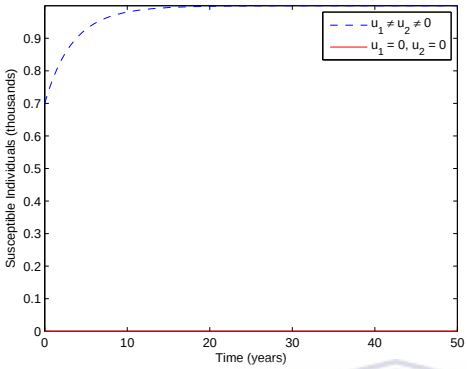
Strategy A: Optimal use of screening control (u_1) and parental care (u_2) on individuals.
The screening control (u_1) and parental care (u_2) are used to optimize the objective function J. We observe in Fig. 7.1(b) that due to control strategies, the number of infected individuals I decreases to zero at time $t = 19$ while the population of infectious increases when there is no control. Also in Fig. 7.1(c), the number of HIV individuals decreases to zero at $t = 25$ when there is control when no control. AIDS individuals in Fig. 7.1(d) increases and later decreases to zero at $t = 27$ when there is control, and increases when no control. The control profile in Fig. 7.1(e) shows that maximum effort is required on screening control (u_1) till the end of intervention, while parental care (u_2) can be relaxed at a certain period of time.

Strategy B: The use of only screening control (u_1) on individuals.
Here, only screening control u_1 is used to optimize the objective function J while we set the parental care (u_2) to zero. We observe in Fig. 7.2(b) infectives decrease to zero at $t = 20$ with screening control, and decrease to zero at $t = 25$ when no control. It is also noted that population of HIV individuals decrease to zero at $t = 27$ with screening and tends to zero at $t = 30$ when uncontrolled in Fig. 7.2(c). Population of AIDS individuals first increase but later decrease to zero at $t = 30$ with screening and down to zero at $t = 32$ in Fig. 7.2(d) when no control. The control profile in Fig. 7.2(e) also shows that maximum effort is required by screening control (u_1) even in the absence of parental care. All these imply no much difference between controlled and uncontrolled in the case of screening control.

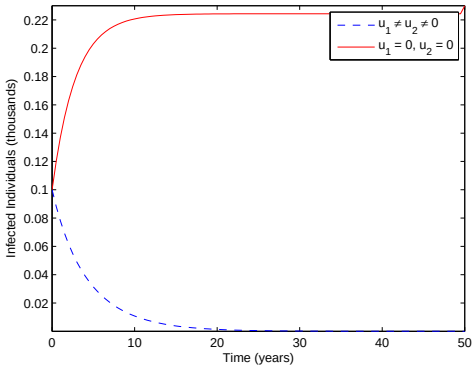
Strategy C: The use of only parental care (u_2) on individuals.
Simulations here are similar to that of strategy A with only slight difference. Only the parental care (u_2) is used to optimize the objective function J while screening control (u_1) is set to zero. We observe in Fig. 7.3(b) that due to control strategies, the number of infected individuals I decrease to zero at time $t = 21$ while the population of infectious increases when there is no control. Similarly in Fig. 7.3(c), the number of HIV individuals decrease to zero at $t = 26$ when there is parental care, but increase when no control. AIDS individuals in Fig. 7.3(d) increase from initial 0 to 750 and later decrease to zero at $t = 29$, but increase rapidly when there is no control. The control profile in Fig. 7.3(e) also shows that maximum effort is required on screening control (u_1) throughout the period, while that of parental care (u_2) can be

Figure 7.1: Simulations of the HIV/AIDS model showing the effect of optimal control strategies using screening control and parental care on individuals.

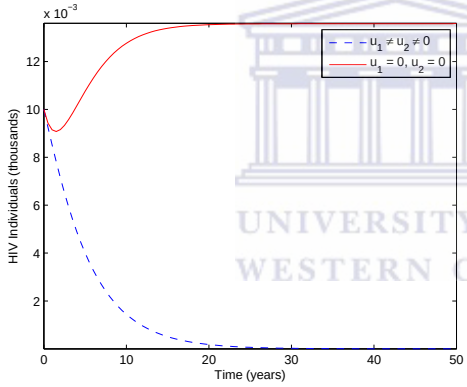
(a)



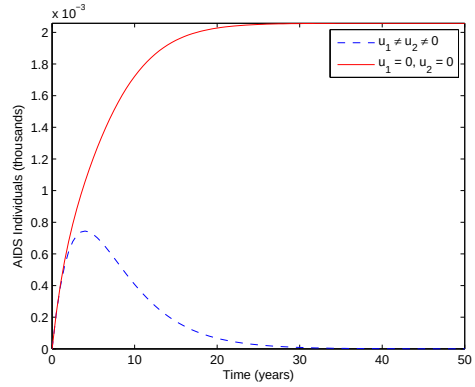
(b)



(c)



(d)



(e)

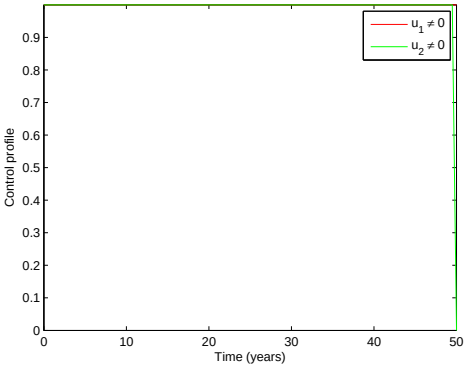
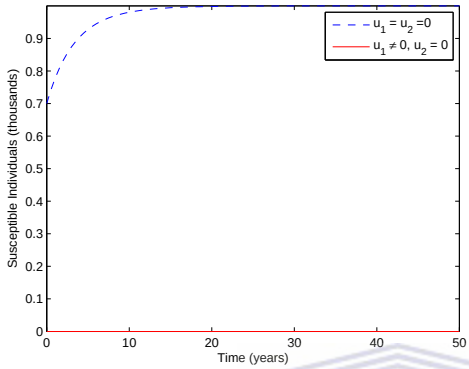
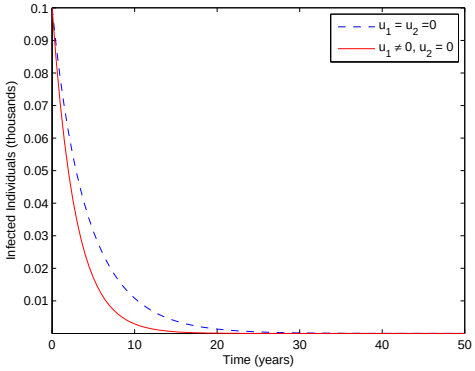


Figure 7.2: Simulations of the HIV/AIDS model showing the effect of optimal control strategies using only screening control (without parental care) on individuals.

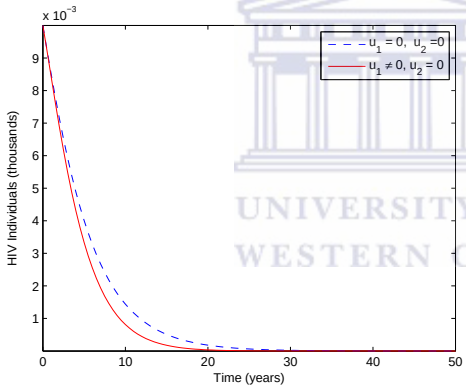
(a)



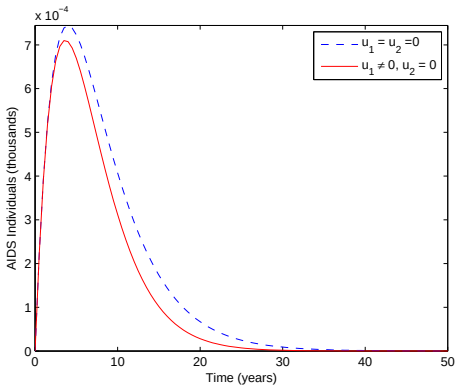
(b)



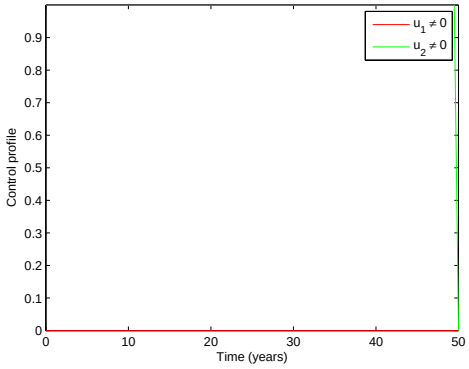
(c)



(d)



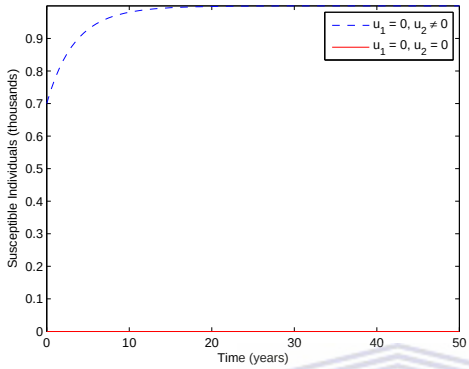
(e)



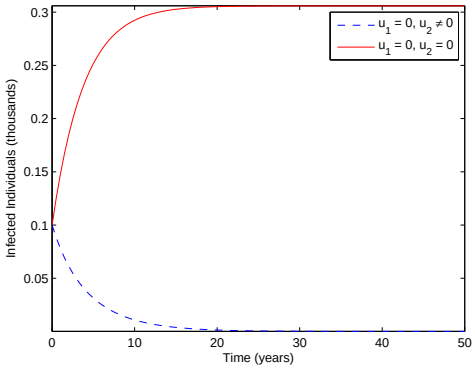
relaxed at a certain period of time.

Figure 7.3: Simulations of the HIV/AIDS model showing the effect of optimal control strategies using only parental care (without screening control) on individuals.

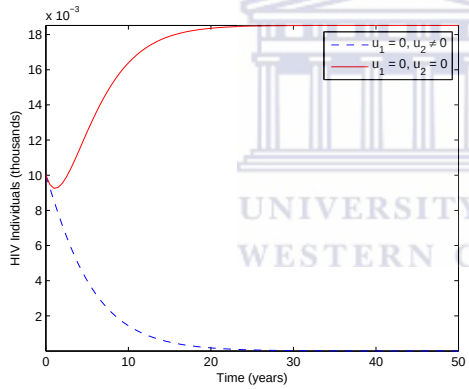
(a)



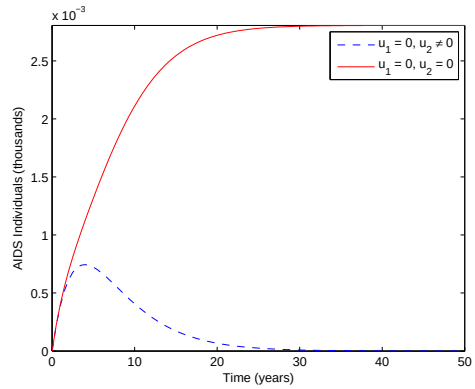
(b)



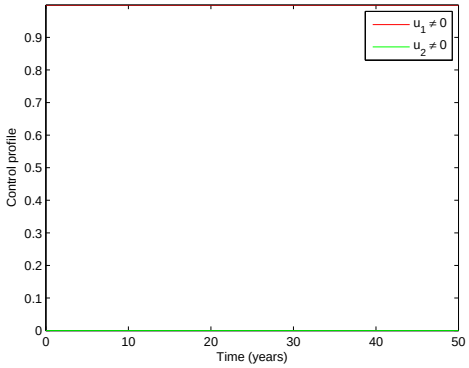
(c)



(d)



(e)



Chapter 8

Optimal control analysis of public-health campaign and infectives withdrawal

In this Chapter, we want to investigate the optimal level of efforts that would be needed to control HIV/AIDS with the use of public-health campaigning and infectives withdrawal. For this to be achieved, we proceed to the study of the optimal control of our model in Chapter 5. We include into the model time dependent control measures for preventive interventions that is public-health and infective withdrawal. Then we apply optimal control method using Pontryagin's Maximum Principle to determine the necessary conditions for the control of HIV/AIDS.

8.1 The control problem

We propose an objective functional J, in terms of which we shall minimize the number of human infectives and AIDS individuals.

$$J = \int_0^\tau [M_0 I_1 + M_1 I_2 + M_2 A + M_3 q^2 + M_4 \alpha^2] dt \tag{8.1}$$

where M_1, M_2, M_3, M_4 are positive weights. With the given objective function $J(q, \alpha)$, our goal here is also to minimize the number of infectives $(I_1(t), I_2(t))$ and AIDS $A(t)$ individuals, while also minimizing the cost of control $q(t), \alpha(t)$ and we also choose quadratic cost on the controls which is similar to other

literature on epidemic controls. Like in Chapter 7, the squares in the integrand of J ensures that the Hamiltonian is convex with respect to the control variables. We choose optimal control q, α such that

$$J(q^*, \alpha^*) = \min\{J(q, \alpha) | q, \alpha \in U\}, \tag{8.2}$$

where $U = \{(q, \alpha)$ such that $(q(t), \alpha(t))$ are measurable with $0 \leq q \leq \alpha \leq 1\}$ is the control set. Here we also incorporate the Pontryagin's Maximum Principle. This principle concerns a Hamiltonian function $\mathcal{H}$, which for our problem is as follows

$$\begin{aligned}
&\mathcal{H} = M_0 H + M_1 I + M_2 A + M_3 q^2 + M_4 \alpha^2 \\
&+\Phi_S[\mu b - \mu S - \lambda(\mathbf{I}, A)S] \\
&+\Phi_{I_1}[\lambda(\mathbf{I}, A)S - (\mu + \sigma)I_1] \\
&+\Phi_{I_2}[\sigma I_1 - (\mu + \rho)I_2] \\
&+\Phi_A[\rho I_2 - (\mu + \delta)A],
\end{aligned} \tag{8.3}$$

where $\Phi_S, \Phi_{I_1}, \Phi_{I_2}$ and Φ_A are the adjoint variables. Applying Pontryagin's Maximum Principle, we obtain the following proposition which characterizes the optimal control.

Proposition 8.1.1. *For the optimal control (q^*, α^*) that minimizes $J(q, \alpha)$, the adjoint variables $\Phi_S, \Phi_{I_1}, \Phi_{I_2}$ and Φ_A satisfy the following odes*

$$\begin{aligned}
-\tfrac{d\Phi_S}{dt} &= (S - b)\ \mu + \tfrac{c\,\beta\,(-(\alpha\, I_1) - \alpha\, I_2\, \eta_1 + A\,(q-1)\,\alpha\,\eta_2)}{\alpha\,(1 + \alpha\, I_1 + \alpha\, I_2\, \eta_1 - A\,(q-1)\,\alpha\,\eta_2)} \\
-\tfrac{d\Phi_{I_1}}{dt} &= (\mu + \sigma)\ I_1 + \tfrac{c\, S\, \beta\,(\alpha\, I_1 + \alpha\, I_2\, \eta_1 - A\,(q-1)\,\alpha\,\eta_2)}{\alpha\,(1 + \alpha\, I_1 + \alpha\, I_2\, \eta_1 - A\,(q-1)\,\alpha\,\eta_2)} \\
-\tfrac{d\Phi_{I_2}}{dt} &= -\,(\sigma\, I_1) + (\mu + \rho)\ I_2 \\
-\tfrac{d\Phi_A}{dt} &= A\ (\delta + \mu) - \rho\, I_2
\end{aligned} \tag{8.4}$$

and with transversality conditions

$$\Phi_S(\tau) = \Phi_{I_1}(\tau) = \Phi_{I_2}(\tau) = \Phi_A(\tau) = 0. \tag{8.5}$$

The optimal controls take the form:

$$\begin{aligned} q^* &= \max\{0, \quad \min(1, \tfrac{\mu\, b\, \Phi_{I_1} + \mu\, b\, \Phi_S}{2\, M_3})\}, \\ \alpha^* &= \max\{0, \quad \min(1, \tfrac{c\, S\, \beta\, M_4\, (I_1 + I_2\, \eta_1 + A\, (1-q)\, \eta_2)\, \phi_S}{2\, (1+\alpha\, (I_1 + I_2\, \eta_1 + A\, (1-q)\, \eta_2))})\}. \end{aligned} \tag{8.6}$$

Proof. Fleming et al. [25] gives the existence of an optimal control due to the convexity of the integrand of J with respect to q, α, a priori boundedness of the state solutions, and the Lipschitz property of the state system with respect to the variables. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control.

$$\begin{aligned} -\tfrac{d\Phi_S}{dt} &= \tfrac{d\mathcal{H}}{dS} = (S - b)\ \mu + \tfrac{c\, \beta\, (-(\alpha\, I_1) - \alpha\, I_2\, \eta_1 + A\, (q-1)\, \alpha\, \eta_2)}{\alpha\, (1 + \alpha\, I_1 + \alpha\, I_2\, \eta_1 - A\, (q-1)\, \alpha\, \eta_2)} \\ -\tfrac{d\Phi_{I_1}}{dt} &= \tfrac{d\mathcal{H}}{dI_1} = (\mu + \sigma)\ I_1 + \tfrac{c\, S\, \beta\, (\alpha\, I_1 + \alpha\, I_2\, \eta_1 - A\, (q-1)\, \alpha\, \eta_2)}{\alpha\, (1 + \alpha\, I_1 + \alpha\, I_2\, \eta_1 - A\, (q-1)\, \alpha\, \eta_2)} \\ -\tfrac{d\Phi_{I_2}}{dt} &= \tfrac{d\mathcal{H}}{dI_2} = -(\sigma\, I_1) + (\mu + \rho)\ I_2 \\ -\tfrac{d\Phi_A}{dt} &= \tfrac{d\mathcal{H}}{dA} = A\, (\delta + \mu) - \rho\, I_2 \end{aligned} \tag{8.7}$$

By standard control arguments involving the bounds on the controls, we conclude

$$q^* = \begin{cases} 0 & \text{if } \zeta_1^* \leq 0, \\ \zeta_1^* & \text{if } 0 < \zeta_1^* < 1 \\ 1 & \text{if } \zeta_1^* \geq 1 \end{cases}$$

$$\alpha^* = \begin{cases} 0 & \text{if } \zeta_2^* \leq 0, \\ \zeta_2^* & \text{if } 0 < \zeta_2^* < 1 \\ 1 & \text{if } \zeta_2^* \geq 1 \end{cases}$$

where

$$\begin{aligned} \zeta_1^* &= \tfrac{\mu\, b\, \Phi_{I_1} + \mu\, b\, \Phi_S}{2\, M_3}, \\ \zeta_2^* &= \tfrac{c\, S\, \beta\, M_4\, (I_1 + I_2\, \eta_1 + A\, (1-q)\, \eta_2)\, \phi_S}{2\, (1+\alpha\, (I_1 + I_2\, \eta_1 + A\, (1-q)\, \eta_2))}. \end{aligned} \tag{8.8}$$

The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of (8.1) and (8.2) with characterization (8.3). □

8.2 Numerical results and discussion

Here we generate some numerical solutions to our control problem using forth order Runge-Kutta scheme. This method is also tested for convergence. We use the scheme to solve our transversality conditions in (8.5) and update our control with the combination of previous controls and values from characterization (8.6). The process is repeated while iterations stop when unknown values of the previous iterations are very close to the present ones, see also [55]. A number of different numerical simulations are carried out for comparisons in Fig. (8.1) to Fig. (8.3). The values of parameter used in the simulations are presented in Table 8.1 and some of these parameters are varied to test the robustness of our methods.

We use our model to study the effects of public-health campaigns (α) and infectives withdrawals (q) on each of the classes. We also investigate numerically the effect of the following optimal control strategies on the spread of HIV/AIDS in a population.

- Strategy A: Optimal use of public-health campaigns (α) and infectives withdrawals (α) on individuals.
- Strategy B: The use of only public-health campaigns (α) on individuals.
- Strategy C: The use of only infectives withdrawals (q) on individuals.

Here we choose a set of weight factors M_1=920, M_2=25, M_3=80 together with initial variables $S(0)$=400, $I_1(0)$=400, $I_2(0)$=500, $A(0)$=600 to illustrate the effect of different optimal control strategies on the spread of HIV/AIDS. Thus, we have considered the spread of HIV/AIDS in an endemic population.

Strategy A: Optimal use of public-health campaigns (α) and infectives withdrawals (q) on individuals.
The infectives withdrawals (q) and public-health campaigns (α) are used to

Table 8.1: Parameter values used in simulating education model

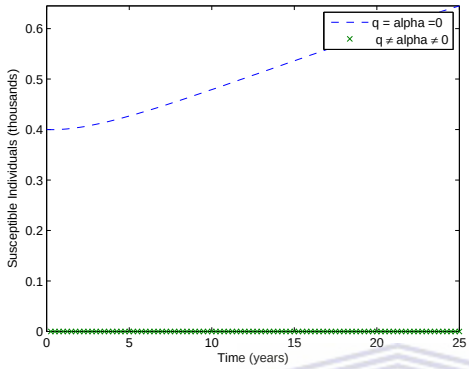
Parameter	Parameter description	value	Source
c	Partner acquisition rate	1.5	[73]
q	Proportion of withdrawals by AIDS	0.5	[73]
σ	Rate of becoming symptomatic	0.14	[73]
μ	Natural death rate	0.02	[16]
ρ	Rate of developing AIDS	0.05	[73]
β	Probability of transmission	0.5	[73]
(η_1, η_2)	Enhancement factor	1,2	[16]
δ	Disease-induced death rate	0.33	[73]

optimize the objective function J. We observe in Fig. 8.1(b) that due to control strategies, the number of asymptomatic infectives individuals I_1 decreases to zero at time t=25 while the population increases when there is no control. Also in Fig. 8.1(c), the number of symptomatic infectives individuals I_2 first increases from initial 500 but later decreases to zero at t=25 when there is control while decreases to zero at t=26. This implies that there is only slight difference between when there is control and when no control in the case of symptomatic infectives individuals I_2. Both control overlap in AIDS individuals in Fig. 8.1(d) and decrease from initial 600 to 0 at t=15. The control profile in Fig. 8.1(e) shows that maximum effort is required on public-health campaigns (α) till the end of intervention, while infectives withdrawals (q) can be relaxed at a certain period of time.

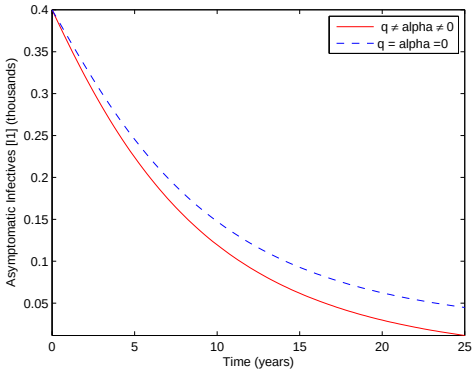
Strategy B: The use of only public-health campaigns (α) on individ-

Figure 8.1: Simulations of the HIV/AIDS model showing the effect of optimal control strategies using public-health campaigns and infectives withdrawal on individuals.

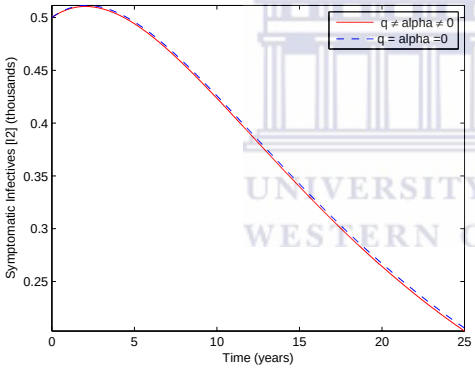
(a)



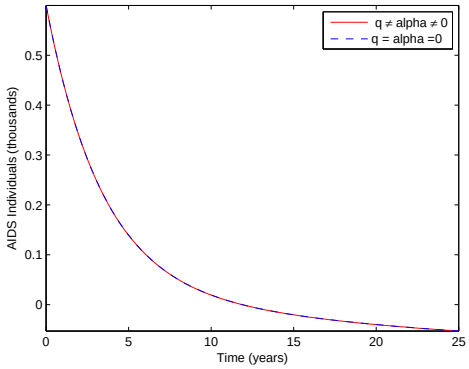
(b)



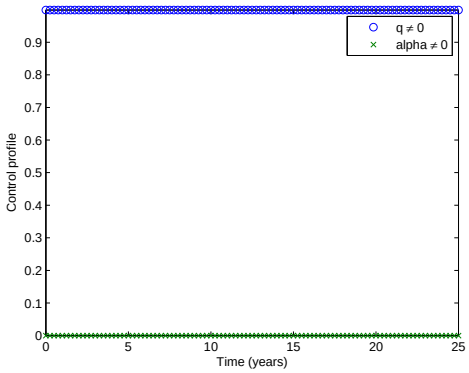
(c)



(d)



(e)

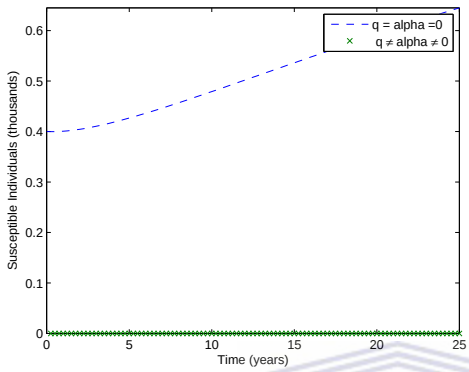


uals.
Here, only public-health campaigns α is used to optimize the objective function J while we set infectives withdrawal (q) to zero. We observe overlapping in each of the classes showing that no much difference between controlled and uncontrolled. It is also noted that there is a rapid increase in population of asymptomatic infectives individuals I_1, symptomatic infectives individuals I_2 and AIDS individuals A in Fig. 8.2(b), 8.2(c), and 8.2(d) respectively. The control profile in Fig. 8.2(e) also shows that maximum effort is required on public-health campaigns (α) till the end of intervention even in the absence of infectives withdrawal (q).

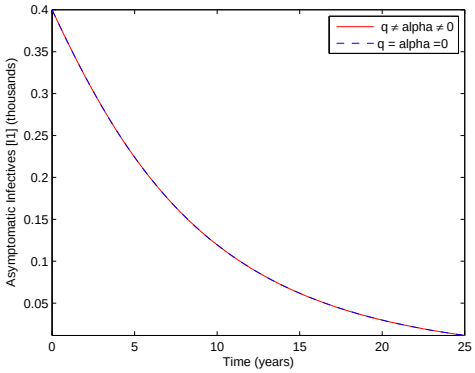
Strategy C: The use of only infectives withdrawal (q) on individuals.
Simulations here are similar to that of strategy A with only slight difference. Only the infectives withdrawals (q) is used to optimize the objective function J while public-health campaigns (α) is set to zero. We observe in Fig 8.1(b) that due to control strategies, the number of asymptomatic infectives individuals I_1 decreases to zero at time t=25 while the population increases when there is no control. Also in Fig. 8.1(c), the number of symptomatic infectives individuals I_2 first increases from initial 500 but later decreases to zero at t=25 when there is control while decreases to zero at t=25. This implies that there is only slight difference between when there is control and when no control in the case of symptomatic infectives individuals I_2. Both control overlap in AIDS individuals in Fig. 8.1(d) and decrease from initial 600 to 0 at t=17. The control profile in Fig. 8.1(e) still showing that maximum effort is required on public-health campaigns (α) till the end of intervention, while infectives withdrawal (q) can be relaxed at a certain period of time.

Figure 8.2: Simulations of the HIV/AIDS model showing the effect of optimal control strategies using only public-health campaigns (without infectives withdrawal) on individuals.

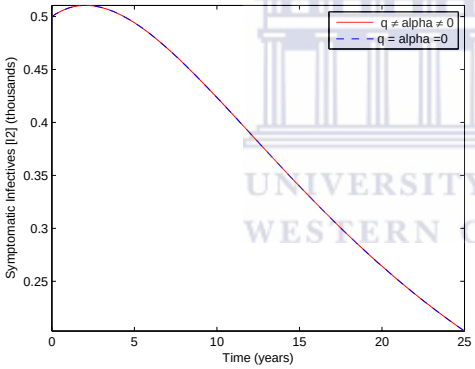
(a)



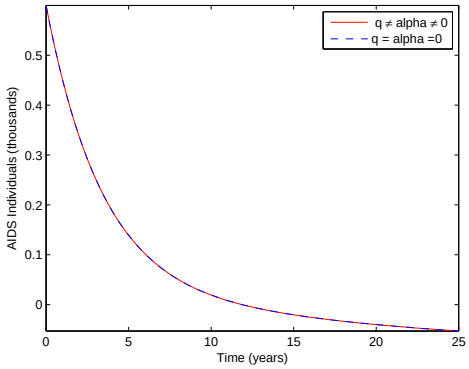
(b)



(c)



(d)



(e)

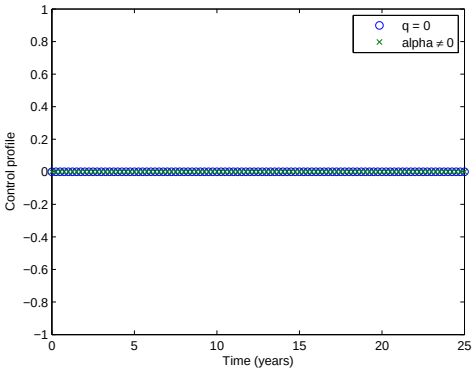
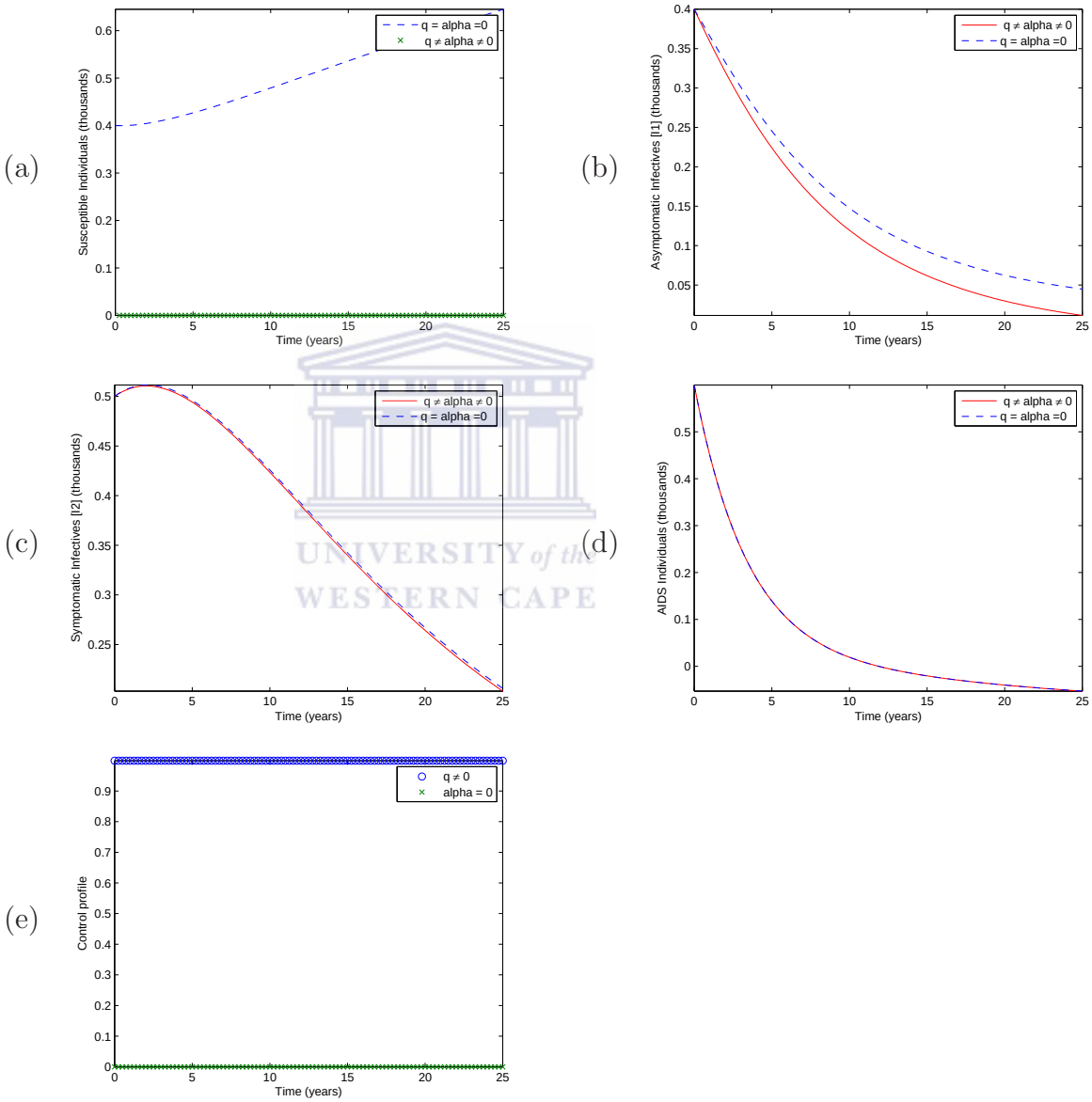


Figure 8.3: Simulations of the HIV/AIDS model showing the effect of optimal control strategies using infectives withdrawal (without public-health campaigns) on individuals.



Chapter 9

Conclusion

9.1 Observation of this research

In this study, we derived and analyzed various deterministic models for the transmission of HIV/AIDS. In Chapter 4, we analyzed HIV/AIDS model with carefree susceptibles and treatment. We analyzed the model for the existence of diseases-free and endemic equilibrium points. We discovered the model cannot have disease free equilibrium if careful susceptibles enlightenment control is not maintained. Hence it has an endemic equilibrium point in which the disease persists in the population. We also carried out the sensitivity analysis for reproduction number R_0. From this analysis, we found out that the most sensitive parameter is the probability of careful susceptible contact with infectives and least is the natural mortality related to HIV/AIDS.

In Chapter 5, we analyzed HIV/AIDS model with public-health campaigns and infectives voluntary withdrawal. We analyzed the model for the existence of diseases-free and endemic equilibrium points. We discovered the model cannot have disease free equilibrium if infectives individuals refuse to withdraw from sexual activities. Hence has an endemic equilibrium point in which disease persists in the population. We also carried out the sensitivity analysis for both R_0 and state variables. This analysis showed that the most sensitive parameter is the partner acquisition rate and the least is proportion of withdrawals by AIDS cases. Sensitivity analysis of the state variables was also carried out and there we noticed that probability of transmission (β) is more sensitive on AIDS (A^*) than on asymptomatic infectives on (I_1^*). We also noticed that partner acquisition rate (c) is more sensitive on (S^*) than on (A^*).

In Chapter 6, we derived and analyzed a deterministic model for the transmission of HIV/AIDS. We also analyzed the model for the existence of disease-free and endemic equilibrium points. We discovered that the model cannot have a disease free equilibrium in the presence of immigration of infected and/or infectious youths and it has an endemic equilibrium point in which the disease persists in the community. This discovery agrees with Brauer and van den Driessche [14] on general SIR model with infective immigrants. We also found from the sensitivity indices analysis that the most sensitivity parameters are number of contact with AIDS individuals (c_3), transmission probability of getting AIDS (β_3) and natural death rate (μ). The sensitivity analysis for the state variable shows that the natural death rate (μ) is sensitive on S^*, I^* and H^*.

In Chapter 7, we analzed the effect of screening control and parental care on the transmission of the disease by performing optimal control analysis on our model. We derived and analyzed the conditions for optimal control of the disease with screening control and parental care on youths.
From our numerical results, the control profiles in each of the strategies used explained that maximum effort is required on screening control through the intervention while parental care can be relaxed after a period of time. We further found that infected immigrants have no strong impact in the disease transmission, if there is effective parental care or control over the youths. However, the combination of the screening of infected immigrants and parental care applied together give best and more efficient results in controlling the spread of HIV/AIDS.

In Chapter 8, we examined the effect of public-health campaign and infectives withdrawal on the transmission of the disease by performing optimal control analysis on the model. We also derived and analyzed the conditions for optimal control of the disease with public-health campaign and infectives withdrawal. Our numerical results shows that the control profiles in each of the strategies used explained that maximum effort is required on public-health campaigns through the intervention while infectives withdrawal can be relaxed after a period of time. We also found that public-health campaigns have no strong impact in the disease transmission if there is effective infectives withdrawal. However, the combination of public-health campaigns and infectives withdrawal applied together offer the best and more efficient results in controlling the spread of HIV/AIDS. Hence the control programs that follow these

strategies can also reduce the spread of HIV/AIDS.

In general this thesis contributes to understanding HIV population dynamics, and informing optimal strategies for intervention. Therefore control programs that follow these strategies can effectively reduce the spread of HIV/AIDS.

9.2 Possible continuation

Our model does not consider some factors and approach below which may influence the spread of HIV/AIDS. Considering these factors properly may provide a better understanding of the disease and its control.

Stochastic approach: Our model and approach in this thesis is deterministic. Reviewing all analyses and comparing the results obtained with stochastic modelling and approach will enable us to choose the best approach in controlling HIV/AIDS.

Culture/Religion: The impact of religion and culture on transmission of HIV/AIDS allows us to investigate the relationship between the spread of HIV/AIDS and religion.

Co-infection: The impact of co-infection in the dynamics of infectious disease cannot be neglected in our present day. This will allow us to study Malaria and HIV/AIDS co-infection and how best to control them.

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