Cape Peninsula
University of Technology

# MODELLING THE OPTIMAL EFFICIENCY OF INDUSTRIAL LABOUR FORCE IN THE PRESENCE OF HIV/AIDS PANDEMIC

by

**ISAAC TAKAIDZA**

(Student Number 210266384)

BSc Hons, MSc (University of Zimbabwe)

**Thesis submitted in fulfilment of the requirements for the degree**

**Doctor of Technology: Mechanical Engineering**

**Faculty of Engineering**

**Cape Peninsula University of Technology**

**Supervisor: Professor O. D. Makinde**

**Institute for Advanced Research in Mathematical Modelling and Computations**

**Bellville Campus**

Date submitted: November 2012

## DECLARATION

I, **Isaac TAKAIDZA**, declare that the contents of this thesis represent my own work, and that the thesis has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology.

**Signed** **Date**

## ABSTRACT

In this thesis, we investigate certain key aspects of mathematical modelling to explain the epidemiology of HIV/AIDS at the workplace and to assess the potential benefits of proposed control strategies. Deterministic models to investigate the effects of the transmission dynamics of HIV/AIDS on labour force productivity are formulated. The population is divided into mutually exclusive but exhaustive compartments and a system of differential equations is derived to describe the spread of the epidemic. The qualitative features of their equilibria are analyzed and conditions under which they are stable are provided. Sensitivity analysis of the reproductive number is carried out to determine the relative importance of model parameters to initial disease transmission. Results suggest that optimal control theory in conjunction with standard numerical procedures and cost effective analysis can be used to determine the best intervention strategies to curtail the burden HIV/AIDS is imposing on the human population, in particular to the global economy through infection of the most productive individuals. We utilise Pontryagin's Maximum Principle to derive and then analyze numerically the conditions for optimal control of the disease with effective use of condoms, enlightenment/educational programs, treatment regime and screening of infectives. We study the potential impact on productivity of combinations of these conventional control measures against HIV. Our numerical results suggest that increased access to antiretroviral therapy (ART) could decrease not only the HIV prevalence but also increase productivity of the infected especially when coupled with prevention, enlightenment and screening efforts. We conclude that the successful screening especially of unaware infectives has a significant impact in reducing the endemicity of HIV/AIDS.

We initially investigate the productivity of organizational labour force in the presence of HIV/AIDS with three intervention strategies, enlightenment/monitoring, preventive and HAART treatment measures, in enhancing workforce output. The model is used to estimate the cost of the non-productive susceptibles and the non-productive infectious individuals (depressed) to organizations as well as project the benefits when the non-productive and depressed employees have access to interventions. We first consider the constant control case, calculate the basic reproduction number and investigate 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.

The model used to analyze recruitment effects of susceptible and infected people in order to assess the productivity of organizational labour force in the presence of HIV/AIDS with

screening, enlightenment, preventive and HAART treatment measures in enhancing workforce output is found to exhibit backward and Hopf bifurcations implying that for the disease to be eradicated, the basic reproductive number must be below a critical value less than one. Cost effectiveness analysis results indicate that putting in efforts on recruitment (HIV screening of applicants, etc.) is not necessarily the most cost-effective strategy to enhance productivity in organizational labour force. Hence, to enhance employees' productivity, effective education programs and strict adherence to preventive measures should also be promoted.

We also study the impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives on the transmission dynamics of the disease in a homogeneous population with constant immigration of susceptibles. The model of [113] is modified by incorporating use of condoms, treatment and screening of unaware infectives as time dependent control measures. The model is found to exhibit trans-critical bifurcation. Formulating the appropriate optimal control problem, we investigate the necessary conditions for the disease control in order to determine the role of unaware infectives in the spread of HIV/AIDS. We found that unawareness by infectives has a great cost impact on the community. We investigate the impact of a combination of these strategies in the control of HIV/AIDS. The costs associated with these strategies are investigated through the formulation of the costs function problem, and then we use the Maximum Principle to solve the resulting optimal control problem and determine optimal strategies for controlling the spread of the disease. Carrying out cost-effectiveness analysis, we found that the most cost-effective strategy is the combination of all the control strategies.

## ACKNOWLEDGEMENTS

I am indebted to my supervisor, Prof Oluwole Daniel Makinde, for his contribution to this thesis. I would like to thank you for offering mentorship, encouragement and expertise in the application of ideas from dynamical systems, stability theory and numerical analysis to the field of HIV epidemiology. Your modelling experience and generosity in sharing your ideas had a profound influence on my work.

I extend gratitude and heartfelt thanks to Dr Oare Kazeem Okosun, a Senior Lecturer and colleague at Vaal University of Technology, for mentoring and guiding me throughout the study.

I cannot thank my wife, Samkeliso, and the boys (Isheanesu, Simbarashe, Takudzwanashe and Tatenda) enough for their unwavering support and inspiration. I sincerely hope that this will also inspire you.

My colleagues and fellow students, Lazarus Rundora and Solly Lebelo, deserve a mention for your moral support. My good friend, Dr Gift Muchatibaya, thanks for always being hospitable to us when we visited Cape Town for consultation. VUT Maths Department colleagues, thank you for ensuring that work continued in our absence.

I also extend special thanks to my parents and siblings for all the support and encouragement starting from the foundational stages through high school and then the undergraduate years. To my in-laws, the Moyo family, I am truly thankful.

To those I may not have mentioned by name, there are many more people to thank, but like stars, some shine bright for all to see and others fade in the background aiding in the beauty of the night sky. Thank you all very much.

## TABLE OF CONTENTS


**Declaration** ii
**Abstract** iii
**Acknowledgements** v
**Glossary** xi
**Publications and Conference Presentations** xii

**CHAPTER ONE: GENERAL INTRODUCTION**

**1.1 Introduction** 1
**1.1.1 HIV/AIDS Biological History** 1
**1.1.2 HIV/AIDS Impact** 4
**1.1.3 Impact on Firms** 8
**1.2 Mathematical Epidemiology** 11
**1.3 Literature Review** 13
**1.4 Statement of the Problem** 15
**1.5 Aim of the Study** 15
**1.6 Research Objectives** 16
**1.7 Significance of the Study** 16
**1.8 Outline of Thesis** 17

**CHAPTER TWO: BASIC MATHEMATICAL CONCEPTS**

**2.1 Model Formulation** 18
**2.1.1 Compartmental Modelling** 19
**2.1.2 Incidence/Transmission** 20
**2.2 Stability Analysis** 22
**2.3 Sensitivity Analysis** 24
**2.4 Optimal Control** 25
**2.4.1 The General Optimal Control Problem** 25
**2.4.2 Pontryagin's Maximum Principle** 26
**2.5 Numerical Analysis** 27
**2.6 Cost Effective Analysis** 27

**CHAPTER THREE: LABOUR FORCE PRODUCTIVITY IN THE PRESENCE OF HIV/AIDS**

**3.1 Introduction** 30
**3.2 Model Formulation** 33
**3.3 Existence and Stability of Equilibria** 35
**3.3.1 Stability of the Disease-Free Equilibrium (DFE)** 35
**3.3.2 Existence of Endemic Equilibrium** 35
**3.4 Sensitivity Analysis** 37
**3.5 Analysis of Optimal Control** 39
**3.6 Numerical Results and Discussions** 41
**3.6.1 Condom Use (Prevention) Control Set to Zero** 42
**3.6.2 Enlightenment/Monitoring Control Set to Zero** 44
**3.6.3 HAART Treatment Control Set to Zero** 47
**3.6.4 All Controls Optimized** 49

**3.7 Cost Effective Analysis** **51**
**3.8 Conclusion** **52**

**CHAPTER FOUR: ANALYSIS OF RECRUITMENT AND INDUSTRIAL HUMAN RESOURCES MANAGEMENT FOR OPTIMAL PRODUCTIVITY IN THE PRESENCE OF THE HIV/AIDS EPIDEMIC**

**4.1 Introduction** **53**
**4.2 Model Formulation** **54**
**4.3 Analysis of Equilibria** **55**
**4.3.1 Productive Susceptible Recruits Only** **57**
**4.3.2 Susceptible Recruits Only** **58**
**4.3.3 Productive Recruits Only** **59**
**4.4 Optimal Control Analysis** **61**
**4.5 Numerical Results and Discussion** **65**
**4.5.1 Strategy A** **66**
**4.5.2 Strategy B** **68**
**4.5.3 Strategy C** **70**
**4.5.4 Strategy D** **72**
**4.5.5 Strategy E** **74**
**4.5.6 Strategy F** **76**
**4.5.7 Strategy G** **77**
**4.5.8 Strategy H** **79**
**4.5.9 Strategy I** **81**
**4.5.10 Strategy J** **83**
**4.5.11 Strategy K** **84**
**4.6 Cost Effective Analysis** **86**
**4.7 Conclusion** **90**

**CHAPTER FIVE: IMPACT OF OPTIMAL CONTROL ON THE TREATMENT OF HIV/AIDS AND SCREENING OF UNAWARE INFECTIVES**

**5.1 Introduction** **91**
**5.2 Model Formulation** **93**
**5.3 Mathematical Analysis of the HIV/AIDS model** **95**
**5.3.1 Positivity and Boundedness of Solutions** **95**
**5.3.2 Stability of the Disease-Free Equilibrium** **95**
**5.3.3 Existence of Endemic Equilibrium** **96**
**5.4 Modified Model** **97**
**5.4.1 Stability of the Disease-Free Equilibrium** **99**
**5.4.2 Existence of Endemic Equilibrium** **100**
**5.4.3 Global Stability of the Endemic Equilibrium for $\alpha = 0$** **104**
**5.5 Optimal Control Analysis** **105**
**5.6 Numerical Results and Discussion** **108**
**5.6.1 Screening and Treatment Only** **110**
**5.6.2 Screening and Condom Use Only** **112**
**5.6.3 Condom Use and Treatment Only** **114**
**5.6.4 Condom Use, Screening and Treatment** **116**
**5.7 Cost Effective Analysis** **118**
**5.8 Conclusion** **120**

**CHAPTER SIX: CONCLUDING REMARKS** **121**

**BIBLIOGRAPHY** **123**

## LIST OF FIGURES

Fig 1.1: A schematic diagram of the pathogenic events that occur from initial infection with HIV to the development of clinical disease. 3

Fig 1.2: Typical course of HIV infection. Patterns of $CD4^+$ T-cell decline and virus load increase 4

Fig 1.3: HIV Prevalence in Adults in Africa 7

Fig 1.4: Global HIV Prevalence in 2007 7

Fig 1.5: Global Prevalence of HIV in 2009 8

Fig 1.6: Impact of HIV/AIDS on a Company 11

Fig 3.1: Flow diagram for HIV/AIDS transmission 34

Fig 3.2: Simulations of the model showing the effect of enlightenment and treatment 43

Fig 3.3: Simulations of the model showing the effect of prevention and treatment 45

Fig 3.4: Simulations of the model showing the effect of prevention and enlightenment 47

Fig 3.5: Simulations of the model showing the effect of prevention, enlightenment and treatment 49

Fig 4.1: Flow diagram for HIV/AIDS disease transmission 55

Fig 4.2: Simulations of the state system (4.1) for $Q = 100$, $\mu = 0.04$, $\pi_3 = 0.03$, $\gamma = 0.288$, $\rho = 0.2$, $\sigma = 0.04$, $\delta = 0.8$, $\alpha = 0.81$. 60

Fig 4.3: Simulations of the state system (4.1) for $Q = 100$, $\mu = 0.04$, $\pi_3 = 0.03$, $\gamma = 0.288$, $\rho = 0.2$, $\sigma = 0.04$, $\delta = 0.8$, $\alpha = 0.81$ 61

Fig 4.4: Simulations of the model showing the effect of control strategy A 66

Fig 4.5: Simulations of the model showing the effect of control strategy B 68

Fig 4.6: Simulations of the model showing the effect of strategy C 71

Fig 4.7: Simulations showing the effect of strategy D 72

Fig 4.8: Simulations showing the effect of strategy E 74

Fig 4.9: Simulations showing the effect of strategy F 76

Fig 4.10: Simulation results showing the effect of strategy G 78

Fig 4.11: Simulations showing the effect of strategy H 79

Fig 4.12: Simulations showing the effect of strategy I 81

Fig 4.13: Simulations showing the effect of strategy J 83

Fig 4.14: Simulations showing the effect of strategy K 84

Fig 5.1: Flow diagram for HIV/AIDS disease transmission model 94

Fig 5.2: Flow diagram for the modified HIV/AIDS disease transmission model 98

Fig 5.3: Simulation of the model (5.11) showing contour plots of the reproduction number $R_h$ as a function of $\theta$ and $\pi$ at steady state. 109

Fig 5.4: The projected $I_1 - I_2$ phase plane of the phase space 109

Fig 5.5: Simulations showing the effect of screening and treatment on HIV/AIDS spread 111

Fig 5.6: Simulations showing the effect of condom use and screening 113

Fig 5.7: Simulations showing the effects of condom use and treatment 114

Fig 5.8: Simulations showing the effects of all controls on the spread of HIV/AIDS 116

Fig 5.9: Simulations showing the effect of the number of sexual partners ($c_1$) and ($c_2$) on AIDS spread. 117

Fig 5.10: Simulations showing the effect of the number of sexual partners ($c_3$) and ($c_h$) on AIDS spread. 118

## LIST OF TABLES

Table 1.1: Costs of HIV/AIDS in the workforce 10

Table 3.1: Sensitivity indices for $R_0$ 38

Table 3.2: Model parameter values 42

Table 4.1: Cases averted and associated costs for intervention strategies 90

Table 5.1: HIV/AIDS model parameter values 110

## GLOSSARY

| Terms/Acronyms/Abbreviations | Definition/Explanation |
|---|---|
| AIDS | Acquired Immune Deficiency Syndrome |
| Basic reproduction number, $R_0$ | The average number of secondary infections caused by a typical infected individual during his entire period of infectiousness, in a completely susceptible population, in the absence of any interventions. |
| HAART | Highly Active Anti-Retroviral Therapy |
| HIV | Human Immunodeficiency Virus |
| ICER | Incremental Cost Effectiveness Ratio |
| ILO | International Labour Organization |
| Incidence | The number of new cases occurring over a period of time. |
| Incidence rate | The number of new cases per person per unit time |
| Prevalence | The fraction of a population (or number of individuals) infected with the disease at a particular point in time. |
| UN | United Nations |
| UNAIDS | Joint United Nations Programme on HIV/AIDS |
| WHO | World Health Organization |

## PUBLICATIONS AND CONFERENCE PRESENTATIONS

This thesis was built around the following papers and presentations at conferences:

1. K.O. Okosun, O. D. Makinde and I. Takaidza. Impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives, Appl. Math. Modell. (2012), http://dx.doi.org/10.1016/j.apm.2012.08.004

2. I. Takaidza, K.O. Okosun and O. D. Makinde. Modelling the optimal efficiency of industrial labour force in the presence of HIV/AIDS epidemics. Journal of Industrial and Management Optimization (2012). Submitted

3. K.O. Okosun, O. D. Makinde and I. Takaidza. Analysis of the recruitment and industrial human resources management for optimal productivity in the presence of HIV/AIDS epidemic. Journal of Biological Physics (2012), DOI 10.1007/s10867-012-9288-2

4. Optimal Control, Unaware Infective and Treatment, Poster Presentation by I. Takaidza, Clinic on the Meaningful Modelling of Epidemiological Data, 27 May - 08 June 2012, Muizenberg

5. Computational Modelling and Optimal Control of HIV/AIDS Impact on Industrial Labour Productivity, Paper Presentation by I. Takaidza, 55$^{th}$ SAMS Congress, 31 October – 02 November 2012, Stellenbosch University

# CHAPTER ONE

# GENERAL INTRODUCTION

## 1.1 Introduction

### 1.1.1 HIV/AIDS Biological History

AIDS, caused by the lentivirus HIV, is a condition in humans in which the immune system begins to fail leading to life-threatening opportunistic infections [124, 34]. Lentiviruses are characteristically responsible for long-duration illnesses with a long incubation period [75]. Infection with HIV occurs by the transfer of bodily fluids such as blood, semen, vaginal fluid, pre-ejaculate or breast milk. Within these fluids, HIV is present as both free virus particles and virus within infected immune cells. The major routes of transmission are unsafe sex, contaminated needles, from a mother to her baby during pregnancy, birth (prenatal transmission) and breast feeding. Therefore, the most susceptible individuals at risk of acquiring infection include people having sexual contacts with the HIV infected, babies of infected parents, homosexual and bisexual individuals, intravenous drug abusers and people transfused with contaminated blood.

HIV only replicates in dividing cells and primarily infects a class of white blood cells or lymphocytes called CD4 T-cells, but it also infects other cells such as dendritic cells. When the CD4 T-cell count, normally around 1 000 per $\mu L$, decreases to 200 per $\mu L$ or below, a patient is characterized as having AIDS [90]. HIV works by infecting the cells of the immune system, using them to make more viruses, and then killing them. Some antibodies that the body produces actually work to enhance HIV replication.

There is no cure for HIV/AIDS besides anti-retroviral therapy (ART) which helps boost the immune system of the infected against secondary infections thereby significantly prolonging their life span [127]. However, for far too many people HIV infection eventually progresses to AIDS and ultimately death [79]. HIV infection has four basic stages: incubation period, acute infection, latency stage and AIDS. HIV progresses to AIDS at a variable rate affected by viral, host and environmental factors. Most people will progress to AIDS within 10 years of HIV infection while some will have progressed much sooner and yet others will take much longer [16]. Even after HIV has progressed to diagnosable AIDS, the average survival time with antiretroviral therapy was estimated to be more than 5 years as of 2005 [110]. Without antiretroviral therapy, someone who has AIDS typically dies within a year [88]. Antiretroviral

treatment reduces both the mortality and the morbidity of HIV infection, but routine access to antiretroviral medication is not easily available in all countries [96].

The initial incubation period upon infection is asymptomatic and usually lasts between two and four weeks. The second stage, acute infection, lasts an average of 28 days and can include symptoms. This is a period of rapid viral replication that immediately follows the individual's exposure to HIV leading to an abundance of virus in the peripheral blood with levels of HIV commonly approaching several million viruses per mL [100]. During this stage (usually 2-4 weeks post-exposure) most individuals (80% to 90%) develop an influenza or mononucleosis-like illness called acute HIV infection, the most common symptoms of which may include fever, lymphadenopathy (swollen lymph nodes), pharyngitis (sore throat), rash, myalgia (muscle pain), malaise, mouth and esophageal sores, and may also include, but less commonly, headache, nausea and vomiting, enlarged liver/spleen, weight loss, thrush, and neurological symptoms. Infected individuals may experience all, some, or none of these symptoms. The duration of symptoms varies, averaging 28 days and usually lasting at least a week [60]. Because of the nonspecific nature of these symptoms, they are often not recognized as signs of HIV infection. Even if patients go to their doctors or a hospital, they will often be misdiagnosed as having one of the more common infectious diseases with the same symptoms. As a consequence, these primary symptoms are not used to diagnose HIV infection, as they do not develop in all cases and because many are caused by other more common diseases. However, recognizing the syndrome can be important because the patient is much more infectious during this period [26].

The latency stage, which occurs third, shows few or no symptoms and can last anywhere from two weeks to twenty years and beyond. A strong immune defence reduces the number of viral particles in the blood stream, marking the start of secondary or chronic HIV infection. During this phase of infection, HIV is active within lymph nodes, which typically become persistently swollen, in response to large amounts of virus that becomes trapped in the follicular dendritic cells (FDC) network [17]. During this stage of infection early initiation of antiretroviral therapy significantly improves survival, as compared with deferred therapy [68]. AIDS, the fourth and final stage of HIV infection shows as symptoms of various opportunistic infections.

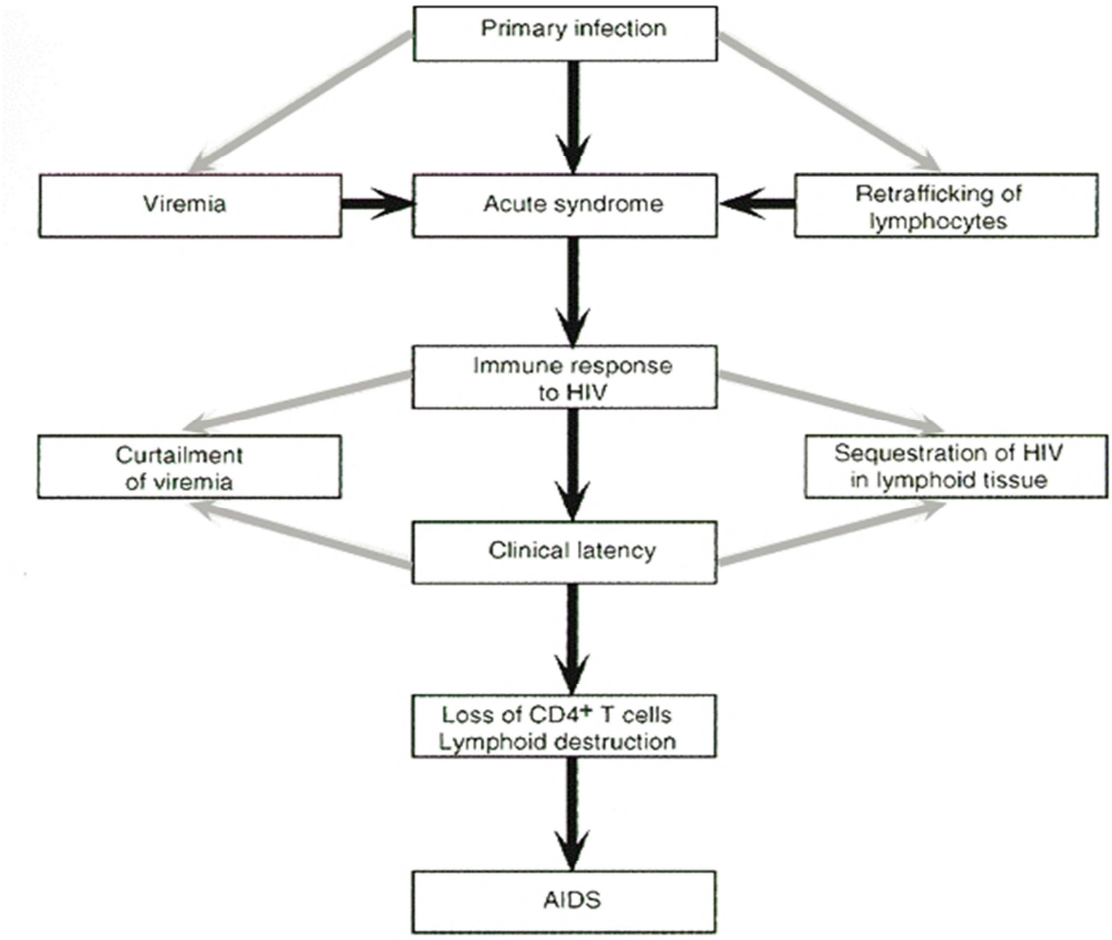



Fig 1.1: Pathogenesis of HIV infection. A schematic diagram of the pathogenic events that occur from initial infection with HIV to the development of clinical disease. (Modified from [97])

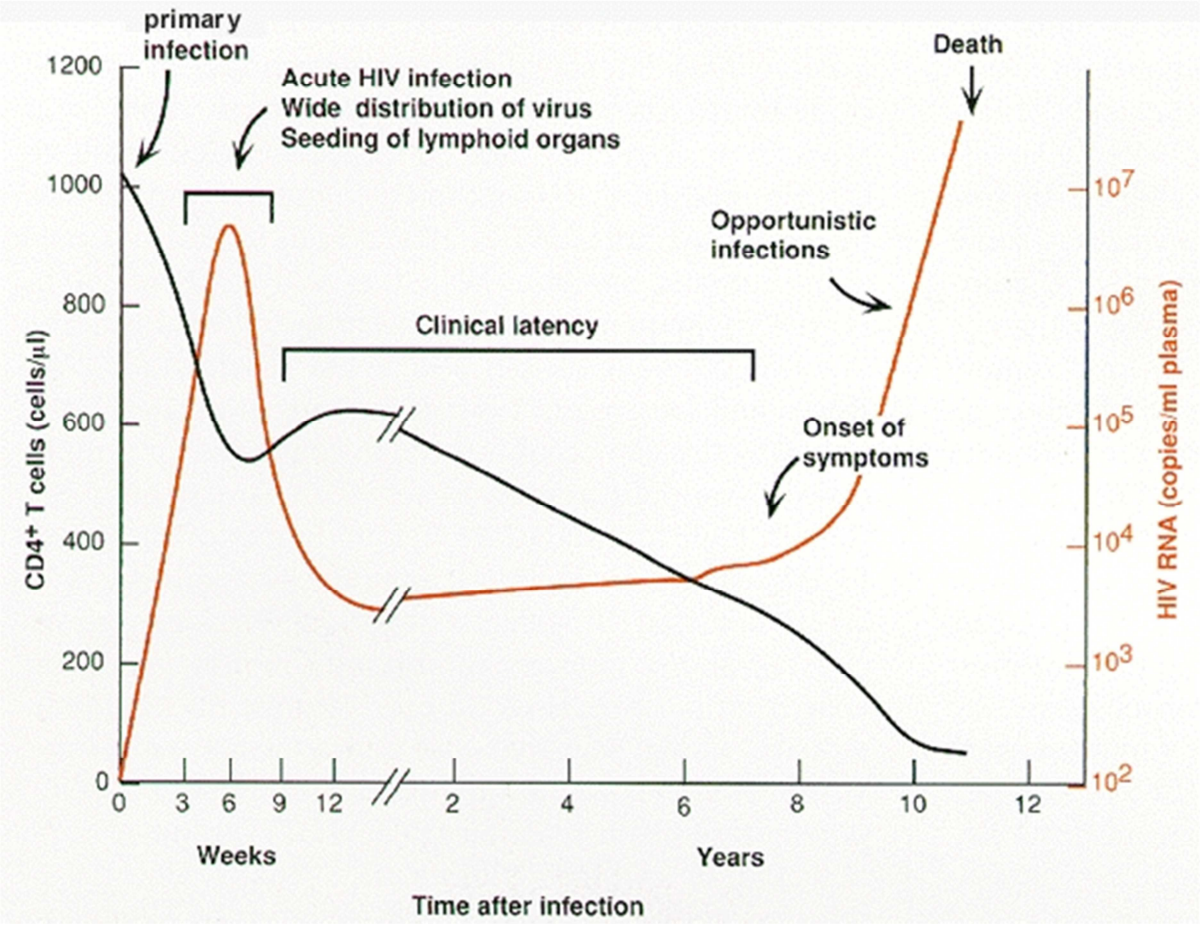



Fig 1.2: Typical course of HIV infection. Patterns of $CD4^+$ T-cell decline and virus load increase vary greatly from one patient to another, as do the actual values of viral RNA load. (Modified from [97])

### 1.1.2 HIV/AIDS Impact

AIDS is one of the deadliest epidemics ever encountered in the history of mankind as it compromises the body's defence from infections and diseases [66]. HIV/AIDS is the greatest single public health challenge that humanity has ever faced, is considered pandemic by the World Health Organization (WHO) and it continues largely unabated. Timely control and prevention of HIV/AIDS, and other infectious diseases, are among the key global health priorities in light of the available statistics which starkly expose the severity of the pandemic.

Global databases consistently demonstrate the higher incidence, prevalence, mortality and burden of HIV/AIDS. In 2006 HIV infected about 0.6% of the world's population [54]. If 2007 trends persisted, it was projected that 60 million more HIV infections would occur by 2015 and the annual number of new infections could increase by 20% or more by 2012 [42]. Today, an estimated 33.3 million people live with HIV and AIDS worldwide and more than 25 million people have died from AIDS since the first cases of AIDS were identified in 1981. Besides the human cost, HIV/AIDS is having profound effects on productive employment and

economic development in Africa, and hence on its ability to cope with the pandemic [12]. Globally, around 2.6 million people became infected with HIV in 2009 whilst an estimated 1.8 million people died as a result of AIDS in the same year [7]. Sub-Saharan Africa is more heavily affected by HIV and AIDS than any other region of the world with an estimated 22.5 million people living with HIV in the region, around two thirds of the global total.

The HIV epidemic touches on almost every aspect of society, is unevenly distributed in the population and has a tremendous impact on morbidity (illness) and mortality [92]. HIV/AIDS has socio-economic and psychological implications on patients, their families and the community as a whole [65].

The social and economic consequences of the AIDS epidemic are widely felt, not only in the health sector but also in education, industry, agriculture, transport, human resources and the economy in general [118]. HIV has affected both the demand for and supply of education (respectively, number of students and teachers), a critical factor for development and the generation of human capital. This is particularly the case in some African and Asian countries that already face significant challenges in their educational systems [62]. Ultimately, the quality of education may be compromised. While deaths among teachers are occurring in large numbers in highly affected countries, frequent bouts of sickness of either teachers or family members take away many person hours from classroom teaching. Even worse, the stress of sickness and the knowledge of impending death reduce the quality of lecture preparation and delivery. The end result is the poor quality of people flowing from the education system in relation to the demands of the workplace and society [85]. The AIDS epidemic in sub-Saharan Africa continues to devastate communities, rolling back decades of development progress as families lose income earners leaving behind orphans who are often cared for by members of the extended family.

Labour is dramatically affected, which in turn slows down economic activity and social progress since employers have to train other staff to replace those at the workplace that become too ill to work. For instance, given agriculture's reliance on labour, illness and death directly affect productivity and, therefore, affect crop yields, the types of crops being cultivated, income and, ultimately, food security. The impact of HIV/AIDS on economic growth is a critical area to examine, yet difficult to measure, as it is tied to job creation, higher living standards and the resources governments have available - all of which have implications for overall development. Studies of some of the worst affected countries show that their Gross Domestic Product (GDP— a commonly used measure of economic growth) grew more slowly than it would have without AIDS [9, 19, 115].

Other than inflicting physical pain, HIV/AIDS imposes a significant psychological burden to both the infected and the affected [91]. On one hand, infected individuals often suffer from depression and anxiety as they adjust to the impact of their diagnosis. On the other, those who live and work with the HIV infected also experience some form of stress as a result of fear of being infected or heavy workload experienced due to slowdown of the infected colleagues [99].

The spread of HIV/AIDS is a threat to national economies globally as the pandemic has weakened the human capital base (has led to poor mental health and poor physical health) across all sectors, a situation that undoes efforts to reduce poverty through improvements in labour productivity [91]. However, despite the potential adverse impact of HIV/AIDS, its economic impact is largely unknown as little empirical evidence exists on this issue. This study hopes to fill this gap by undertaking a detailed mathematical epidemiology analysis relating HIV/AIDS to industrial labour productivity.

In addition to the enormous socio-economic burden it imposes, AIDS is now the leading cause of death in sub-Saharan Africa, and has cut the life expectancy in a number of countries in this region [47]. In 2009, around 1.3 million people died from AIDS in sub-Saharan Africa and 1.8 million people became infected with HIV. Since the beginning of the epidemic, 14.8 million children have lost one or both parents to HIV/AIDS [118]. In 2005, AIDS claimed an estimated 2.4 - 3.3 million lives, of which more than 570 000 were children. A third of these deaths occurred in sub-Saharan Africa, retarding economic growth and increasing poverty [44]. At that time, it was estimated that HIV would infect 90 million people in Africa, resulting in a minimum estimate of 18 million orphans [53].

The greatest burden of the HIV/AIDS scourge is in southern Africa. In 2010, the HIV prevalence in South Africa was pegged at 17.8% while the national adult HIV prevalence rate in three other southern African countries exceeded 20%. These countries are Botswana, Lesotho and Swaziland with prevalence rates of, respectively, 24.8%, 23.6% and 25.9% [118]. Swaziland and Botswana have the highest and second highest prevalence in the world among the 15 - 49 year olds. In 2001, about 20% of the entire adult population aged 15 - 49 was infected in nine southern African countries — Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Zambia and Zimbabwe [102]. An estimated 5.6 million people were living with HIV and AIDS in South Africa in 2009, more than in any other country [118]. It is believed that in 2009, an estimated 310 000 South Africans died of AIDS. The impact of the AIDS epidemic is reflected in the dramatic change in South Africa's mortality rates. The overall number of annual deaths increased sharply from 1997, when 316 559 people died, to 2006 when 607 184 people died [6]. In 2003, projections of the future

HIV/AIDS burden in South Africa underscored the importance of immediate action to reduce the number of new infections and plan for medical and social care needs [105]. Studies show that HIV/AIDS is now the number one overall cause of death in Africa, yet, only less than one percent of those infected receive combination antiretroviral therapy [46, 69].

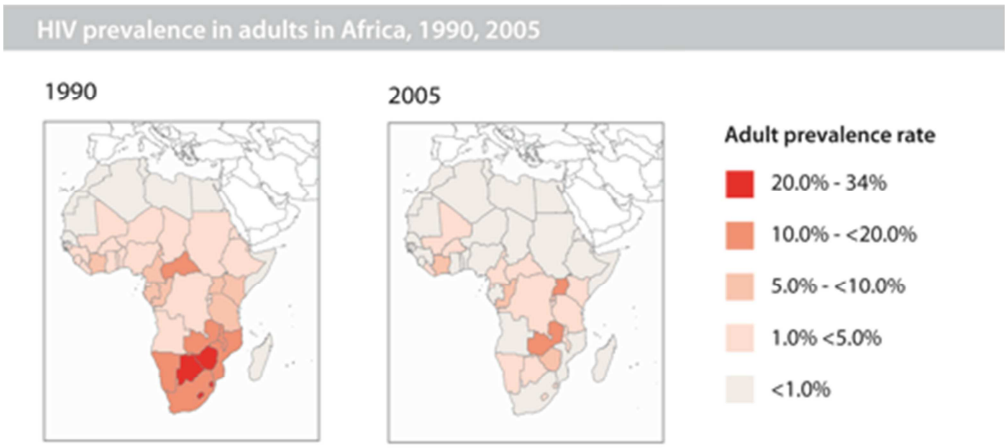



Fig 1.3: HIV Prevalence in Adults in Africa [116]

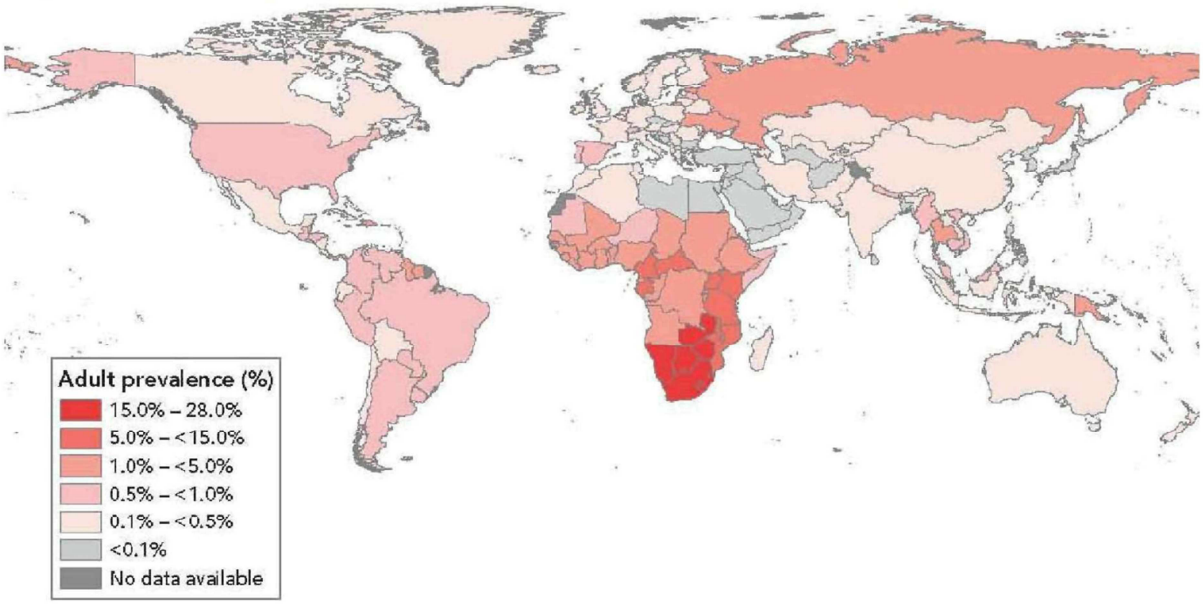



Fig 1.4: Global HIV Prevalence in 2007 [117]

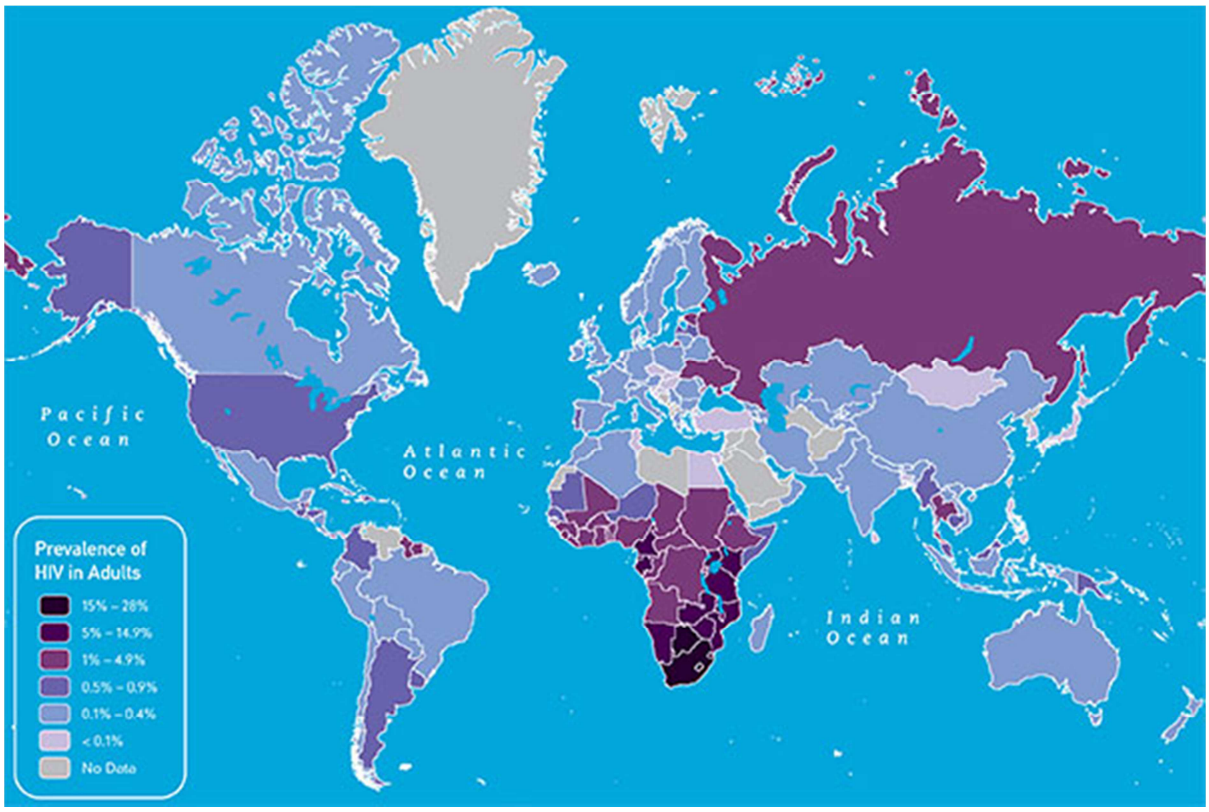



Fig 1.5: Global Prevalence of HIV in 2009 [118]

### 1.1.3 Impact on Firms

The impact of the HIV/AIDS epidemic goes far beyond the household level. The virus does not discriminate as personnel from hotel staff, business people, migrant workers to public servants are all affected, but while their lives may be different, work stands out as a unifying activity. Firms and businesses are, without doubt, also affected as HIV-infected people are usually in the prime working years and are involved in the process of production.

"*Especially in its early stages, the epidemic tended to strike urban centres, the better educated, the elite in leadership and the most productive members of society." (*Kofi Annan, Secretary General of the United Nations, 12/01/2004 *in [126]).*

Many businesses realize that the rapid spread of HIV/AIDS negatively affects their workforce, market and, ultimately ability to earn a profit [51]. These organizations understand that HIV/AIDS is not only a health issue, but a core business issue. A business may decide to address HIV/AIDS for purely economic reasons. A study on the financial impact of the epidemic on six corporations in South Africa and Botswana revealed that the "AIDS tax" - increased medical costs, decreased productivity, and other costs associated with HIV/AIDS in the work force - was as much as 5.9% of the corporations' labour costs [49]. According to the mathematical model the researchers used, all six companies in the study would have

earned positive returns on their investments and reduced this "AIDS tax" by as much as 40.4% if they had provided antiretroviral drugs at no cost to employees with HIV/AIDS. Findings from a survey conducted by the World Economic Forum revealed that of the 10 993 business leaders polled globally, 22% of respondent firms reported experiencing impacts from the virus [18]. In hard-hit sub-Saharan Africa, 65% of respondent firms reported some impact while 21 % reported serious impact.

One result of ill-health associated with HIV/AIDS is that it affects the physical and mental health of the infected and affected persons. Poor health reduces labour productivity, work effort and discourages the maintenance of human and social capital [106, 123]. In a business or manufacturing enterprise, the worker's health concerns such as worries, expressed or unexpressed, as a result of the risks of exposure to HIV/AIDS, or about their HIV-positive status or that of their family members or fellow workers could be a source of mental distractions and can adversely affect labour productivity [21, 35]. Since HIV induced ill-health is irreversible and poses a high mortality risk, the potential loss in productivity as a result of mortality and days lost due to poor health can be substantial. Furthermore, the poor health may limit the ability to work, which may mean less output per worker, reduced sales and diminished profitability. Social capital, labour relations and employee morale could also be adversely affected when employees are contending with HIV/AIDS [91].

Another area of concern is the effect of the pandemic on the competitiveness of enterprises in the production of quality goods and services. Losses in labour time and skills will reduce the quantity and quality of outputs produced. This can directly affect the quality of products and services, leading to reputation losses and ultimately a reduction in customers [85]. Also, what happens in one sector could impact events in another sector. For example, skills losses and interruption of production in say the information technology and telecommunications sectors may lead to production losses in all other sectors using these services.

Previous research provides little evidence on employer and employee concerns about HIV/AIDS and the effects of the concerns on labour productivity. The present study is therefore an important empirical contribution to an understanding of the impact of HIV/AIDS on labour productivity of the firms. In general, labour productivity would be affected by HIV/AIDS because of the loss of skilled workers, an increase in absenteeism and the entry into the labour market of less experienced young people and older persons who have not worked before [24]. At micro level, the impact is more apparent as results are based on surveys of enterprises. The study by Coulibaly, through national surveys and reports, showed that worker productivity declined as AIDS progressed, especially in the last years

before death. The costs to any organization arising from an employee becoming infected are not immediate but delayed as the virus can incubate for 3 - 5 years before the infected person begins to suffer HIV-related illnesses and, if unable to get adequate treatment, suffers increasing bouts of more severe and varied opportunistic illnesses and, ultimately, death 5 - 10 years after infection [83]. The company therefore does not incur any costs during the initial period of about 1 - 8 years from infection. When sickness starts, the company incurs illness-related costs (absenteeism, productivity, management time, medical care and insurance). The employee will ultimately leave the workforce due to either death or retirement wherein the organization incurs costs associated to funeral expenses, pay-out from the retirement fund as well as loss of experience and morale. The company may choose to either replace the employee or not, in which case they incur turnover costs (vacancy, recruiting, training, reduced productivity). The organization's total workforce-related costs due to HIV/AIDS may be calculated as the aggregate of direct and indirect costs as explained in Table 1.1.

| | Direct (out of pocket) Costs | Indirect (productivity) Costs |
|---|---|---|
| From one employee (Individual Costs) | • Benefits payments<br>• Medical care<br>• Recruitment and training of a replacement employee | • Reduced on-the-job productivity<br>• Increased leave and absenteeism<br>• Supervisor's time<br>• Vacancy until replacement is hired<br>• Poorer performance while new employee learns the job |
| From many employees (Organizational Costs) | • Benefits premiums<br>• Accidents<br>• Legal costs | • Senior management time<br>• Production disruptions<br>• Loss of workforce morale, cohesion and experience<br>• Deteriorating labour relations |

Table 1.1: Costs of HIV/AIDS in the workforce, [108]

HIV/AIDS affects corporations by increasing costs and reducing productivity, as outlined in Fig 1.6.

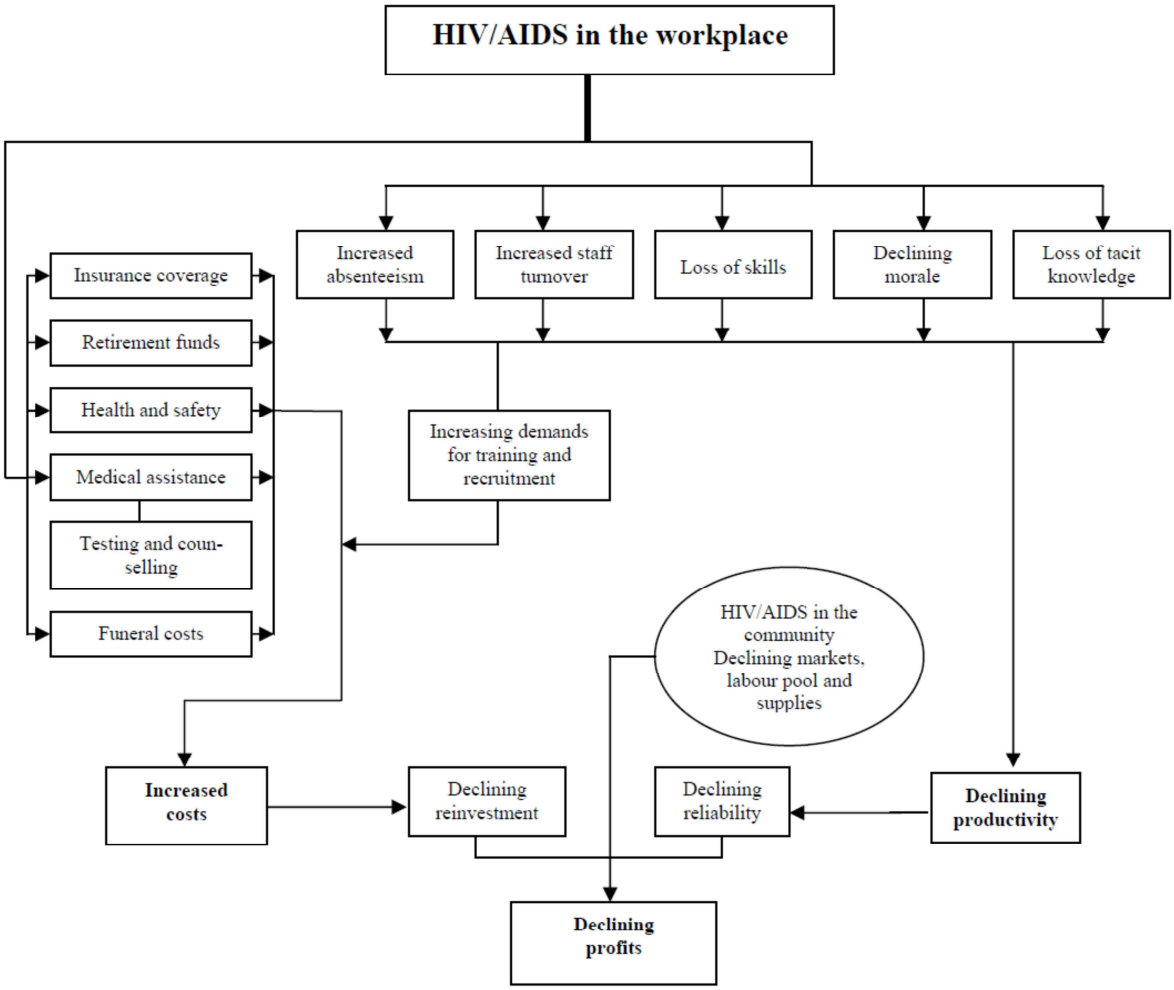



Fig 1.6: Impact of HIV/AIDS on a Company, [27]

In the absence of increased access to antiretroviral therapy, the International Labour Organization estimated that global labour force losses due to HIV could reach 45 million by 2010 and expected the number to peak at 64 million by 2015 [52].

### 1.2 Mathematical Epidemiology

Epidemiology is the study of the spread of diseases in populations, and primarily the human population is of interest. Mathematical epidemiology is concerned with the quantitative aspects of the study, often consisting of the following activities:

i) model formulation,
ii) estimation of parameters,
iii) investigation of the sensitivity of the model to changes in the parameters, and
iv) simulations.

All these activities are expected to give us information about the spread of the disease in the population, the possibility to control this spread and maybe how to make the disease disappear from the population.

The diseases which are modelled most often are the so called infectious diseases, that is, diseases that are contagious and can be transferred from one individual to another through contact. Examples of such diseases are measles, chicken pox, sexually transmitted diseases (HIV/AIDS, gonorrhea, syphilis, etc), hepatitis, tuberculosis, and the very familiar influenza. What constitutes a contact so that the disease can be transmitted in each case is different. For example, we know that the common flu can be obtained by just being physically close to a person who already has it. In sexually transmitted diseases, in most cases, a sexual contact is necessary for transmission.

Mathematical models are extremely important in scientific and industrial investigations as they can be used to predict results. Models are generally aimed at predicting a result or investigating a question of interest [101]. A good mathematical model attempts to describe part of the real world through equations. Mathematical models provide an explicit framework within which to develop and communicate an understanding of infectious disease transmission dynamics. Mathematical models can also be used to estimate the expected costs and benefits of alternative disease prevention, diagnostic, and treatment interventions and, ultimately, to aid policy makers with allocating limited disease-control resources [78].

The process of describing a system like the spread of an infectious disease forces one to recognise the assumptions made and the data available in order to estimate parameter values, and allows for qualitative or quantitative predictions that can be tested. Thus, the central role of creating and analysing mathematical models is to develop our understanding of a system. Once the transmission dynamics of an infectious disease are appropriately described by a model it is possible to evaluate the potential impact of proposed interventions. Models should assist in the identification of successful interventions, their necessary scale, and the role or ability of new technologies to deliver public health benefits [41].

Mathematical models have been proposed as an aid to understanding the immune dynamics underlying AIDS. However, theoretical and clinical models of AIDS that assume that HIV has a central role in disease progression have not met expectations [25]. Deterministic mathematical modelling of infectious diseases on the molecular level is still a relatively new field. Mathematicians and immunologists have begun to work together to create models that attempt to predict the progression of disease in an individual. Classical epidemiologic models use variables to describe the state of being of individuals within a population that has been

exposed to an infectious disease. The standard categories include susceptible, infectious, recovered, immune and exposed (but not infectious) individuals. The number of variables to be incorporated depends on the particular disease being studied as well as on the desired complexity of the model. Parameters incorporated into the equations represent fundamental quantities such as birth rate, rate of transmission of infectious agent, death rate, and so forth. Simplicity allows a better understanding of the intrinsic properties of the models. However, oversimplified models may not be able to capture the reality of epidemiological disease transmission. Thus, it is necessary to use models that are complex enough to capture the finest details of disease transmission.

### 1.3 Literature Review

The human immune system is complex and not fully understood, and no model, mathematical or otherwise can fully capture every facet of its phenomenology. Nevertheless, mathematical modelling of HIV infection has proven to be instrumental for the current understanding of the AIDS pathogenesis [55]. Generally, mathematical models and computer simulations are crucial in analyzing the spread and control of infectious diseases [79]. Mathematical models of transmission dynamics of HIV play an important role in better understanding of epidemiological patterns for disease control as they provide short and long term prediction of HIV and AIDS incidence [113]. HIV epidemic projection is essential in determining the type of services that will be needed to prevent new infections and treat, care for, and support sufferers in the future. Without this kind of modelling, it would be impossible to determine how much funding will be needed to control the spread of HIV.

There are many research studies about modelling HIV/AIDS using different approaches and epidemiological apparatus and instruments in determining the prevalence of the disease and to come up with effective alternative ways to control and prevent the proliferation of the disease. Anderson, Medley, May and Johnson, [4], presented a simple mathematical HIV transmission model to investigate the effects of various factors on the overall pattern of the AIDS epidemic. Nikolaos, Dietz and Schenzle, [93], proposed a detailed analysis of a dynamical model to describe the pathogenesis of HIV infection. Christopher and Jorge, [23], derived a simple two-dimensional SIS (susceptible-infected-susceptible) model with vaccination and multiple endemic states. Li and Jin, [77], studied the global dynamics of an SEIR (susceptible-exposed-infected-recovered) epidemic model in which latent and immune states were infective. Mukandavire, Gumel, Garira and Tchuenche, [89], proposed and examined a deterministic model for the co-infection of HIV and malaria in a community. Tripathi, Naresh and Sharma, [113], proposed a mathematical model to study the effect of screening of unaware infectives on the spread of HIV infection.

Elaiw, [36], conducted a study on the global properties of a class of HIV models. A model with exposed state and a model with nonlinear incidence rate are also analyzed and Lyapunov functions are constructed to establish the global asymptotic stability of the uninfected and infected steady states. In a control system framework, a model incorporating the effect of Highly Active AntiRetroviral Therapy (HAART) is shown to be globally asymptotically controllable to the uninfected steady state.

Karrakchou, Rachik and Gourari, [63], investigated the fundamental role of chemotherapy treatment in controlling the virus reproduction in an HIV patient, while Adams, Banks, Kwon and Tran, [1], derived HIV therapeutic strategies by formulating and analyzing an optimal control problem using two types of dynamic treatments. Hattaf, Rachik, Saadi and Yousfi, [48], applied optimal control to a system of ordinary differential equations modelling the Hepatitis B Virus (HBV) infection. They used Pontryagin's maximum principle to characterize the optimal controls representing the efficiency of drug therapy in inhibiting viral production and preventing new infections. Gajic, [40], considered a nonlinear third-order mathematical model of HIV-virus dynamics and proposed an efficient control strategy to keep the number of HIV virons under a pre-specified level and to reduce the total amount of medications that patients receive.

Greenhalgh, [45], dealt with a model for controlling an epidemic by removal and isolation of infected people with the objective of maximizing the expected number of people removed at some terminal time. Wickwire, [125], conducted a survey on the applications of mathematical optimization theory to the optimal control of pests and infectious diseases. Jung, Iwami, Takeuchi and Jo, [58], studied the prevention of pandemic influenza to evaluate the time-dependent optimal prevention policies, which are associated with elimination policy and quarantine policy, considering its execution cost. Miller Neilan, Schaefer, Gaff, Fister and Lenhart, [87], formulated a model for cholera disease to include components such as a hyperinfectious, short-lived bacterial state, a separate class for mild human infections, and waning disease immunity. Using optimal control theory, parameter sensitivity analysis and numerical simulations, a cost-effective balance of multiple intervention methods was compared for two endemic populations.

Dhar and Dhar, [30], considered an optimal control problem on the use of condoms, taken as control, so as to attain a specified reduced value of the infected population of HIV within a certain stipulated time under the minimization of the cost of the control with the aid of a maximum principle by incorporating statistical knowledge on VCTC report in the mathematical model. Fister, Lenhart and McNally, [38], examined an ordinary differential system modelling the interaction of the HIV virus and the immune system of the human body. They considered an optimal control representing a percentage effect the chemotherapy had on the interaction of the CD4+T cells with the virus. They maximized the benefit based on the

T cell count and minimized the systemic cost based on the percentage of chemotherapy given. The existence of an optimal control was proven, and the optimal control was uniquely characterized in terms of the solution of the optimality system. Bowong, [13], dealt with the problem of optimal control for the transmission dynamics of tuberculosis using a model which incorporated the essential biological and epidemiological features of the disease: susceptible, latently infected (exposed to TB but not infectious) and infectious (has active TB). Landi et al, [71], considered a variant of the Wodarz and Nowak mathematical model, adding “aggressiveness” as a new state variable in order to quantify the strength of the virus and its response to drugs. They found out that though relatively simple, the model may be useful in predicting the impact of the effectiveness of therapy on HIV dynamics. Mathieu et al, [82], introduced and defined a non-homogeneous semi-Markov (NHSM) model in continuous time for the evolution of HIV-1 infected patients.

Various studies on applied optimal control methods to investigate viral infections such as HIV/AIDS, Tuberculosis and Rabies have been conducted extensively [28, 5, 57].

### 1.4 Statement of the Problem

The negative impacts of the HIV/AIDS scourge are quite varied as highlighted in the preceding sections of this chapter to the extent that the disease affects global economies. Hence, the upper-most question is: How does an infected and/or affected employee cope? Specifically, we can ask the following further questions: What is the impact of HIV/AIDS on individual labour productivity during disease progression in the absence of intervention? How healthy and, by extension, productive does the labour force become when screening, prevention, enlightenment and treatment interventions are implemented? Using these interventions, is it possible to optimally control the disease? Which combination of the intervention strategies is cost effective given the tight budgetary constraints organizations and governments operate on? What are the implications regarding human resources policies on especially recruitment of employees in light of the need for staff wellness?

### 1.5 Aim of the Study

Many mathematical models already exist describing HIV/AIDS dynamics, and we propose adopting and refining some of these models to monitor the dynamics of HIV/AIDS in the workplace. The aim of the study is thus to describe and control the epidemiology of HIV and AIDS at the workplace. The plan is to make use of well-known mathematical concepts and techniques to propose cost effective intervention strategies towards curtailing the impact of the HIV/AIDS pandemic in industry.

## 1.6 Research Objectives

Despite the magnitude of the problem, little rigorous empirical research on the micro level effects of HIV/AIDS at the firm and industry levels has been published in the literature on African development. Though numerous studies have been undertaken, there is no ample theoretical study on the optimal control of the impact of the HIV/AIDS epidemic on labour productivity.

The baseline objective of this study is to assess the impact of HIV/AIDS on firms. In order to achieve this objective, the study addresses the questions raised in the problem statement. The study is geared not only at estimating the future economic and health outcomes under different control scenarios but also to determine the optimal allocation of limited resources between competing interventions. The main thrust of this investigation is thus to suggest an optimal method of controlling the HIV/AIDS pandemic given the known facts about the transmission and progression process especially since a cure remains elusive with a view to enhancing the productivity of labour force.

Actually, this research project aims to accomplish several objectives. The first and foremost is an examination of how a firm's productivity changes as a consequence of exposure of employees to health risks associated with HIV/AIDS. We will also examine whether firms' responses to HIV concerns of workers, for example, through interventions that reduce risks of contracting HIV/AIDS or activities that support or treat infected workers affect performance of firms.

Although we undertake theoretical analysis using empirical data in literature, this study seeks to add value to the scant literature on the application of compartmental modelling to investigate effects of HIV/AIDS on firm productivity and to a wider epidemiology literature in several key aspects. The study adapts existing mathematical techniques in creative ways thus making it possible to deal with the common prevention and intervention strategies of HIV/AIDS in the improvement of productivity whilst ensuring cost effectiveness. The study intends to show that the optimal control approach can be used to consistently estimate mathematical models of effects of HIV/AIDS on the productivity of labour at firms.

## 1.7 Significance of the Study

Mathematical modelling is used to provide a description of the current situation of the HIV epidemic and its future projection at the workplace. The findings can be used by a wide range of parties in planning HIV and AIDS intervention programmes in a better and more

directed way. The results of this study will be useful in informing government and organizational policies on HIV/AIDS issues. Furthermore, it is also expected that the epidemic modelling can also be used as a basis for evaluating the implementation of a variety of on-going HIV and AIDS prevention programmes and conducting advocacy to enhance the commitment of a number of parties directly and indirectly involved in the programmes [8]. It is hoped that the modelling results can be used as a basis for making concerted efforts of preventing and controlling HIV and AIDS. In particular, this work should, in some small measure, contribute towards helping organizations, governments, public-health agencies and health care providers to determine how best to allocate scarce resources for the treatment and prevention of HIV and AIDS.

### 1.8 Outline of the Thesis

In this thesis, we derive and analyze HIV/AIDS transmission mathematical models which incorporate the productivity of labour. We incorporate controls into the models, namely the use of condoms, screening, enlightenment and treatment, with appropriate cost functions in order to study and determine the possible impacts of these strategies for controlling the epidemic. We further define and obtain the mathematical expression of the basic reproduction number, $R_0$, as a function of state and control variables as well as model parameters. The role or impact of the control strategies on the value of $R_0$ is investigated. We carry out optimal control analyses of the models to determine optimal strategies for the control of the disease. We identify the necessary conditions for optimal control of the disease using Pontryagin's Maximum Principle.

In Chapter 1, a general background of HIV/AIDS is provided, citing the various stages in the development of the disease, factors contributing to the spread of the epidemic and highlighting the impact on society and the economy. It is in this chapter where we review some studies done on modelling HIV/AIDS. In Chapter 2, we give some mathematical preliminary definitions and concepts needed in the later chapters to gain valuable insights into disease dynamics with emphasis on the analytical and numerical techniques. In Chapter 3, we formulate a deterministic compartmental model to investigate the productivity of organizational labour force in the presence of HIV/AIDS while considering susceptible recruits. In Chapter 4, we extend the model to analyze recruitment effects of susceptible and infected people in order to assess the productivity of organizational labour force. In Chapter 5, we study the impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives on the transmission dynamics of the disease.

# CHAPTER TWO

# BASIC MATHEMATICAL CONCEPTS

*In this chapter, we discuss the various approaches used in gaining valuable insights into the dynamics of infectious diseases. The theoretical nature of this study entails that both numerical and analytical techniques will be employed to tackle models under consideration. Mathematical tools to be applied include: i) Compartmental Modelling, a generalized differential equations approach used to model disease dynamics and control, ii) Stability Theory, iii) Optimal Control Theory, allowing resource management to be optimized with respect to suitably defined objective functions and iv) Numerical solutions aided by the MATLAB and MAPLE software packages*

## 2.1 Model Formulation

A variety of models ranging from simple linear models and decision/probability trees to complex network-based simulations can be used to analyze such problems. Markov models with single or multiple decision epochs, individual microsimulation models, population-level dynamic compartmental models (both deterministic and stochastic) and linear programming models are also possible approaches [78]. The fact that infectious diseases are *dynamic* (epidemics evolve over time), *nonlinear* (the rate of new infection is approximately a function of the number of people who are infective multiplied by the number of people who are susceptible), and *stochastic* (many factors, such as behavioural and biological factors that influence the transmission and progression of a disease vary across individuals and over time) is key to determining the appropriate mathematical framework approach.

All the other approaches fail to appropriately capture disease transmission in the population except dynamic compartmental models and network models which are better suited for projecting the evolution of an epidemic over time. In compartmental models, the population is divided into a set of mutually exclusive but collectively exhaustive compartments with individual transitions between subclasses modelled by a system of nonlinear difference or differential equations. Deterministic compartmental models are useful when considering large populations, where model parameters for an *average* individual are sufficient whereas stochastic epidemic models are particularly useful when random variations in model parameters are important, or if the population under consideration is small and/or heterogeneous [78]. Besides, stochastic models can become computationally intensive as is the case with network models wherein each individual in the population is modelled as well

as his or her partnerships. In this study deterministic ordinary differential equations model formulations are developed to describe the state system making use of the appropriate form of infection.

### 2.1.1 Compartmental Modelling

In 1927, Kermack and McKendrick wrote a pioneering article discussing the application of nonlinear dynamic systems to epidemic control. In 1979, Anderson and May applied this theory to many modern infectious diseases [2, 84]. The underlying idea behind a deterministic model is to characterize the epidemic by the number of susceptible and infected individuals over time. This approach for modelling the transmission of infectious diseases in human populations involves subdivision of the population under consideration into a number of epidemiological classes called compartments and the resulting models are thus called compartmental models. The primary classes usually considered are the following:

*Susceptible (S)*: This group consists of those individuals in a population who are not infected but are however capable of contracting the disease under appropriate conditions.

*Exposed (E)*: This class comprises of individuals who are infected with the disease pathogen, but are not yet able to infect others. They are still in the incubating stage, and do not possess immunity. This group is also known as the latent class.

*Infected (I)*: This is a collection of individuals who have contracted the disease or infection. These people are infectious with the disease pathogen, that is, they can transmit the disease after a contact with a susceptible individual.

*Recovered/removed (R)*: This is a set of individuals who possess temporary or permanent immunity and may not contract or transmit the disease, either because they are no longer infectious, have been vaccinated or may be dead.

Compartmental models have provided valuable insights into the epidemiology of so many infectious diseases including AIDS. Diseases that confer immunity have a different compartmental structure from diseases without immunity [94]. For diseases which confer immunity, the SIR terminology is used to describe the transition of individuals from the susceptible to the infected and then to the removed/recovered class. The term SIS describes a disease with no immunity against re-infection, indicating the movement of individuals from the susceptible to infective and then back to the susceptible class. Other possibilities include SEIR and SEIS models with an exposed period of being infected and becoming infective, and SIRS models with temporary immunity on recovery from infection [15].

The sizes of each class at any time $t$ are represented by $S(t)$, $E(t)$, $I(t)$, $R(t)$ respectively with $N(t)$ denoting the total population size, that is, $N(t) = S(t) + E(t) + I(t) + R(t)$. Some other classes may be adopted to increase accuracy of the model.

Deterministic compartmental models with few disease states can often be solved analytically. As the number of disease states increases, a compartmental model can more realistically capture the subtleties of disease transmission and progression. However, the model can become analytically intractable. In this case, numerically solving the system of differential equations is the best alternative. After specifying initial conditions for each equation, the ordinary differential equations system can be solved by using numerical solution techniques such as the Runge-Kutta methods [78].

The transmission of diseases may be through horizontal incidence, from infectives to susceptibles, and/or vertical transmission, for example from mothers to babies. The probability, per unit time, at which susceptible members of the population are infected is called the *force of infection* and is generally viewed as a function of the total number of infectives. Epidemic measures such as incidence, prevalence and the basic reproduction number are relevant for models of infectious disease control. *Incidence* refers to the number of individuals in the population who become infected in a given period of time. It is often referred to as incidence rate, which is actually the number of new cases per person per unit time. *Prevalence* is defined as the proportion of the population that is infected at a given point in time. The basic reproduction number, $R_0$, is defined as the average number of secondary infections caused by a typical infected individual during his entire period of infectiousness, in a completely susceptible population, absent any interventions [78]. It represents the strength of an infectious disease at sustaining itself in a population: when $R_0 < 1$ the disease will die out in the long run; when $R_0 > 1$ the disease will remain endemic in the population. In cases where $R_0 = 1$, the disease becomes endemic, meaning the disease remains in the population at a consistent rate, as one infected individual transmits the disease to one susceptible [114]. In general, higher values of $R_0$ correspond to diseases that are more difficult to eliminate. $R_0$ is clearly a theoretical outcome, derived from mathematical analyses as described later, given that the population is no longer entirely susceptible by the time a new epidemic raises public health concerns.

### 2.1.2 Incidence/Transmission

The probability of transmission in a given time period may be regarded as either a function of the number of infectious individuals in a given area or as a function of the prevalence of infection in the population. In the former case, the contact rate depends on the size of the total host population and thus models are said to represent *mass action* (density dependent)

transmission. This type of incidence has been used in modelling several infectious diseases and is mostly suitable when a small population size is considered. In the latter case, the contact rate is assumed to be constant. Transmission models for this scenario are said to be for *standard* (frequency dependent) transmission.

While modelling the transmission of measles in 1906, William Hamer observed that the incidence of new cases in a time interval was proportional to the product $SI$ of the number of susceptibles and infectives in the population. This conceptualization, called mass action in analogy to its origin in chemical reaction kinetics, is fundamental in the modern theory of deterministic epidemic modelling [107]. It offers convenience and it is a reasonable assumption for complex contact processes especially for low population densities.

A single susceptible individual in a homogeneously mixing population contacts other members at a rate $c$. The proportion of these contacts that are with infectious individuals is $I/N$. If the probability of infection given contact is $\beta$, then the rate of transmission of infection to susceptibles is $\beta cI/N$. The rate of infection for the susceptible population is then $\beta cSI/N$. Terms such as $\beta I/N$ and $\beta SI/N$ are frequent in literature given that the contact rate is, quite often, a function of population density. In particular, $c$ may either be proportional to $N$ or may be constant. The contact rate function $c$ can be subsumed into $\beta$, which is then no longer a probability but a transmission coefficient.

In modelling the HIV/AIDS dynamics, the population $\mathrm{N(t)}$ is divided into various subclasses, for example, of HIV negatives but susceptibles $S(t)$, HIV positives or infectives $I(t)$, individuals undergoing treatment $T(t)$ and that of AIDS patients $A(t)$, i.e.

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

Susceptibles are assumed to become infected via sexual contacts with infectives and infectives move with a constant rate to develop AIDS. The resulting systems of equations are derived based on the assumptions applicable based on the interaction and progression from one subclass to the other. It is important to note that models should rely on assumptions that are consistent with empirical evidence. Existing models of nominal heterosexual HIV transmission for sub-Saharan Africa have not accurately portrayed the epidemiological situation. Deuchert and Brody [29] implore modelers to realistically simulate HIV spread by ensuring that parameter values are based on the most accurate data.

Other feasible compartmental models will be derived and these will be analyzed using stability theory of differential equations as well as numerical simulation. The model analysis will incorporate comparison of the theoretical results with known HIV data. Investigations in

the necessary conditions for controlling the disease will be undertaken by initially formulating the appropriate optimal control problems.

## 2.2 Stability Analysis

For an autonomous system of ordinary differential equations

$$\dot{\boldsymbol{x}} = \frac{d\boldsymbol{x}}{dt} = \boldsymbol{f}(t, \boldsymbol{x}),$$

where $\boldsymbol{x} = \begin{pmatrix} x_1 \\ x_2 \\ \vdots \\ x_n \end{pmatrix}$ and $\boldsymbol{f} = \begin{pmatrix} f_1 \\ f_2 \\ \vdots \\ f_n \end{pmatrix}$, any point $\boldsymbol{x}_*$ such that $\boldsymbol{f}(\boldsymbol{x}_*) = \boldsymbol{0}$ is referred to as an *equilibrium point*.

Equilibrium points represent stationary conditions for the dynamics of a system. Typically, equilibrium points govern long time behaviour of physical models. In particular, solutions tend to approach stable equilibrium points as time gets large, and to move away from unstable equilibrium points. A general method for studying stability regards the consideration of eigenvalues.

**Definition 2.1**: The equilibrium point $\boldsymbol{x}_*$ is

- stable if $\forall\, \epsilon > 0\ \exists\, \delta(\epsilon) > 0$ such that $|\boldsymbol{x}(0) - \boldsymbol{x}_*| < \delta \implies |\boldsymbol{x}(t) - \boldsymbol{x}_*| < \epsilon, \forall\, t > 0$
- unstable if it is not stable
- asymptotically stable if it is stable and $\delta$ can be chosen such that $|\boldsymbol{x}(0) - \boldsymbol{x}_*| < \delta \implies \lim_{t\to\infty} \boldsymbol{x}(t) = \boldsymbol{x}_*$.

$\boldsymbol{x}_*$ is said to be a locally or simply stable equilibrium point if initial conditions that start near $\boldsymbol{x}_*$ remain close to $\boldsymbol{x}_*$. In other words, no eigenvalue of the Jacobian matrix of $\boldsymbol{f}(\boldsymbol{x}_*)$ has a positive real part.

**Definition 2.2**: Let $\boldsymbol{x}_*$ be an asymptotically stable equilibrium point of the system $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$, where $\boldsymbol{f}$ is a locally Lipschitz function defined on a domain $\boldsymbol{D} \subset \mathbb{R}^n$ ($\boldsymbol{x}_* \in \boldsymbol{D}$).

- The region of attraction is the set of all points $\boldsymbol{x}_0$ in $\boldsymbol{D}$ such that the solution of $\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x})$, $\boldsymbol{x}(0) = \boldsymbol{x}_0$ is defined for all $t \geq 0$ and converges to $\boldsymbol{x}_*$ as $t$ tends to infinity.
- $\boldsymbol{x}_*$ is said to be globally asymptotically stable if the region of attraction is the whole of $\mathbb{R}^n$.

The region of attraction is also referred to as the region of asymptotic stability, domain of attraction or basin. Steady state solutions where there is no disease in the population are

called disease-free equilibrium (DFE) points whereas steady state solutions where the disease persists are called endemic equilibrium (EE) points. Many epidemiological models have disease-free and endemic equilibrium points.

A major task in deterministic epidemiological modelling of heterogeneous populations is to identify conditions for local and global stability of the equilibria and to work out the relations among these stability conditions, the threshold of epidemic take-off, and endemicity, and the basic reproduction [111]. Thus, after formulating the models, stability analysis will be given by computing the basic reproduction number, $R_0$, by using the definition which is to be verified by the condition for stability of the disease free equilibrium. $R_0$ is a threshold for stability of a disease-free equilibrium and is related to the peak and final size of an epidemic [119]. It is characterized by regarding the infection transmission as a 'demographic process', where causing a new infection through transmission is treated as an 'epidemiological birth'. The infection process is then viewed in terms of consecutive 'generations of infected individuals' [33]. Subsequent generations growing in size then indicate a growing population (i.e. an epidemic), and the growth factor per generation indicates the potential for growth. This growth factor is then the mathematical characterization of $R_0$. A matrix that relates the numbers of newly infected individuals in the various categories in consecutive generations is then defined. This matrix, usually denoted by $\boldsymbol{K}$, is called the next-generation matrix (NGM). It was introduced by Diekmann et al [32] who proposed to define $R_0$ as the dominant eigenvalue of $\boldsymbol{K}$.

The natural basis for the definition and calculation of $R_0$ is the next-generation matrix (NGM) [33]. To compute the basic reproduction number we only consider the states that apply to infected individuals. One begins with those equations of the ODE system that describe the production of new infections and changes in state among infected individuals. The first step is to linearize the so-called infected subsystem of nonlinear ODEs about the infection-free steady state, that is, the disease-free equilibrium. This linearized infected subsystem is the starting point of calculations. Using the fact that any linear system of ODEs can be described by a matrix, the matrix is decomposed as $\boldsymbol{F} - \boldsymbol{V}$, where $\boldsymbol{F}$ is the transmission part, describing the production of new infections, and $\boldsymbol{V}$ is the transition part, describing changes in state (including removal by death). Next, the dominant eigenvalue, or more precisely the spectral radius $\rho$, of the matrix $\boldsymbol{K} = \boldsymbol{F}\boldsymbol{V}^{-1}$ is computed [33, 120].

In addition, the disease free and endemic equilibrium points of the models are to be computed from which the conditions for local and global stability will be established. The conditions for local stability will be established using the Jacobian matrix by incorporating Routh-Hurwitz criteria while the global stability conditions can be established via the

Lyapunov function. In particular, an equilibrium point is locally asymptotically stable if the trace and the determinant of the Jacobian matrix evaluated at the equilibrium point are, respectively, negative and positive. It has been established that if $R_0 < 1$, then the DFE is locally asymptotically stable, and the disease cannot invade the population, but if $R_0 > 1$, then the DFE is unstable and invasion is always possible [50].

### 2.3 Sensitivity Analysis

In determining how best to reduce mortality and morbidity due to any disease, it is necessary to know the relative importance of the different factors responsible for its transmission. Essential to any mathematical model of disease progression, thus, is a sensitivity analysis to gauge the impact of parameters on solutions. This analysis allows for the impact of varying parameters to be explored. Since initial disease transmission is directly related to $R_0$, we calculate the sensitivity indices of the reproductive number to the parameters in the model. These indices tell us how crucial each parameter is to disease transmission. Sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values since there are usually errors in data collection and presumed parameter values [22]. Here we use it to discover parameters that have a high impact on $R_0$ and these should be targeted by intervention strategies.

Sensitivity indices allow us to measure the relative change in a state variable when a parameter changes. We make use of the normalized forward sensitivity index of a variable to a parameter, a ratio of the relative change in the variable to the relative change in the parameter. When the variable is a differentiable function of the parameter, the sensitivity index is defined as follows:

**Definition 2.3**: The normalized forward sensitivity index of a variable, $u$, that depends differentiably on a parameter, $p$, is defined as:

$$\zeta_p^u = \frac{\partial u}{\partial p} \times \frac{p}{u}$$

As we have an explicit formula for $R_0$, we derive an analytical expression for the sensitivity of $R_0$ to each of the different parameters described in the model. However, some of the expressions for the sensitivity indices might be complex with little obvious structure. In this case, we evaluate the sensitivity indices using the baseline parameter values.

It is sometimes desirable to also calculate the sensitivity indices of the endemic equilibrium point to the model parameters given that disease prevalence is directly related to the endemic equilibrium point.

## 2.4 Optimal Control

Optimal control theory, an extension of the calculus of variations, is a mathematical optimization method for deriving control policies. It has been a powerful mathematical technique useful in decision making regarding complex biological systems. The technique deals with the problem of finding a control law for a given system such that a certain optimality criterion is achieved. The method is used to solve for an extremum value of an objective functional, $J\big(t, \boldsymbol{x}(t), \boldsymbol{u}(t)\big)$, involving dynamic variables which are divided into two classes: state variables, $\boldsymbol{x}$, and control variables, $\boldsymbol{u}$. This maximizing or minimizing process is accomplished by adjusting the control variables, $\boldsymbol{u}$, until the maximum or minimum is attained. The control set which yields the extreme value is denoted by $\boldsymbol{u}^*$ and is called an optimal control. These control variables, which in our case are functions of time, can be used in many modelling situations and could be functions of any controllable variable [86]. When dealing with a finite dimensional system in time, the states of infection are described by ODEs and the control is deterministic. Initial conditions for the state variables should always be provided and sometimes explicit intra-temporal constraints. Optimal control problems can be solved more easily using the vehicle of the Hamiltonian.

There are a number of different methods for calculating the optimal control for specific models. Pontryagin's Maximum Principle, for example, allows the calculation of the optimal control for an ordinary differential equations model with given constraints. In particular, the optimal control can be derived from the necessity conditions using Pontryagin's maximum principle [103] and sufficiency conditions by solving the Hamilton-Jacobi-Bellman equation. In [61, 72], other powerful optimal control techniques have been derived for partial differential equations and difference equations.

### 2.4.1 The General Optimal Control Problem

We consider a system whose state at any time $t$ is described by a vector $\boldsymbol{x} = \boldsymbol{x}(t) \in \mathbb{R}^n$. The system evolves in time, and we have the ability to influence its evolution through a vector-valued control $\boldsymbol{u}(t) \in \mathbb{R}^m$. The evolution of the system is determined by a set of ordinary differential equations given by

$$\dot{\boldsymbol{x}}(t) = \boldsymbol{f}\big(t, \boldsymbol{x}(t), \boldsymbol{u}(t)\big);\ \boldsymbol{x}(0) = \boldsymbol{x}_0$$

and the goal is to choose the function $\boldsymbol{u}(t)$ for $0 < t < T$ so as to maximize some utility or minimize some cost, the objective functional e.g.

$$J = \int_0^T \boldsymbol{h}\big(t, \boldsymbol{x}(t), \boldsymbol{u}(t)\big)dt + g\big(T, \boldsymbol{x}(T)\big).$$

The problem is determined by specifying the dynamics $\boldsymbol{f}$, the initial state $\boldsymbol{x}_0$, the final time $T$, the "running utility" $\boldsymbol{h}$ and the "final utility" $g$. The problem is solved by finding the optimal control $\boldsymbol{u}(t)$ for $0 < t < T$ and the value of the extremum.

### 2.4.2 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 cost function.This principle converts the maximization/minimization of the objective functional, $J$, coupled with the state variable into maximizing/minimizing point-wise a corresponding Hamiltonian with respect to the controls.

**Theorem 2.1**: *If $\boldsymbol{u}^*(t)$ and $\boldsymbol{x}^*(t)$ are optimal for the problem, then there exists piece-wise differential adjoint variables $\boldsymbol{\lambda}(t) \in \mathbb{R}^n$ such that*

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

*for all controls $u_j$ at each time $t$, where the Hamiltonian $H$ is given by*

$$H = \boldsymbol{h}\big(t, \boldsymbol{x}(t), \boldsymbol{u}(t)\big) + \boldsymbol{\lambda}'(t)\boldsymbol{f}\big(t, \boldsymbol{x}(t), \boldsymbol{u}(t)\big),$$

*and*

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

*constitute the adjoint system,*

$$\frac{\partial H}{\partial u_j} = 0$$

*provide the stationary conditions for the controls while*

$$\lambda_i(T) = 0$$

*specify the transversality conditions.*

The adjoint variable $\lambda_i(t)$ is the shadow price or co-state variable which denotes the increase of the objective function due to marginal increase of the state variable $x_i, i = 1, \ldots n$. At any time, the decision maker can use the control variable to generate direct contributions to the objective function (represented by the cost function term $\boldsymbol{h}\big(t, \boldsymbol{x}(t), \boldsymbol{u}(t)\big)$ in the Hamiltonian), or he/she can use the control variable to change the value of the state variable in order to generate contributions to the objective function in the future. These indirect contributions are measured by the term $\boldsymbol{\lambda}'(t)\boldsymbol{f}\big(t, \boldsymbol{x}(t), \boldsymbol{u}(t)\big)$ in the Hamiltonian, where $\boldsymbol{\lambda}'(t)$ is the transpose of $\boldsymbol{\lambda}$.

## 2.5 Numerical Analysis

Solutions to ordinary differential equations cannot be determined uniquely without some outside condition, typically an initial value or a boundary value. The optimality system consisting of the state and adjoint systems will be solved computationally using an iterative scheme. In particular, the fourth order Runge-Kutta scheme will be used because it is quite accurate, stable, relatively easy to program and does not require a lot of computing effort. This numerical technique is reasonably simple and robust and is a good general candidate for numerical solution of differential equations when combined with an intelligent adaptive step-size routine [104].

The Runge-Kutta fourth order method is based on the following:

$$\boldsymbol{x}_{n+1} = \boldsymbol{x}_n + (a_1 k_1 + a_2 k_2 + a_3 k_3 + a_4 k_4)h$$

Knowledge of the value of $\boldsymbol{x}_n = \boldsymbol{x}(t_n)$ is used to approximate the value of $\boldsymbol{x}_{n+1} = \boldsymbol{x}(t_{n+1})$, where $h = t_{n+1} - t_n$. Comparing the approximation to the first five terms of the Taylor series of $\boldsymbol{x}_{n+1}$ about $\boldsymbol{x}_n$, the technique is then specified by the following algorithm:

$$\boldsymbol{x}_{n+1} = \boldsymbol{x}_n + \frac{h(k_1 + 2k_2 + 2k_3 + k_4)}{6}$$

where

$$k_1 = \boldsymbol{f}(t_n, \boldsymbol{x}_n);\ k_2 = \boldsymbol{f}\left(t_n + \tfrac{h}{2}, \boldsymbol{x}_n + \tfrac{k_1}{2}\right);\ k_3 = \boldsymbol{f}\left(t_n + \tfrac{h}{2}, \boldsymbol{x}_n + \tfrac{k_2}{2}\right);\ k_4 = \boldsymbol{f}(t_n + h, \boldsymbol{x}_n + k_3)$$

Another frequently used scheme uses

$$k_1 = \boldsymbol{f}(t_n, \boldsymbol{x}_n);\ k_2 = \boldsymbol{f}\left(t_n + \tfrac{h}{2}, \boldsymbol{x}_n + \tfrac{k_1}{2}h\right);\ k_3 = \boldsymbol{f}\left(t_n + \tfrac{h}{2}, \boldsymbol{x}_n + \tfrac{k_2}{2}h\right);\ k_4 = \boldsymbol{f}(t_n + h, \boldsymbol{x}_n + k_3 h)$$

Computational programming software such as MATLAB and MAPLE will be employed to implement simulation of the data into models so as to analyze and interpret the dynamics of the models graphically.

## 2.6 Cost Effective Analysis

The goal of modelling infectious disease epidemics is not only to estimate future economic and health outcomes under different control scenarios but also to determine the optimal allocation of limited resources between competing interventions [78]. Before determining the optimal disease-control policy, decision makers must choose the appropriate decision criteria. In other words, they must choose how to select programs based on the cost-

effectiveness information. The choice of criteria must take into consideration the appropriate constraints. These may include budget constraints, limitations on allowable allocations of resources, etc.

To quantify the cost-effectiveness of disease control measures, it is important to examine the cost effectiveness ratios of the strategies, so as to draw our conclusions. There are three types of cost effectiveness ratios: 1) Average Cost-Effectiveness Ratio (ACER) which deals with a single intervention and evaluates that intervention against its baseline option (e.g. no intervention or current practice). It is calculated by dividing the net cost of the intervention by the total number of health outcomes prevented by the intervention. 2) Marginal Cost-Effectiveness Ratio (MCER) for the assessment of the specific changes in cost and effect when a program is expanded or contracted. 3) Incremental Cost-Effectiveness Ratio (ICER) used to compare the differences between the costs and health outcomes of two alternative intervention strategies that compete for the same resources and is generally described as the additional cost per additional health outcome [95]. This involves a comparison of the costs and health effects of an intervention to assess the extent to which it can be regarded as providing value for money with a view to informing decision-making in order to determine where to allocate limited healthcare resources.

Cost effectiveness analysis is a standard tool for comparing the costs and benefits of two or more medical interventions [43]. The incremental cost effectiveness ratio (ICER) is calculated as the marginal cost of an intervention divided by the marginal benefit. It measures how much additional “bang for the buck” could be achieved by switching from one intervention to another. This can be written as

$$ICER = \frac{Costs_{with\ intervention} - Costs_{without\ intervention}}{Benefits_{with\ intervention} - Benefits_{without\ intervention}}$$

This allows us to compare the cost-effectiveness of combinations of at least two of the control strategies, e. g. screening, preventive, enlightenment and treatment of infective individuals. When comparing competing intervention strategies incrementally, one intervention should be compared with the next less-effective alternative. The ICER numerator includes the differences in intervention costs, averted disease costs, costs of prevented cases and averted productivity losses if applicable. While, ICER’s denominator is the difference in health outcomes (e.g. total number of infection averted, number of susceptibility cases prevented).

Alternative interventions are ranked by their incremental cost effectiveness ratio, from most favourable to least favourable. The decision maker can go down the list and select interventions until a predefined budget is exhausted [78]. If medical interventions offer substantial gains in health benefits, perhaps it is wise to increase the funds available for such interventions. These considerations make this way of implementation difficult in practice.

An alternative and preferred approach is to rank interventions by their gains in health benefits from least favourable to most favourable, and then calculate incremental cost effectiveness ratios. The cost of a medical intervention includes the direct cost of the intervention itself e.g., prescription drug cost, prevention program cost, etc. as well as all indirect costs of related health care e.g., hospital visits, ancillary services, etc. The counterpart to an intervention's cost is the expected health benefit it generates in the population. Outcomes specific to a particular disease or intervention such as number of infections averted or number of people who die are often relevant when comparing interventions for controlling a particular disease, but not when comparing different diseases.

# CHAPTER THREE

# LABOUR FORCE PRODUCTIVITY IN THE PRESENCE OF HIV/AIDS

*In this chapter, we investigate the productivity of organizational labour force in the presence of HIV/AIDS with enlightenment/monitoring, preventive and HAART treatment measures in enhancing workforce output. We formulate a mathematical productivity epidemiological model for the transmission dynamics of HIV/AIDS that includes the three intervention strategies. We use the model to estimate the cost of the non-productive susceptibles and the non-productive infectious individuals (depressed) to organizations as well as project the benefits when the non-productive and depressed employees have access to interventions.*

*We first consider the constant control case, calculate the basic reproduction number and investigate 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. We also investigate, by calculating the sensitivity indices, the sensitivity of the basic reproductive number to the model's parameters. In the time dependent control case, we use 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.*

## 3.1 Introduction

The productivity of labour force is a key variable in the profitability of any organizational venture. Productivity can also be influenced by factors such as skill level, motivation, satisfaction and schedule pressure. The question now is how motivated and productive would an employee be in the face of HIV/AIDS infection?

HIV/AIDS is not only beyond a health issue but is a substantial threat to socio-economic development, imposing a heavy burden on families, communities and economies. The pandemic has affected most countries in the world. In 2003, about 26 million of the estimated 38 million HIV-positive persons were workers between the ages of 15 and 49, the most productive age group [115]. This has great implications for families and economies in terms of employment, productivity and labour market changes [51].

In 2005, about 3.1 million people died from AIDS world-wide and 4.9 million people became infected with HIV, bringing to 40.3 million the number of people living with the virus across the world [116]. In 2010, a total of 34 million people (30.1 million adults) were living with HIV,

2.7 million were new infections (2.3 million adults) and 1.8 million (1.5 million adults) died due to AIDS [119]. HIV infection, which causes AIDS, is a global problem which has shown a high degree of prevalence in populations all over the world especially in sub-Saharan Africa. The most susceptible individuals at risk of acquiring infection include people having sexual contacts with HIV infected, homosexual and bisexual men, intravenous drug abusers and persons transfused with contaminated blood.

HIV is preventable but not curable. Highly Active Anti-Retroviral Therapy (HAART) is not a cure, but the use of drugs to halt the decline in immune deficiency and prevent disease progression and death. HAART suppresses viral replication, and successful treatment helps in slowing or halting the disease progression, prevention of drug resistance, and improvement in the quality of life. Although the number of infected people receiving HAART in low and middle- income countries increased dramatically, optimal disease management is not well defined. Despite substantial progress in access to treatment, only 20% of adults who needed HAART were receiving it in 2008 [11]. By 2010, of the estimated 15 million people living with HIV in low- and middle-income countries who need treatment, 5.2 million had access, which translated into fewer AIDS-related deaths. For the estimated 33.3 million people living with HIV after nearly 30 years into a very complex epidemic, the gains are real but still fragile [118].

There is still an on-going intensive search for an anti-HIV vaccine. The use of chemotherapies is aimed at killing or halting the pathogen, but treatment which can boost the immune system can serve to help the body fight infection on its own [56]. The new treatments are aimed at reducing viral population and improving the immune response. This brings new hope to the treatment of HIV infection, and we are exploring strategies for such treatments using optimal control techniques.

A host of social, economic, cultural and political factors facilitate the spread of HIV through populations. HIV spreads more widely where wrong perspectives or attitudes about HIV are common. An example is an extensive organizational (office) sexual network, where a person is having sex with more than one partner in an office location. Having multiple partners concurrently creates a node of transfer from one sexual network to another. Where sexual networks are smaller and more circumscribed, HIV can spread but less widely. The challenges posed by the peoples' attitude and ignorance to the disease dynamics call for a better understanding of the disease transmission and development of effective and optimal strategies for prevention and control of the spread of HIV/AIDS disease. Research has also shown that behavioural or attitudinal change has a great influence in disease spread.

In an organizational work place, individuals are recruited blindly without knowledge of their HIV/AIDS status. In other words, it is not known whether the individual would become an asset (productive) or a liability (non-productive) to the company. The non-productive employees can be associated with their lifestyle choices such as carelessness, alcoholism, wrong value perception, office politicking and multiple sexual partners. It is clear from various studies that interventions designed to support employment, or economic policy, or a national HIV/AIDS strategy cannot be implemented without considering the particular impact HIV and AIDS are having on the economically active and productive population. As very little is known about the impact of HIV/AIDS on the labour force structure and productivity, this study then seeks to fill some of the gaps in this knowledge.

The impact of AIDS in economic sectors is significant. Studies done in some countries have shown that AIDS will continue to have adverse effects on agriculture, including loss of labour supply and remittance income. Agriculture, which accounts for a large portion of production and large employment opportunities and is the largest sector in most African economies, bears the brunt of HIV/AIDS. The loss of a few workers at the crucial periods of planting and harvesting can significantly reduce the size of the harvest [80]. AIDS related illnesses and deaths to employees affect firms by both increasing expenditures and reducing revenues. Expenditures are increased for health care costs, burial fees and training and recruitment of replacement employees. Revenues may be decreased because of absenteeism due to illness or attendance at funerals and time spent on training. Labour turnover can lead to a less experienced labour force that is less productive [121].

Minimal or no attention has been paid to study models which incorporate classes such as productive and non-productive individuals (susceptibles and infected) which may be helpful in determining the productivity level of labour force in organizations in the presence of HIV/AIDS. What is considered here is an improved dynamical system model through the inclusion of a productive susceptible class, productive HIV infected class and time dependent control parameters. We study and determine the possible impact of optimal enlightenment and HAART treatment for enhancing productivity on the spread of HIV. We carry out detailed qualitative optimal control analysis of the resulting model and we determine the necessary conditions for optimal control of the disease using Pontryagin's Maximum Principle in order to identify optimal strategies for controlling the spread of the disease.

Our main goal is to set up an optimal control problem related to the model. In order to do this, we use the following: preventive measures on susceptibles $u_1$, enlightenment or educational parameter $u_2$, HAART treatment rate of individuals with HIV $u_{3,}$ as time dependent control parameters in the model. Hence, we investigate the role of productive susceptibles,

productive infected, optimal prevention (through condom use), enlightenment (through counselling, mentoring, training, screening, educational campaigns) and HAART treatment on the spread of HIV/AIDS.

### 3.2 Model Formulation

We consider a standard compartmental model of HIV/AIDS in which three time dependent control measures are incorporated simultaneously, the following: i) preventive measure (condom use), ii) enlightenment campaign, iii) HAART treatment of HIV individuals for enhanced productivity. The total workforce population at any time $t$, denoted by $N(t)$, is sub-divided into the following five classes: susceptible productive workers ($S_p(t)$), susceptible non-productive workers ($S_n(t)$), infected non-productive workers ($I_n(t)$), infected productive individuals on HAART treatment ($I_p(t)$) and individuals with full blown AIDS ($A(t)$), so that

$$N(t) = S_p(t) + S_n(t) + I_n(t) + I_p(t) + A(t).$$

Susceptibles are individuals who have not contracted the infection but may be infected through sexual contacts. The susceptible non-productive are individuals whose lifestyle places them at high risk of contracting the disease. We assume that individuals with AIDS are sexually inactive.

The organization recruits workers at a rate $Q$, where the proportion of susceptible non-productive workers are recruited at a rate $\pi Q$. The per capita contact rate for susceptible non-productive individuals is $\beta$ while the susceptible productive workers have a per capita contact rate of $\beta_1 := \rho\beta < \beta$, where $\rho$ is the modification parameter due to right values perception of the susceptible productive workers. When susceptible non-productive individuals are enlightened (through counselling, mentoring or monitoring) and their attitudes change, they progress to the susceptible productive class at a rate $u_2\alpha$, where $u_2$ is the control efforts on enlightenment. We assume that unprotected sexual contact between any type of susceptible and any type of infective would eventually land the susceptible into the infected non-productive class. The infected non-productive individuals on HAART treatment progress at a rate $u_3\sigma$ to the infected productive class, where $\sigma$ is the proportion of the infected non-productive individuals on HAART treatment for enhanced productivity, $u_3$ is the control efforts on HAART treatment to enhanced productivity. Infected non-productive workers not on HAART treatment progress to the full blown AIDS class at a rate of $\delta$ while $\gamma$ is the rate of progression of infected productive individuals to full blown AIDS, where $\gamma < \delta$.

The term $\eta$ is the modification parameter due to HAART treatment and right values perception of the infected productive individuals. The disease induced death rate of individuals with AIDS is denoted by $\kappa$ while μ is the natural mortality rate unrelated to HIV/AIDS. We assume, as already stated, that the AIDS class is sexually inactive and non-productive.

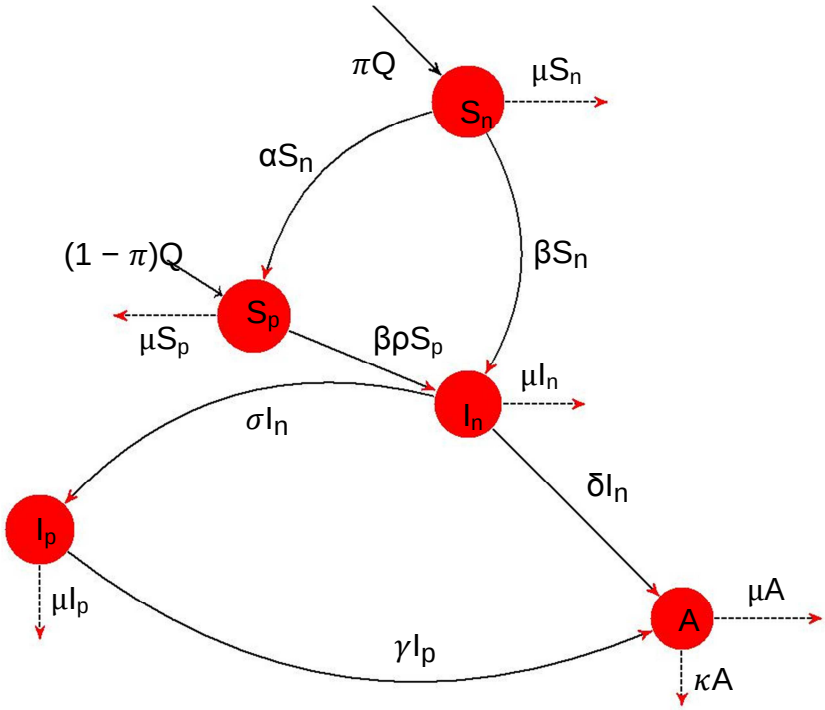



Fig 3.1: Flow diagram for HIV/AIDS transmission

The resulting **state system** of ordinary differential equations is the following:

$$\left.\begin{aligned}
\frac{dS_p}{dt} &= (1-\pi)\mathrm{Q} - (1-\mathrm{u}_1)\rho\beta\phi_I\mathrm{S_p} + \mathrm{u}_2\alpha\mathrm{S_n} - \mu\mathrm{S_p}\\
\frac{dS_n}{dt} &= \pi\mathrm{Q} - (1-\mathrm{u}_1)\beta\phi_I\mathrm{S_n} - \mathrm{u}_2\alpha\mathrm{S_n} - \mu\mathrm{S_n}\\
\frac{dI_n}{dt} &= (1-\mathrm{u}_1)\beta\phi_I\phi_S - (\mathrm{u}_3\sigma + \delta + \mu)\mathrm{I_n}\\
\frac{dI_p}{dt} &= \mathrm{u}_3\sigma\mathrm{I_n} - \gamma\mathrm{I_p} - \mu\mathrm{I_p} = \mathrm{u}_3\sigma\mathrm{I_n} - (\gamma+\mu)\mathrm{I_p}\\
\frac{dA}{dt} &= \delta\mathrm{I_n} + \gamma\mathrm{I_p} - \kappa\mathrm{A} - \mu\mathrm{A} = \delta\mathrm{I_n} + \gamma\mathrm{I_p} - (\kappa+\mu)\mathrm{A}
\end{aligned}\right\} \qquad (3.1)$$

where $\phi_I = \mathrm{I_n} + \eta\mathrm{I_p}$ is the force of infection and $\phi_S = \rho\mathrm{S_p} + \mathrm{S_n}$ is susceptibility to infection.

### 3.3 Existence and Stability of Equilibria

#### 3.3.1 Stability of the Disease-Free Equilibrium (DFE)

Disease-free equilibrium entails setting $I_n = I_p = A = 0$ and also assumes steady-state, i.e. $\frac{d(\cdot)}{dt} = 0$. The DFE of our HIV/AIDS model exists and is given by

$$\xi_0 = (S_p^0, S_n^0, I_n^0, I_p^0, A^0) = \left(\frac{(u_2\alpha + \mu - \pi\mu)Q}{\mu(u_2\alpha + \mu)}, \frac{\pi Q}{u_2\alpha + \mu}, 0, 0, 0\right).$$

The control reproduction number, $R_0$, of the model in the presence of non-productive susceptible individuals is calculated using the next generation matrix $FV^{-1}$, where $F$ represents the rate of appearance of new infections in each compartment and is given by

$$F = \begin{bmatrix} (1-\mathrm{u}_1)\beta\phi_S & (1-\mathrm{u}_1)\beta\eta\phi_S & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

while $V$ represents the rate of transfer of individuals out of each compartment and is given by

$$V = \begin{bmatrix} \mathrm{u}_3\sigma + \delta + \mu & 0 & 0 \\ -\mathrm{u}_3\sigma & \gamma + \mu & 0 \\ -\delta & -\gamma & \kappa + \mu \end{bmatrix}.$$

Taking the most positive eigenvalue of $FV^{-1}$ evaluated at the DFE $\xi_0$ gives

$$R_0 = \frac{(1-\mathrm{u}_1)\beta(\gamma+\mu+\eta\mathrm{u}_3\sigma)\{\rho(u_2\alpha+\mu-\pi\mu)+\pi\mu\}\mathrm{Q}}{\mu(\mathrm{u}_3\sigma+\delta+\mu)(\gamma+\mu)(u_2\alpha+\mu)} \tag{3.2}$$

The DFE is locally asymptotically stable if $\mathrm{R}_0 < 1$ and unstable if $\mathrm{R}_0 > 1$.

#### 3.3.2 Existence of Endemic Equilibrium

Calculating the endemic equilibrium point, $\xi^* = (S_p^*, S_n^*, I_n^*, I_p^*, A^*)$, we obtain

$$\left.\begin{aligned} S_p^* &= \frac{(1-\pi)\mathrm{Q}+u_2\alpha S_n^*}{(1-\mathrm{u}_1)\beta\phi_I^*+\mu} \\ S_n^* &= \frac{\pi\mathrm{Q}}{(1-\mathrm{u}_1)\beta\phi_I^*+u_2\alpha+\mu} \\ I_n^* &= \frac{(1-\mathrm{u}_1)\eta\beta I_p^*\phi_S^*}{\mathrm{u}_3\sigma+\delta+\mu-(1-\mathrm{u}_1)\beta\phi_S^*} \\ I_p^* &= \frac{\mathrm{u}_3\sigma I_n^*}{\gamma+\mu} \\ A^* &= \frac{\delta I_n^*+\gamma I_p^*}{\kappa+\mu} \end{aligned}\right\} \tag{3.3}$$

where $\phi_I^* = I_n^* + \eta I_p^*$ is the endemic force of infection and $\phi_S^* = \rho S_p^* + S_n^*$ is the endemic susceptibility.

The endemic equilibrium satisfies the following polynomial equation

$$P(\phi_I^*) = B\,{\phi_I^*}^2 + C\,\phi_I^* + D = 0 \tag{3.4}$$

where

$$\left.\begin{aligned} B &= \rho(\gamma+\mu)(\delta+\mu+\mathrm{u}_3\sigma) \\ C &= \frac{\mu\rho(\gamma+\mu)(\delta+\mu+\mathrm{u}_3\sigma)(\mu+u_2\alpha)}{\pi\mu(1-\rho)+\rho(\mu+u_2\alpha)}(R-R_0) \\ D &= \mu(\gamma+\mu)(\mu+u_2\alpha))(\delta+\mu+\mathrm{u}_3\sigma)(1-R_0) \end{aligned}\right\} \tag{3.5}$$

with

$$R = \frac{(\mu+\rho(\mu+u_2\alpha))(\pi\mu(1-\rho)+\rho(\mu+u_2\alpha))}{\mu\rho(\mu+u_2\alpha)} \tag{3.6}$$

$R > 1$ if and only if

$$\pi > \pi^{\dagger} := \frac{\mu\rho(\mu+u_2\alpha)+\rho(\mu+u_2\alpha)(\mu+\rho(\mu+u_2\alpha))}{\mu(1-\rho)(\mu+\rho(\mu+u_2\alpha))}$$

We obtain the following result:

***Proposition 3.1***:

1. *If $\pi \geq \pi^{\dagger}$, then the state system (3.1) exhibits trans-critical bifurcation.*
2. *If $\pi < \pi^{\dagger}$, then the state system (3.1) exhibits backward bifurcation. That is, there exists $R_c$ in $(0,1)$ such that if*
   - i. $1 \leq R_0$, *then there is one endemic equilibrium point.*
   - ii. $R_c < R_0 < 1$, *then there are two endemic equilibrium points.*
   - iii. $R_0 = R_c$, *then there is one endemic equilibrium point.*
   - iv. $R_0 < R_c$, *then there are no endemic equilibrium points.*

***Proof***:

1. If $\pi \geq \pi^{\dagger}$, then $R \geq 1$. In this case, we have the following:
   i. If $R_0 > 1$, then $C < 0$. In this case (3.4) has a unique positive solution.
   ii. If $R_0 \leq 1$, then $C \geq 0$ and $B \geq 0$ (because $R_0 \leq 1 \leq \sqrt{R}$). This together with $A > 0$ imply that (3.4) has no positive solution.
2. If $\pi < \pi^{\dagger}$, then $\pi^{\dagger} < 1$. In this case, we have that
   i. if $R_0 \geq 1$, then $C \leq 0$ which implies that (3.4) has a unique positive solution.
   ii. if $R_0 < \sqrt{R}$, then $B \geq 0$ and $C > 0$. This implies that (3.4) has no positive solution.
   iii. If $\sqrt{R} < R_0$, we consider the discriminant of (3.4) $\Delta(R_0) = B^2 - 4AC$. One can see that $\Delta(\sqrt{R}) = -4AC < 0$ and $\Delta(1) = B^2 > 0$. Therefore, there exists $R_c \in (\sqrt{R}, 1)$ such that $\Delta(R_c) = 0$ and $\Delta(R_0) < 0$ for $R_0 \in (\sqrt{R}, R_c)$ and $\Delta(R_0) > 0$ for $R_0 \in (R_c, 1)$. In this case we have the following:
      a. If $\sqrt{R} < R_0 < R_c$, then (3.4) has no positive solution.
      b. If $R_0 = R_c$, then $\Delta = 0$ and $B < 0$. This implies that (3.4) has one positive solution.
      c. If $R_c < R_0 < 1$, then (3.4) has two real solutions which are positive since $C > 0$ and $B < 0$. ■

Proposition 3.1 establishes the existence of two endemic equilibria for $R$ in $(R_c, 1)$.

### 3.4 Sensitivity Analysis

Due to uncertainties associated with the estimation of certain parameter values, it is useful to conduct an investigation to determine how sensitive the basic reproductive number is with respect to its parameters. This will also allow us to identify which of the parameters cause the most reduction in $R_0$ and therefore determine the control measure which is the most effective in controlling the disease. For this we compute the normalized forward sensitivity index of the reproduction number with respect to its parameters. This index measures the relative change in a variable with respect to relative changes in its parameters (see [81] for the application of this index to a malaria transmission model).

**Definition 3.1**: If a variable $h$ depends differentiably on a parameter $p$, then the normalized forward sensitivity index of $h$ with respect to $p$, denoted by $\zeta_p$, is defined as

$$\zeta_p = \frac{p}{h}\frac{\partial h}{\partial p}.$$

The sensitivity index of $R_0$ with respect to β and $Q$ is equal to 1. For the other parameters we obtain

$$\zeta_\rho = \frac{\rho(\mu-\pi\mu+u_2\alpha)}{\pi\mu(1-\rho)+\rho(\mu+u_2\alpha)}, \zeta_\delta = -\frac{\delta}{\delta+\mu+u_3\sigma}, \zeta_\pi = \frac{\pi\mu(1-\rho)}{\pi\mu(1-\rho)+\rho(\mu+u_2\alpha)}.$$

Indices for $\mu, \alpha, \gamma$ and $\sigma$ have complex expressions. We observe that the sensitivity indices using the parameter values in Table 3.2 are always constant (even though their expressions depend on $u_2$ and $u_3$). Therefore, we calculate the sensitivity indices of $\pi, \mu, \rho, \alpha, \gamma, \eta, \sigma$ and $\delta$. Their values are given in the table below:

| Parameter | Description | Index |
|---|---|---|
| $\pi$ | recruited proportion in non-productive susceptible class | 0.035 |
| $\mu$ | mortality rate | -0.38 |
| $\rho$ | modification parameter on productive susceptible | 0.96 |
| $\alpha$ | enlightenment rate | -0.02215 |
| $u_3$ | control effort on HAART treatment | -0.0128 |
| $\eta$ | modification parameter on productive infected | 0.00362 |
| $\sigma$ | proportion of non-productive infected on HAART treatment | -0.0128 |
| $\delta$ | rate of progression to AIDS for non-productive infected | -0.82 |
| $u_2$ | control effort on enlightenment | -0.0221 |

Table 3.1: Sensitivity indices for $R_0$

The interpretation of the sensitivity index values is that an increase/decrease of 1% in any of the parameter values in the first column results in a percentage increase/decrease given by the corresponding value in the third column. In particular, an increase in the modification parameter due to productivity mindset $\rho$ or a decrease in the progression rate to AIDS $\delta$ have negative impact in controlling HIV epidemics, and hence productivity, at the workplace. The most sensitive parameters are transmission and recruitment rates β and $Q$. Since $\zeta_\beta = \zeta_Q = 1$, increasing (or decreasing) the transmission probability rate, β, by 10% increases (or decreases) $R_0$ by 10%. Similarly, increasing (or decreasing) the recruitment rate, $Q$, by 10% increases (or decreases) $R_0$ by 10%. Increasing (or decreasing) the modification parameter $\rho$ by 10%, increases (or decreases) $R_0$ by 9.6%. In the same way, increasing (or decreasing) the progression to AIDS rate $\delta$ by 10% results in a decrease (or increase) in $R_0$ of 8.1%.

In the next section, we apply Pontryagin's Maximum Principle to determine the necessary conditions for the optimal control of the non-productive, both susceptible and infected, on the spread of HIV.

### 3.5 Analysis of Optimal Control

We investigate the optimal level of efforts that would be needed to control the disease and optimize productivity, that is, to minimize the number of non-productive susceptible and infectious individuals at a minimal cost of applying the controls $\mathrm{u}_1$, $\mathrm{u}_2$ and $\mathrm{u}_3$ over a finite time interval $[0, T]$. This is achieved by defining the objective functional, $J$, by choosing a quadratic cost on the controls, in accordance with the existing literature on epidemic controls [56, 1, 37, 74, 67].

$$J = \int_0^T (n\mathrm{S_n} + m\mathrm{I_n} + b_1 u_1^2 + b_2 u_2^2 + b_3 u_3^2)dt, \tag{3.7}$$

where $n$, $m$, $b_1$, $b_2$ and $b_3$ are positive weights. With the given objective functional, $J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3)$, our goal is to minimize the number of carefree susceptibles $\mathrm{S_n}$, while minimizing the cost of controls $\mathrm{u}_1(\mathrm{t})$, $\mathrm{u}_2(\mathrm{t})$ and $\mathrm{u}_3(\mathrm{t})$. We thus seek an optimal control triple $\left(u_1^{\#}, u_2^{\#}, u_3^{\#}\right)$ such that

$$J(u_1^{\#}, u_2^{\#}, u_3^{\#}) = \min\{J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3): (\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3) \in \mathcal{U}\}, \tag{3.8}$$

where

$$\mathcal{U} = \{(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3): \mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3 \text{ are measurable with } 0 \le \mathrm{u_i} \le 1, \mathrm{i} = 1, 2, 3 \text{ for } \mathrm{t} \in [0, \mathrm{T}]\}$$

is the control set. The necessary conditions that an optimal control problem must satisfy come from Pontryagin's Maximum Principle [103]. We use this principle to convert the problem of minimization of the objective functional coupled with the state variable into a problem of minimizing point-wise a Hamiltonian, $H$, with respect to the controls $\mathrm{u}_1$, $\mathrm{u}_2$ and $\mathrm{u}_3$.

$$\begin{aligned} H = {} & n\mathrm{S_n} + m\mathrm{I_n} + b_1 u_1^2 + b_2 u_2^2 + b_3 u_3^2 + \lambda_{\mathrm{S_p}}\{(1-\pi)\mathrm{Q} - (1-\mathrm{u}_1)\rho\beta(\mathrm{I_n} + \eta\mathrm{I_p})\mathrm{S_p} + \mathrm{u}_2\alpha\mathrm{S_n} - \mu\mathrm{S_p}\} \\ & + \lambda_{\mathrm{S_n}}\{\pi\mathrm{Q} - (1-\mathrm{u}_1)\rho\beta(\mathrm{I_n} + \eta\mathrm{I_p})\mathrm{S_n} - \mathrm{u}_2\alpha\mathrm{S_n} - \mu\mathrm{S_n}\} \\ & + \lambda_{\mathrm{I_n}}\{(1-\mathrm{u}_1)\rho\beta(\mathrm{I_n} + \eta\mathrm{I_p})\mathrm{S_p} + (1-\mathrm{u}_1)\rho\beta(\mathrm{I_n} + \eta\mathrm{I_p})\mathrm{S_n} - \mathrm{u}_3\sigma\mathrm{I_n} - \delta\mathrm{I_n} - \mu\mathrm{I_n}\} \\ & + \lambda_{\mathrm{I_p}}\{\mathrm{u}_3\sigma\mathrm{I_n} - \gamma\mathrm{I_p} - \mu\mathrm{I_p}\} + \lambda_A\{\delta\mathrm{I_n} + \gamma\mathrm{I_p} - \kappa\mathrm{A} - \mu\mathrm{A}\} \end{aligned} \tag{3.9}$$

where $\lambda_{\mathrm{S_p}}, \lambda_{\mathrm{S_n}}, \lambda_{\mathrm{I_n}}, \lambda_{\mathrm{I_p}}$ and $\lambda_A$ are adjoint or co-state variables. By applying Pontryagin's Maximum Principle and the existence result for the optimal control [39], we obtain

***Proposition 3.2***: *For the optimal control triple* $\left(u_1^{\#}, u_2^{\#}, u_3^{\#}\right)$ *that minimizes* $J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3)$ *over* $\mathcal{U}$, *there exist adjoint variables* $\lambda_{\mathrm{S_p}}, \lambda_{\mathrm{S_n}}, \lambda_{\mathrm{I_n}}, \lambda_{\mathrm{I_p}}$ and $\lambda_A$ *satisfying the following:*

***(i) Adjoint System***

$$\left.\begin{aligned}
\frac{d\lambda_{S_p}}{dt} &= (1-u_1)\rho\beta\left(I_n+\eta I_p\right)\left(\lambda_{S_p}-\lambda_{I_n}\right)+\mu\lambda_{S_p}\\
\frac{d\lambda_{S_n}}{dt} &= -n+(1-u_1)\beta\left(I_n+\eta I_p\right)\left(\lambda_{S_n}-\lambda_{I_n}\right)+(u_2\alpha+\mu)\lambda_{S_n}-u_2\alpha\lambda_{S_p}\\
\frac{d\lambda_{I_n}}{dt} &= -m+(1-u_1)\beta\lambda_{SI}+u_3\sigma\left(\lambda_{I_n}-\lambda_{I_p}\right)+\delta(\lambda_{I_n}-\lambda_A)+\mu\lambda_{I_n}\\
\frac{d\lambda_{I_p}}{dt} &= (1-u_1)\beta\eta\{\rho S_p(\lambda_{S_p}-\lambda_{I_n})+S_n(\lambda_{S_n}-\lambda_{I_n})\}+\gamma(\lambda_{I_p}-\lambda_A)+\mu\lambda_{I_p}\\
\frac{d\lambda_A}{dt} &= (\kappa+\mu)\lambda_A
\end{aligned}\right\} \quad (3.10)$$

*where* $\lambda_{SI}=\rho S_p(\lambda_{S_p}-\lambda_{I_n})+S_n\left(\lambda_{S_n}-\lambda_{I_n}\right)$.

***(ii) Transversality Conditions***

$$\lambda_{S_p}(T)=\lambda_{S_n}(T)=\lambda_{I_n}(T)=\lambda_{I_p}(T)=\lambda_A(T)=0 \quad (3.11)$$

***(iii) Stationary Values***

$$\left.\begin{aligned}
u_1^{\#} &= min\left\{1,max\left\{0,\frac{\beta(I_n+\eta I_p)\{\rho S_p(\lambda_{I_n}-\lambda_{S_p})+S_n(\lambda_{I_n}-\lambda_{S_n})\}}{2b_1}\right\}\right\}\\
u_2^{\#} &= min\left\{1,max\left\{0,\frac{\alpha S_n\left(\lambda_{S_n}-\lambda_{S_p}\right)}{2b_2}\right\}\right\}\\
u_3^{\#} &= min\left\{1,max\left\{0,\frac{\sigma I_n\left(\lambda_{I_n}-\lambda_{I_p}\right)}{2b_3}\right\}\right\}
\end{aligned}\right\} \quad (3.12)$$

***Proof****:*

Corollary 4.1 in [39], gives the existence of an optimal control due to the convexity of the integrand of $J$ with respect to $u_1$, $u_2$ and $u_3$, a *priori* boundedness of the state solutions, and the *Lipschitz* property of the state system with respect to the state variables [39]. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control. In particular

$$\frac{\partial H}{\partial x}=-\frac{dx}{dt}$$

where $x=S_p,S_n,I_n,I_p,A$ establishes the adjoint system and

$$\frac{\partial H}{\partial u_i} = 0$$

gives $\tilde{u}_i$, $i = 1, 2, 3$ and coupled with standard control arguments involving the bounds on the controls

$$u_i^{\#} = \begin{cases} 0, if\ \tilde{u}_i \leq 0 \\ \tilde{u}_{i,}\ if\ 0 < \tilde{u}_i < 1 \\ 1, if\ \tilde{u}_i \geq 1 \end{cases}$$

provide the stationary values.

Due to the a *priori* boundedness of the state system, the adjoint system and the resulting *Lipschitz* structure of the ODEs, we obtain the uniqueness of the optimal control for small $T$. The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of the state system (3.1) and the adjoint system (3.10) characterized by the stationary values (3.12). There is a restriction on the length of time interval in order to guarantee the uniqueness of the optimality system. This smallness restriction of the length on the time is due to the opposite time orientations of the state and adjoint systems; the state problem (3.1) has initial values and the adjoint problem (3.10) has final values. This restriction is very common in control problems (see [56, 37, 74, 67]). ■

### 3.6 Numerical Results and Discussions

In this section, we study numerically an optimal transmission parameter control for the HIV model. The optimal control set is obtained by solving the associated optimality system which consists of state and adjoint equations. An iterative scheme is used for solving the optimality system. We start to solve the state equations (3.1) with a guess for the controls over the simulated time using the fourth order Runge-Kutta scheme. The state equations are solved using a forward method with given initial conditions for the state variables (3.1). The corresponding adjoint system (3.10) is solved using a backward scheme with the transversality conditions (3.11). The controls are updated by using a convex combination of the previous controls and the stationary value characterizations. This process is repeated and iterations stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iterations [72].

We investigate and compare numerical results in the following scenarios: (i) when the preventive control, $\mathrm{u}_1$, is set to zero and the other control parameters optimized (ii) when the enlightenment control, $\mathrm{u}_2$, is set to zero and the other control parameters optimized (iii) when

the HAART treatment control, $\mathrm{u}_3$, is set to zero and the other control parameters optimised (iv) when all controls were optimized.

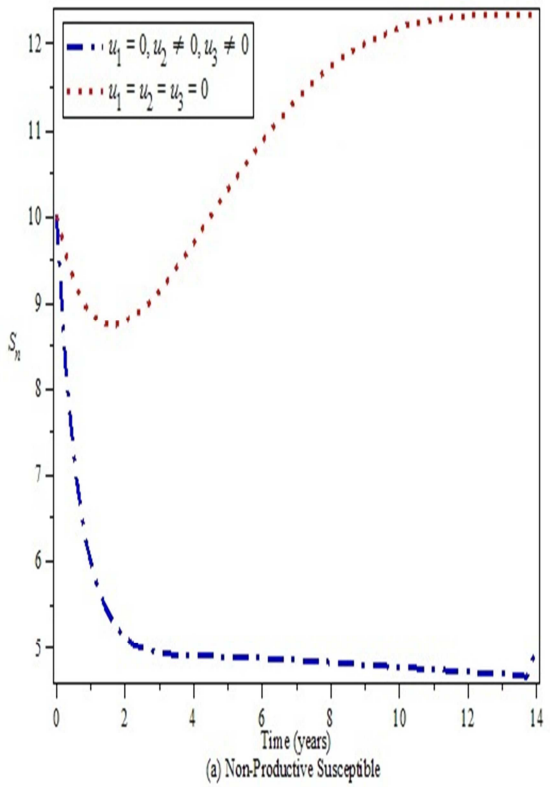
| Parameter | Description | Value | Reference |
|---|---|---|---|
| $\beta$ | contact rate for the non-productive susceptible | 0.344 | [113] |
| $\mu$ | natural mortality unrelated to HIV/AIDS | 0.02 | [113] |
| $\kappa$ | AIDS related death rate | 1 | [113] |
| $\rho$ | productivity mind-set modification parameter | 0.02 | [113] |
| $\delta$ | non-productive susceptibles' AIDS progression rate | 0.1 | [113] |
| $\sigma$ | proportion of non-productive infected on HAART | 0.002 | Assumed |
| $\pi$ | non-productive susceptible recruits proportion | 0.002 | Assumed |
| $\alpha$ | non-productive susceptible enlightened proportion | 0.034 | Assumed |
| $\eta$ | modification parameter on productive infected | 0.4 | Assumed |
| $\gamma$ | rate of progression to AIDS for productive infected | 0.01 | Assumed |

Table 3.2: Model parameter values

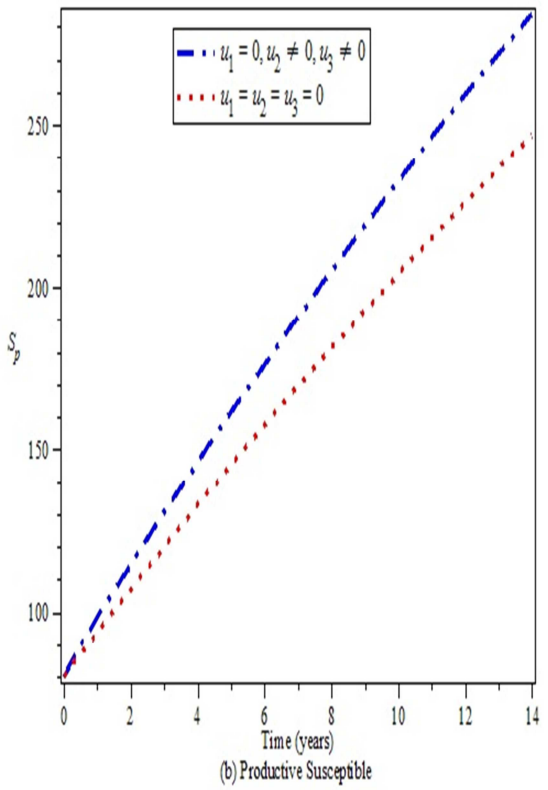
We assume that the weight factor $b_1$ associated with control $\mathrm{u}_1$ is greater than $n$ and $b_2$ which are associated with the control $u_2$. This assumption is based on the fact that the cost associated with $u_1$ will include the cost of prevention (condom use) for the entire population over and above enlightenment, $u_2$, costs related to educating people about the disease dynamics while the cost associated with HAART treatment, $u_3$, will include the cost of drugs, medical examinations and hospitalization for the ill. We have chosen the same set of weight factors: $n = 800, m = 950,\ b_1 = 150,\ b_2 = 30$ and $b_3 = 20$ and initial state variables $\mathrm{S}_p(0) = 800,\ \mathrm{S}_\mathrm{n}(0) = 40, \mathrm{I}_\mathrm{n}(0) = 45,\ I_p(0) = 30$ and $A(0) = 0$ to illustrate the effect of different optimal control strategies on the spread of HIV/AIDS in a population. Thus, we have considered the spread of HIV/AIDS in an endemic population.

### 3.6.1 Condom Use (Prevention) Control Set to Zero

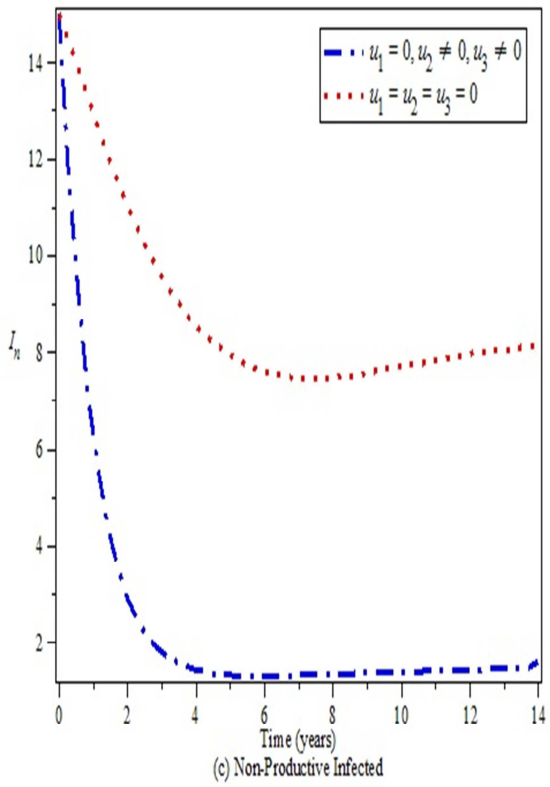
With this strategy, the other controls were used to optimize the objective functional $J$ while the control on prevention,$u_1$, is set to zero. The plots, Fig 3.2 (a) – (h), show a significant difference in the number of HIV/AIDS cases recorded using this strategy compared with the case without any control. The total number of the non-productive infected and AIDS individuals is reduced drastically at the end of final time. The plot for adjoint variables shows that the shadow price of non-productive susceptible workers, $\lambda_{\mathrm{S}_\mathrm{n}}$, is much more damaging to the economy followed by the shadow price on non-productive infected workers, $\lambda_{I_\mathrm{n}}$.



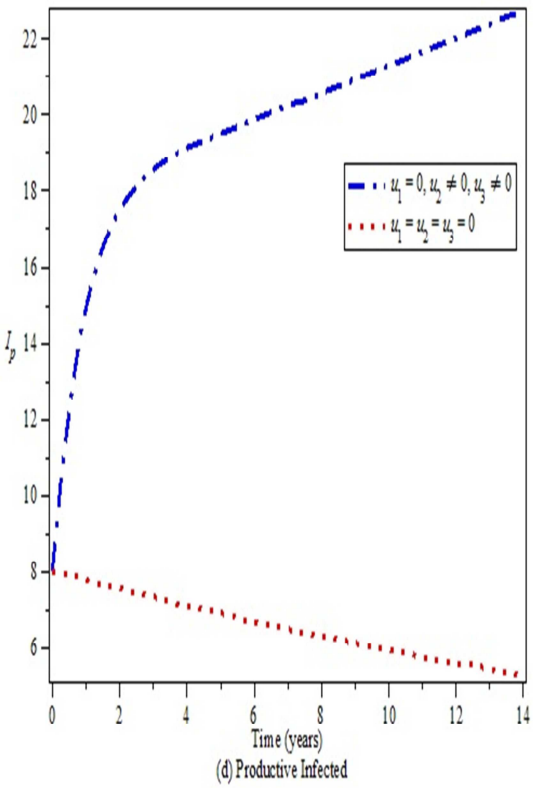
(a) Non-Productive Susceptible



(b) Productive Susceptible



(c) Non-Productive Infected



(d) Productive Infected

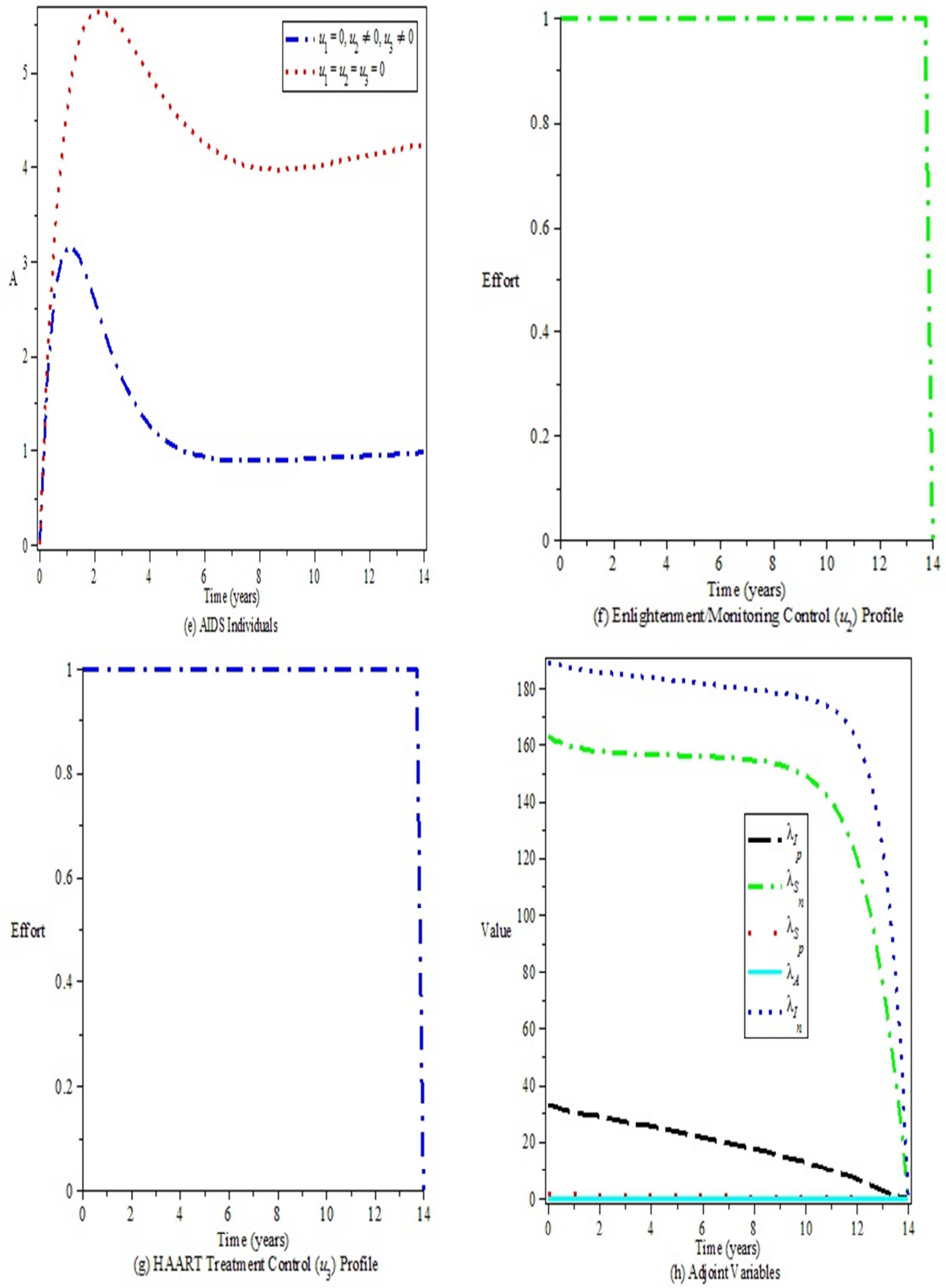
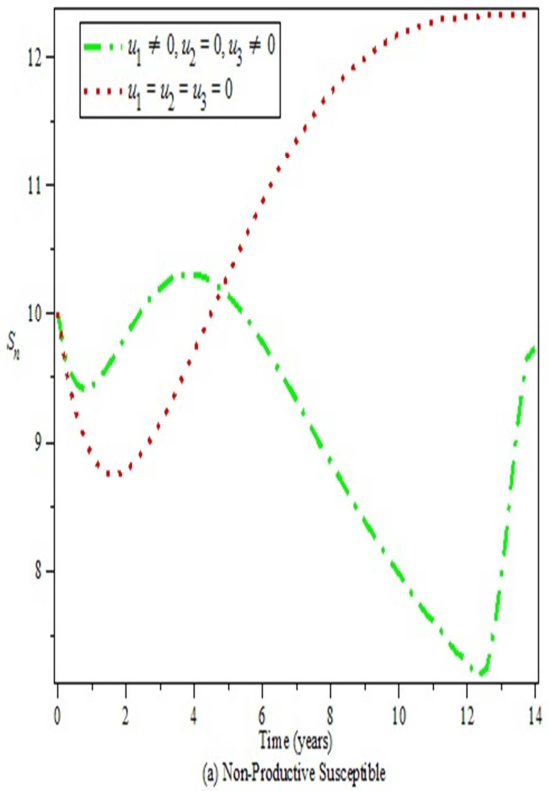



Fig 3.2: Simulations of the model showing the effect of enlightenment and treatment

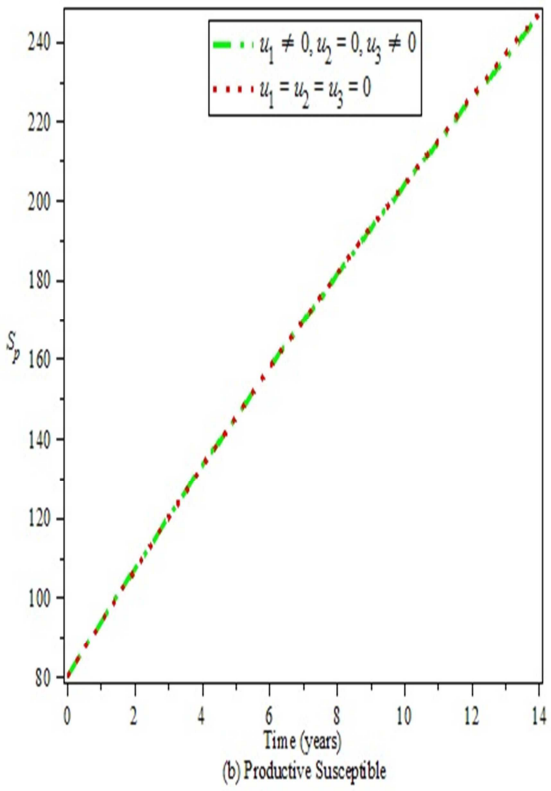
### 3.6.2 Enlightenment/Monitoring Control Set to Zero

With this strategy, the other controls were used to optimize the objective functional $J$ while the control on enlightenment, $u_2$, is set to zero. Plots show a significant difference in the

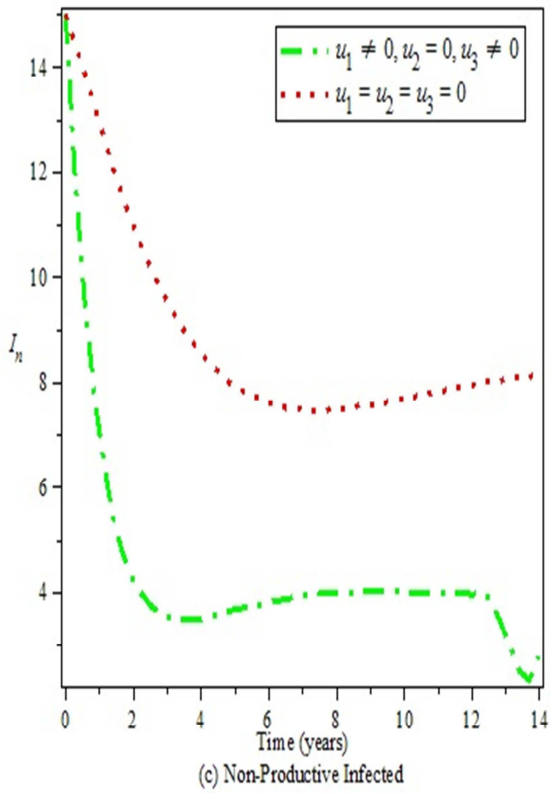
number of HIV/AIDS cases recorded using this strategy compared with the case without control. Under this strategy, the total numbers of the non-productive infected and those with AIDS reduce quite remarkably.



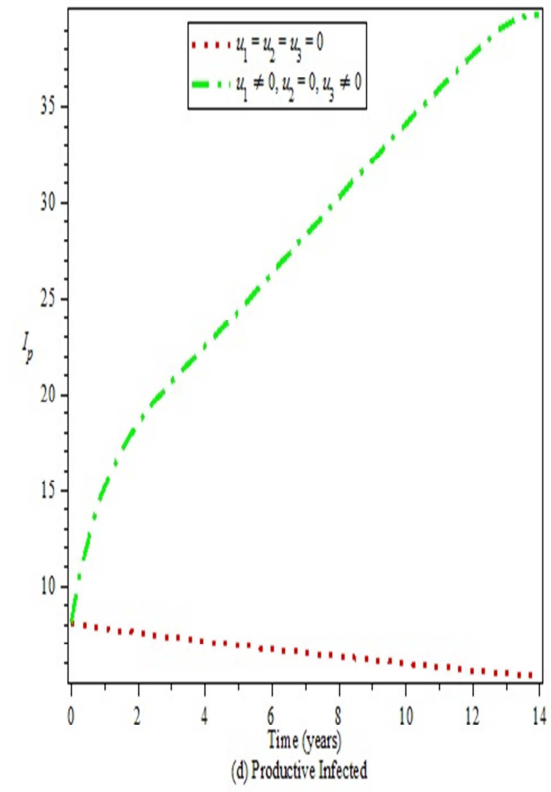
(a) Non-Productive Susceptible



(b) Productive Susceptible



(c) Non-Productive Infected



(d) Productive Infected

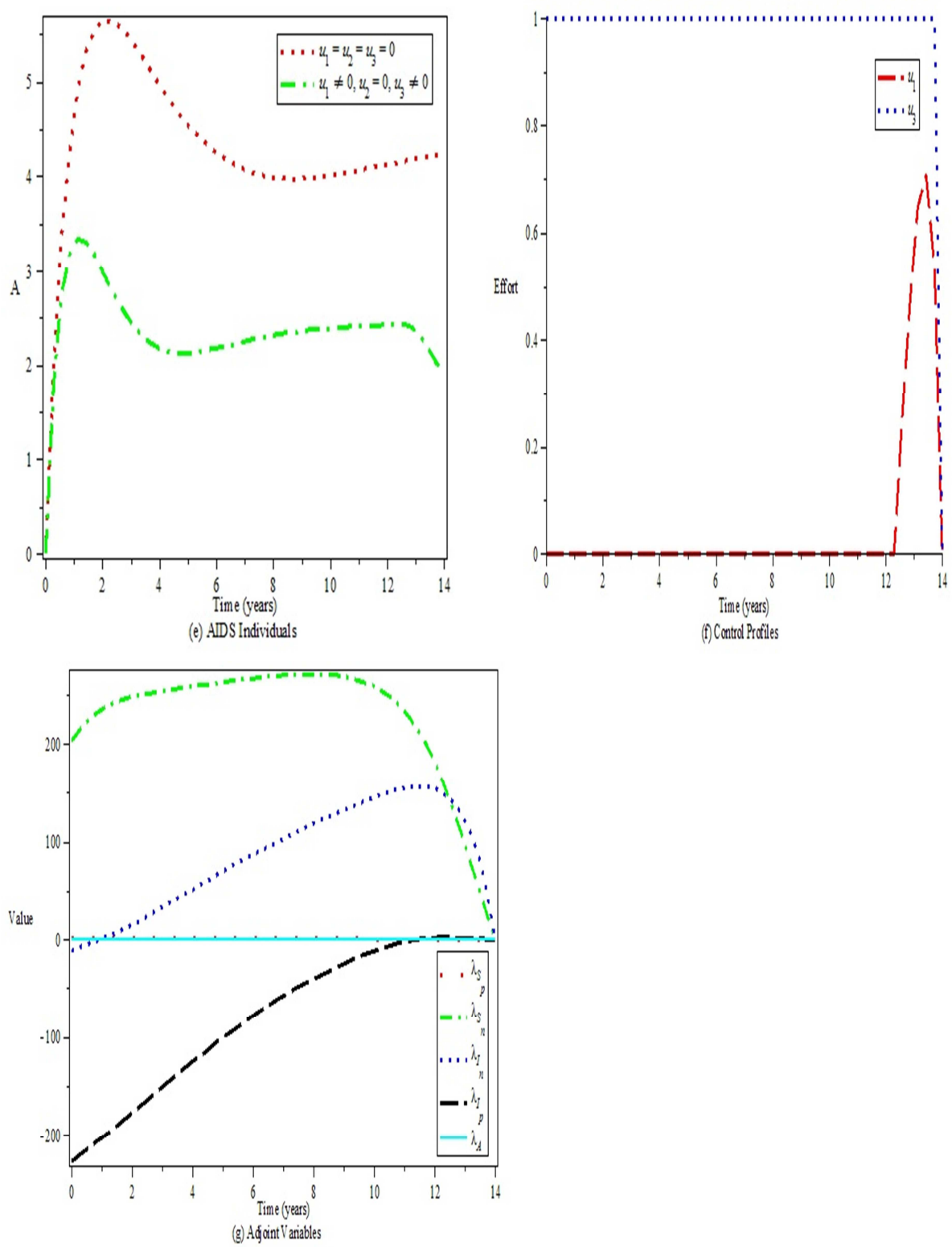
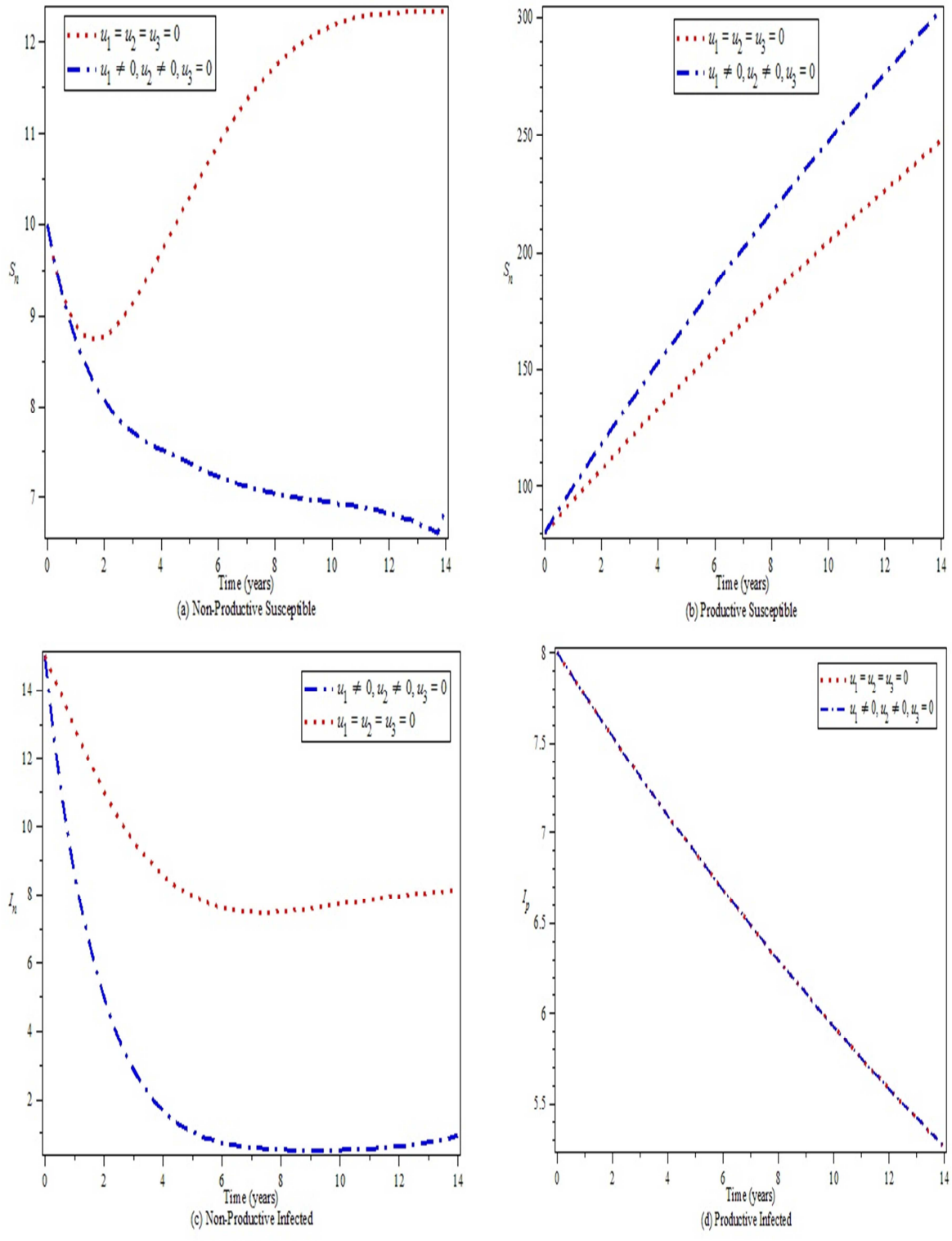



Fig 3.3: Simulations of the model showing the effect of prevention and treatment

Shadow price simulations show that non-productive susceptible individuals have a much more damaging impact on organizational labour productivity followed by the non-productive infected.

### 3.6.3 HAART Treatment Control Set to Zero

With this strategy, the other controls were used to optimize the objective functional $J$ while the control on HAART treatment, $u_3$, is set to zero. Results show a significant difference in the number of HIV/AIDS cases recorded using this strategy compared with the case without control. Under this strategy, the total number of infected and AIDS individuals start to decrease drastically due to control efforts.



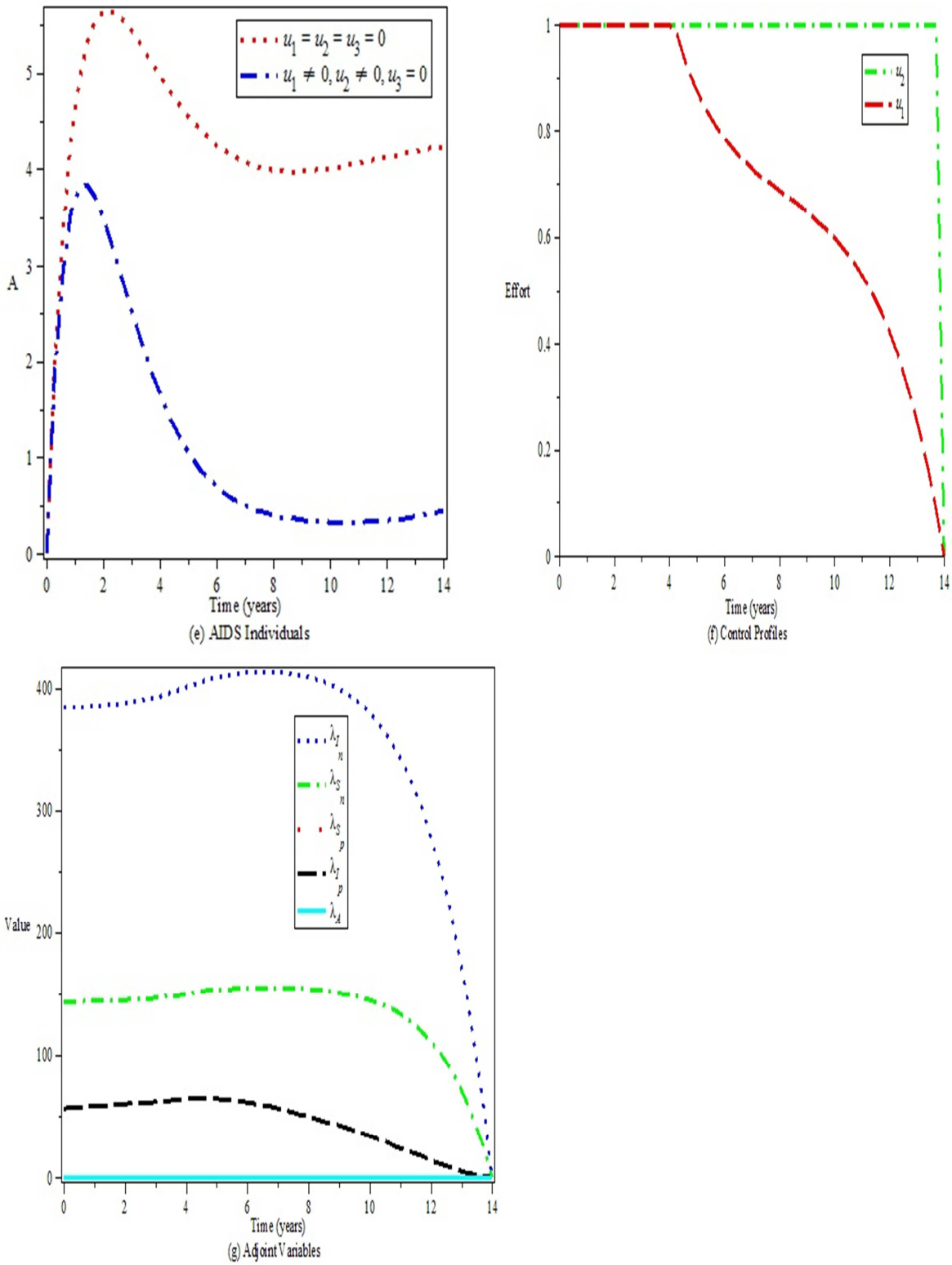
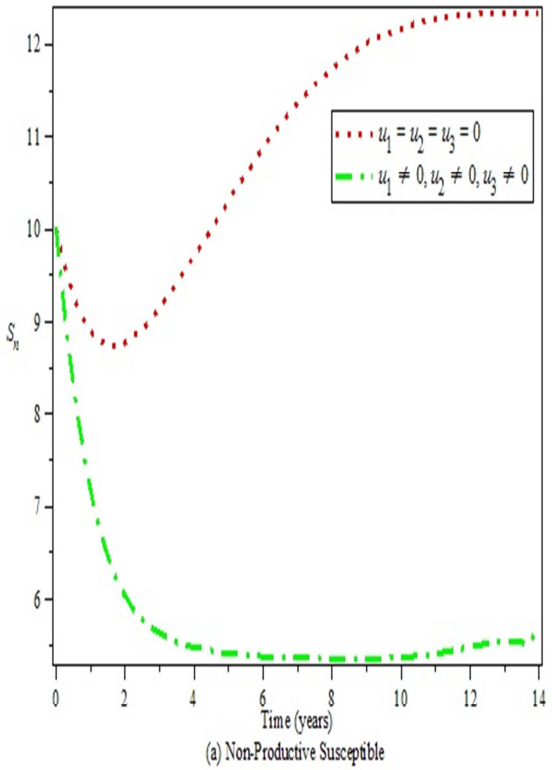



Fig 3.4: Simulations of the model showing the effect of prevention and enlightenment

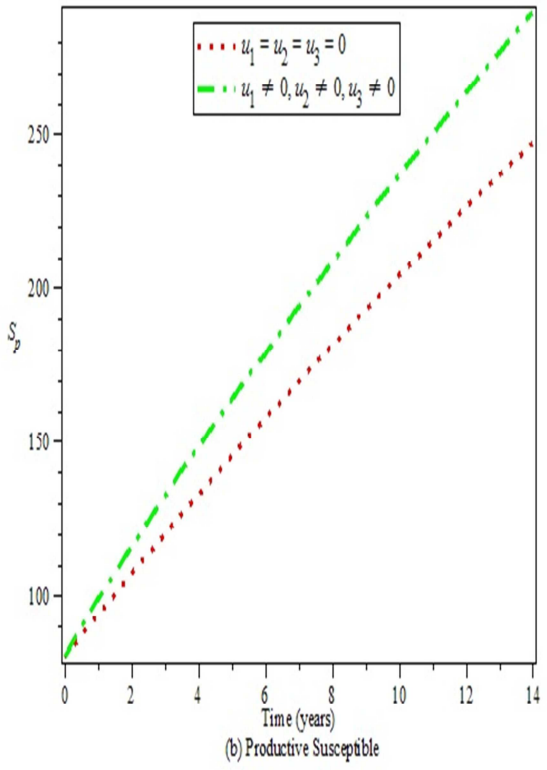
Shadow price dynamics show that the adjoint variable for non-productive infected individuals, $\lambda_{I_n}$, is much higher and more damaging to the organizational outputs followed by the shadow price for the non-productive susceptible, $\lambda_{S_n}$.

### 3.6.4 All Controls Optimized

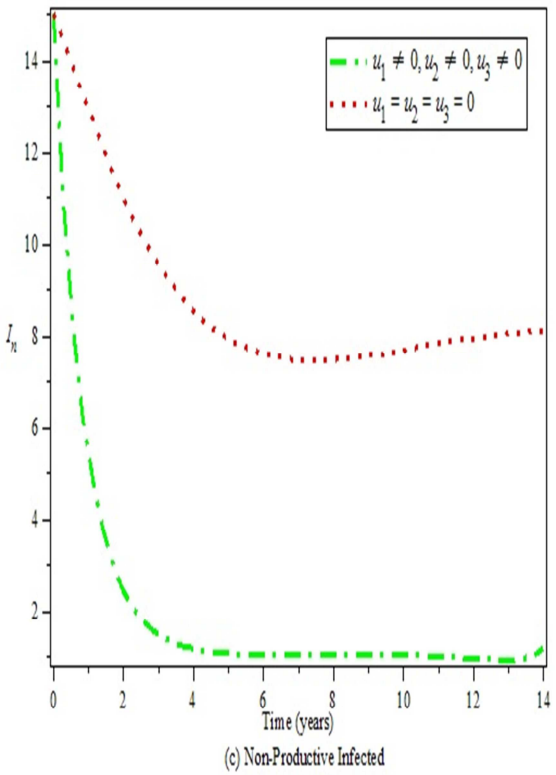
With this strategy, all the three controls were used to optimize the objective functional, $J$. This strategy shows a significant reduction in the non-productive individuals in the population and also reduces the endemicity of the disease. From the figures it easy to notice that the controls help in stabilizing the number of the non-productive infected and AIDS individuals.



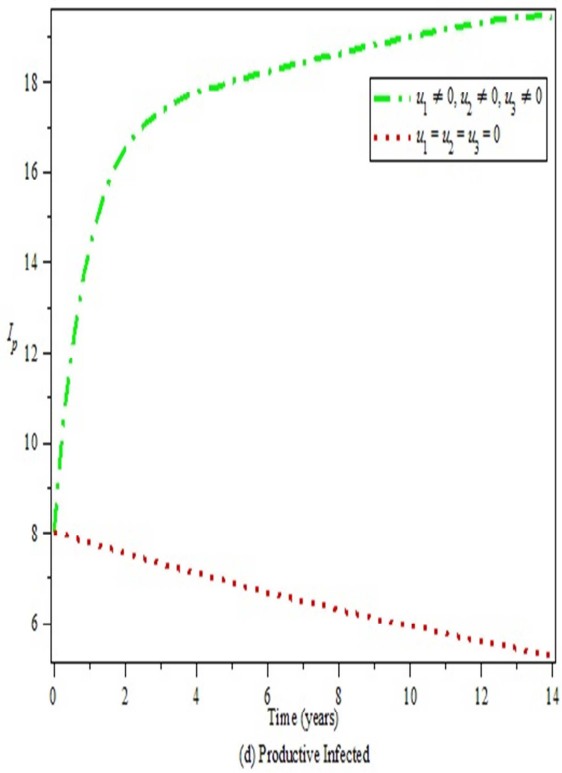
(a) Non-Productive Susceptible



(b) Productive Susceptible



(c) Non-Productive Infected



(d) Productive Infected

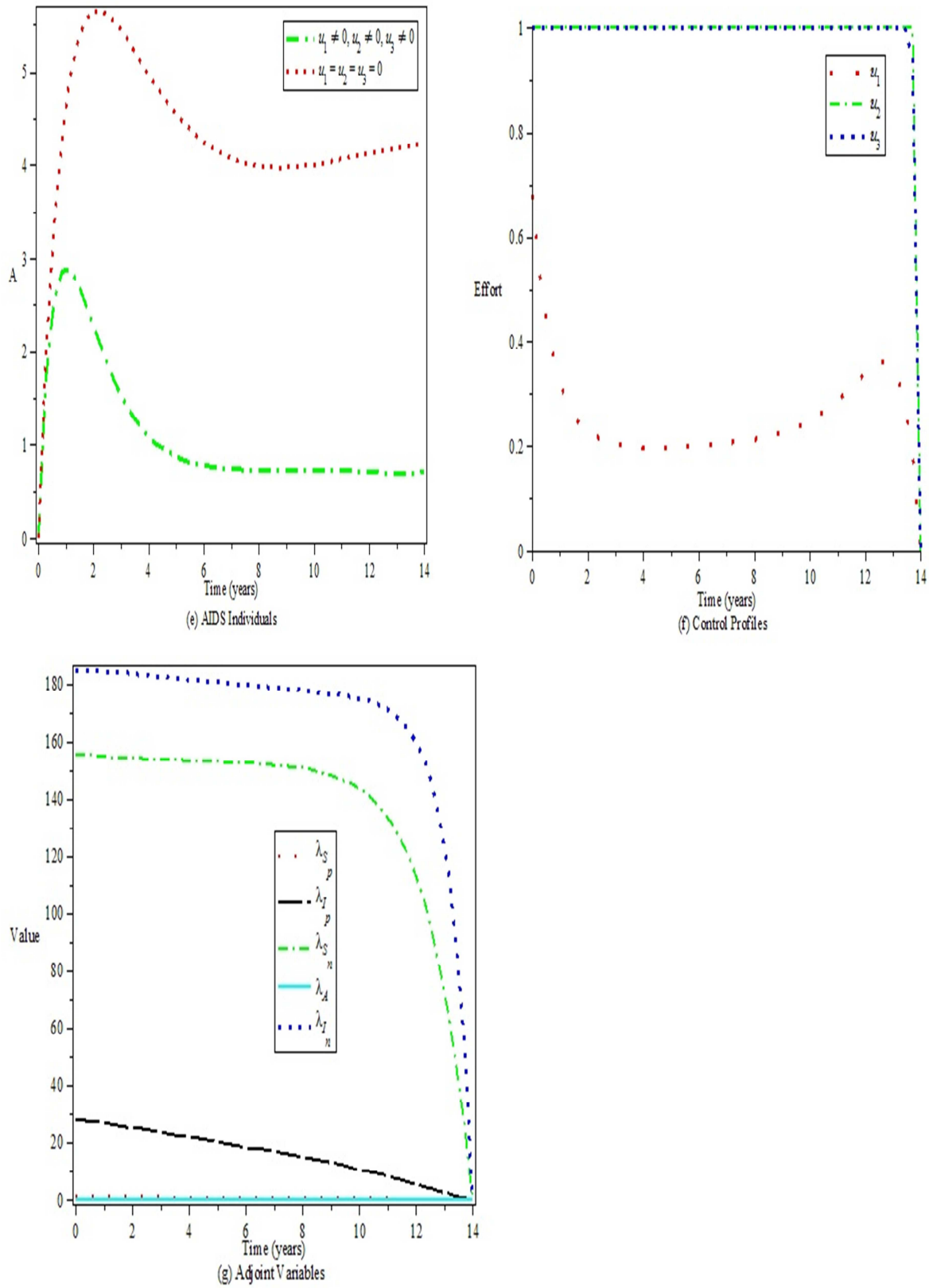



Fig 3.5: Simulations of the model showing the effect of prevention, enlightenment and treatment

Fig 3.5 (g) shows that the shadow price for the non-productive susceptible, $\lambda_{S_n}$, is more damaging to the productivity of an organization followed by the shadow price on the non-productive infected, $\lambda_{I_n}$.

### 3.7 Cost Effective Analysis

We compare the four control scenarios to determine the most cost effective one(s). The key question is: What are the additional benefits to be gained from one strategy to the other and at how much greater cost? In order to answer such a question, we use **incremental cost-effectiveness ratios (ICERs)** calculated as the marginal cost of an intervention divided by the marginal benefit. It measures how much additional "bang for the buck" could be achieved by switching from one intervention to another [78]. This can be written as

$$ICER = \frac{Difference\ in\ costs\ between\ strategies}{Difference\ in\ health\ effects\ between\ strategies}$$

The alternative strategies are ranked according to their effectiveness – on the basis of securing maximum effect rather than considering cost – and ICERs are calculated. Effects are calculated as the reduction in the non-productive (both susceptible and infected) for each of the strategies compared to the case when there are no controls.

***Strategy A – No Prevention***: Averted = 179; Cost = 63 717

***Strategy B – No Enlightenment***: Averted = 92; Cost = 13 892

***Strategy C – No Treatment***: Averted = 147; Cost = 65 519

***Strategy D – All Controls***: Averted = 174; Cost = 41 626

| Strategy | Effects (E) | Costs (C) | Incremental Costs ($\Delta C$) | Incremental Effects ($\Delta E$) | ICER ($\Delta C/\Delta E$) |
|---|---|---|---|---|---|
| B | 92 | 13 892 | 13 892 | 92 | 151 |
| C | 147 | 65 519 | 51 627 | 55 | 938.67 |
| D | 174 | 41 626 | -23 893 | 27 | -884.93 |
| A | 179 | 63 717 | 22 091 | 5 | 4418.2 |

The negative ICER for Strategy D means that by adopting Strategy D rather than Strategy C there is an improvement in cases averted and a reduction in costs. The ICER for Strategy A works out to be 4 418.2 , which means that it costs $4 418.20 to generate each additional case averted compared with Strategy D. Strategy C is followed by a programme that has increased effectiveness and reduced cost, i.e. Strategy C is more expensive and less effective and is therefore excluded. ICERs are then recalculated for Strategies B, D and A.

| Strategy | Effects (E) | Costs (C) | Incremental Costs ($\Delta C$) | Incremental Effects ($\Delta E$) | ICER ($\Delta C/\Delta E$) |
|---|---|---|---|---|---|
| B | 92 | 13 892 | 13 892 | 92 | 151 |
| D | 174 | 41 626 | 27 734 | 82 | 338.22 |
| A | 179 | 63 717 | 22 091 | 5 | 4418.2 |

Strategy A is dominated by Strategy D which in turn is dominated by Strategy B. Therefore Strategy B is the most cost-effective. However, in deciding between B and D, the size of the available budget may be brought to bear.

### 3.8 Conclusion

In this chapter, we derived and analyzed a deterministic model for the transmission of HIV/AIDS disease that includes non-productive susceptible and infected individuals, enlightenment/monitoring campaign of the non-productive susceptible and HAART treatment of non-productive infected individuals. We also performed optimal control analysis of the model employing Pontryagin's Maximum Principle to derive and analyze the conditions for optimal control of the disease with effective HAART treatment regime and enlightenment of non-productive susceptible and infectious individuals.

From the shadow price analysis and the numerical results from the combinations of control strategies, it is clear that the cost and impact of the non-productive susceptible workers in an organization is very high. This will ultimately have a negative effect on the organization profits. The results also suggest that the successful enlightenment/monitoring of employees has a significant impact in reducing the non-productivity of an infected employee in the presence of HIV/AIDS. Therefore, control programs that follow these strategies can effectively reduce the spread of HIV/AIDS and non-productivity among HIV/AIDS individuals in organizational labour force.

# CHAPTER FOUR

# ANALYSIS OF RECRUITMENT AND INDUSTRIAL HUMAN RESOURCES MANAGEMENT FOR OPTIMAL PRODUCTIVITY IN THE PRESENCE OF THE HIV/AIDS EPIDEMIC

*In this chapter, we analyze recruitment effects of susceptible and infected people in order to assess the productivity of organizational labour force in the presence of HIV/AIDS with screening, enlightenment, preventive and HAART treatment measures in enhancing workforce output. We consider constant controls as well as time-dependent controls. In the constant control case, we calculate the basic reproduction number and investigate the existence and stability of equilibria. The model is found to exhibit backward and Hopf bifurcations implying that for the disease to be eradicated, the basic reproductive number must be below a critical value less than one. We also investigate, by calculating sensitivity indices, the sensitivity of the basic reproductive number to the model's parameters. In the time-dependent control case, we use 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. Cost effectiveness analysis results show that putting in efforts on recruitment (HIV screening of applicants, etc.) is not the most cost-effective strategy to enhance productivity in the organizational labour force. Hence, to enhance employees' productivity, effective education programs and strict adherence to preventive measures should be promoted.*

## 4.1 Introduction

The profitability of any organizational venture depends largely on the productivity of its workforce. The main determining factors include skill level, motivation, satisfaction and schedule pressure. The question now is, how would an ineffective employee recruitment policy affect an organization in the face of HIV/AIDS infection?

We, here, consider a scenario where employees may be recruited whilst already infected over and above the susceptible recruits as discussed in the previous chapter. Our main goal is to set up an optimal control problem related to the model. In order to do this, we use the following: recruitment strategy (effective screening of applicants) $u_1$, preventive measures (abstinence, being faithful, condom use) parameter on susceptibles $u_3$, enlightenment or educational parameter $u_2$ and HAART treatment parameter for individuals with HIV $u_4$, as time dependent controls in the model. Hence, we investigate the role of productive susceptibles, productive infected, optimal enlightenment (through counselling, mentoring,

training, screening, educational campaigns) and HAART treatment on the spread of HIV/AIDS.

### 4.2 Model Formulation

We propose a standard compartmental model of HIV/AIDS in which four time dependent control measures are incorporated simultaneously: i) recruitment strategy, ii) preventive measure (condom use), iii) enlightenment campaign, iv) HAART treatment of HIV individuals for enhanced productivity. The total workforce population at any time $t$, denoted by $N(t)$, is sub-divided into the following five classes: productive susceptible workers, $S_p(t)$, non-productive susceptible workers, $S_n(t)$, non-productive infected workers, $I_n(t)$, productive infected individuals on HAART treatment, $I_p(t)$ and individuals with full blown AIDS, $A(t)$, so that

$$N(t) = S_p(t) + S_n(t) + I_n(t) + I_p(t) + A(t).$$

Susceptibles are individuals who have not contracted the infection but may be infected through sexual contacts. The susceptible non-productive are individuals whose lifestyle places them at high risk of contracting the disease.

The organization recruits workers at the rate $Q$, where the proportion of non-productive susceptible, non-productive infected and productive infected workers are recruited at rates $\pi_1$, $\pi_2$ and $\pi_3$ respectively. The parameter $\beta$ is the per capita contact rate for non-productive susceptible individuals. The productive susceptible workers have a per capita contact rate of $\beta_1 = \rho\beta < \beta$, where $\rho$ is the modification parameter due to right values perception of the productive susceptible workers. When non-productive susceptible individuals are enlightened (through counselling, mentoring or monitoring) and their attitude changed they progress to the productive susceptible class at a rate $u_2\alpha$, where $u_2$ is the enlightenment control effort. We assume that unprotected sexual contact between any type of susceptible and any type of infective would eventually land the susceptible into the infected non-productive class. The non-productive infected individuals on HAART treatment progress to the productive infected class at a rate $u_3\sigma$, where $\sigma$ is the proportion of the non-productive infected individuals on HAART treatment for enhanced productivity and $u_3$ is the control effort on HAART treatment to enhanced productivity. Infected non-productive workers not on HAART treatment progress to the full blown AIDS class at a rate $\delta$, while γ is the rate of progression of productive infected individuals into full blown AIDS, here $\gamma < \delta$. The term $\eta$ is the modification parameter due to HAART treatment and right value perceptions of the productive infected individuals. The disease induced death rate of AIDS individuals is denoted by $\psi$ and $\mu$ is the

natural mortality rate unrelated to HIV/AIDS. We also assume the AIDS class to be sexually active, albeit weakly, and non-productive. We denote by $\tau$ the transmission probability of an AIDS individual infecting susceptible humans.

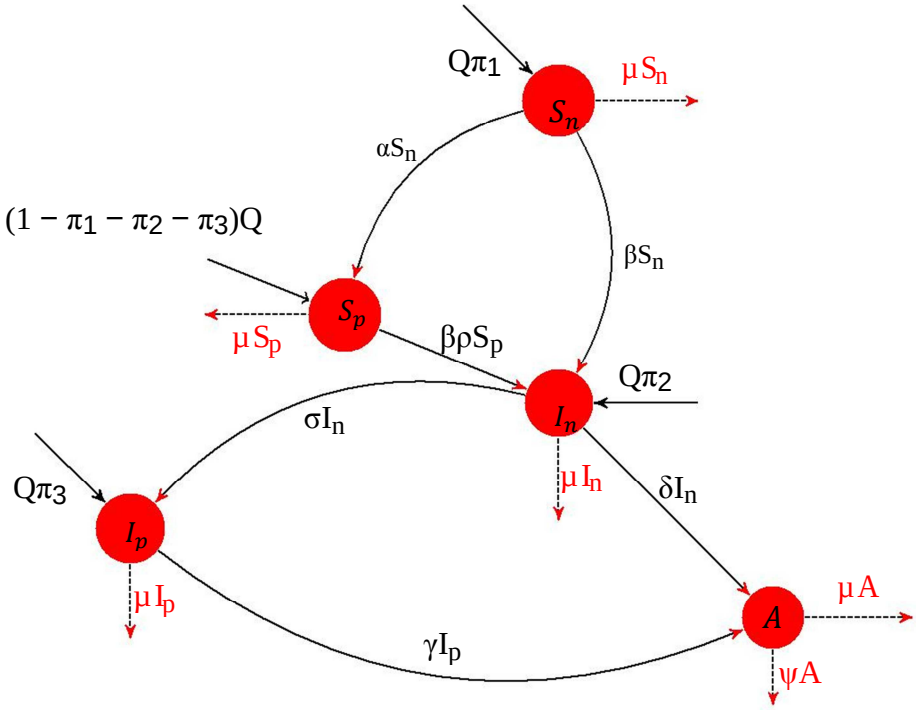



Fig 4.1: Flow diagram for HIV/AIDS disease transmission

The resulting system of equations for the constant control case is as follows:

$$\left.\begin{aligned}
\frac{dS_p}{dt} &= (1-\pi_1-\pi_2-\pi_3)Q-\rho\phi_I S_p+\alpha S_n-\mu S_p\\
\frac{dS_n}{dt} &= \pi_1 Q-\beta\left(I_n+\eta I_p+\tau A\right)S_n-\alpha S_n-\mu S_n=\pi_1 Q-(\phi_I+\alpha+\mu)S_n\\
\frac{dI_n}{dt} &= \pi_2 Q+\phi_I\left(\rho S_p+S_n\right)-(\sigma+\delta+\mu)I_n\\
\frac{dI_p}{dt} &= \pi_3 Q+\sigma I_n-\gamma I_p-\mu I_p=\pi_3 Q+\sigma I_n-(\gamma+\mu)I_p\\
\frac{dA}{dt} &= \delta I_n+\gamma I_p-\kappa A-\mu A=\delta I_n+\gamma I_p-(\psi+\mu)A
\end{aligned}\right\} \qquad (4.1)$$

where $\phi_I=\beta\left(I_n+\eta I_p+\tau A\right)$.

### 4.3 Analysis of Equilibria

The endemic equilibrium point exists and is given by

$$\left.\begin{aligned} S_p^* &= \frac{(1-\pi)Q+\alpha S_n^*}{\mu+\rho\phi_I^*} \\ S_n^* &= \frac{\pi_1 Q}{\mu+\alpha+\phi_I^*} \\ I_n^* &= \frac{\pi_2 Q+\phi_I^*(\rho S_p+S_n)}{\sigma+\delta+\mu} \\ I_p^* &= \frac{\pi_2 Q+\sigma I_n^*}{\gamma+\mu} \\ A^* &= \frac{\delta I_n^*+\gamma I_p^*}{\psi+\mu} \end{aligned}\right\} \tag{4.2}$$

where

$$\phi_I^* = \beta(I_n^* + \eta I_p^* + \tau A^*)$$

The endemic equilibrium satisfies the following polynomial equation

$$P(\phi_I^*) = B_0(\phi_I^*)^3 + B_1(\phi_I^*)^2 + B_2(\phi_I^*) + B_3 = 0 \tag{4.3}$$

where

$$B_0 = \rho(\gamma+\mu)(\delta+\mu+\sigma)(\mu+\psi)$$

$$\begin{aligned} B_1 = {} & (\gamma+\mu)(\delta+\mu+\sigma)(\mu+\psi)(\mu(1+\rho)+\alpha\rho) \\ & - Q\beta\rho\Big[\mu^2+\eta\mu\sigma+\delta\mu\tau+\mu\psi+\eta\sigma\psi \\ & - \Big((1-\eta)\mu(\mu+\psi)-\delta\big(-\mu\tau+\eta(\mu+\psi)\big)\Big)\pi_3 \\ & + \gamma(\mu+(\delta+\sigma)\tau+\psi+(\mu(-1+\tau)-\psi)\pi_3)\Big] \end{aligned} \tag{4.4}$$

$$\begin{aligned} B_2 = {} & \mu(\gamma+\mu)(\mu+\alpha)(\delta+\mu+\sigma)(\mu+\psi) \\ & - Q\beta\mu\big[\{\mu^2+\eta\sigma\psi+\mu(\eta\sigma+\delta\tau+\psi)+\gamma(\mu+(\delta+\sigma)\tau+\psi)\}(\pi_1+\pi_2) \\ & + (\delta+\mu+\sigma)\big(\gamma\tau+\eta(\mu+\psi)\big)\pi_3\big] \\ & - Q\beta\rho[\mu\{\mu^2+\eta\sigma\psi+\mu(\eta\sigma+\delta\tau+\psi)+\gamma(\mu+(\delta+\sigma)\tau+\psi)\}](1-\pi_1)+\alpha\gamma\mu \\ & + \alpha\mu^2+\alpha\eta\mu\sigma+\alpha\delta\mu\tau+\alpha\gamma(\delta+\mu)\tau+\alpha\gamma\psi+\alpha\mu\psi+\alpha\eta\sigma\psi \\ & - \pi_3\Big\{-\mu\Big(\gamma\mu(-1+\tau)-\gamma\psi+(-1+\eta)\mu(\mu+\psi)+\delta\big(-\mu\tau+\eta(\mu+\psi)\big)\Big) \\ & + \alpha\gamma(\mu(-1+\tau)-\psi)+\alpha\Big((-1+\eta)\mu(\mu+\psi)+\delta\big(-\mu\tau+\eta(\mu+\psi)\big)\Big)\Big\} \end{aligned}$$

$$\begin{aligned} B_3 = {} & -Q\beta\mu\big[\big(\mu^2+\eta\sigma\psi+\mu(\eta\sigma+\delta\tau+\psi)+\gamma(\mu+(\delta+\alpha)\tau+\psi)\big)\pi_2 \\ & + (\delta+\mu+\sigma)\big(\gamma\tau+\eta(\mu+\psi)\big)\pi_3\big](\mu+\alpha) \end{aligned}$$

We shall examine the endemic equilibrium polynomial equation under the following three scenarios: (i) when there is recruitment of productive susceptibles only ($\pi_1 = \pi_2 = \pi_3 = 0$), (ii) when there is recruitment of susceptibles only (productive and non-productive, i.e.

$\pi_1 \neq 0, \pi_2 = \pi_3 = 0$) and (iii) when there is recruitment of productive individuals only (susceptible and infected, i.e. $\pi_1 = \pi_2 = 0, \pi_3 \neq 0$).

### 4.3.1 Productive Susceptible Recruits Only

Assuming there is no recruitment of non-productive susceptibles and the infected, that is $\pi_1 = \pi_2 = \pi_3 = 0$, the DFE of the HIV/AIDS model exists and is given by

$$\varepsilon_0 = \left(S_p^0, S_n^0, I_n^0, I_p^0, A^0\right) = \left(\frac{Q}{\mu}, 0, 0, 0, 0\right)$$

The endemic equilibrium polynomial equation then gives

$$\left.\begin{aligned} B_0 &= \rho(\gamma + \mu)(\delta + \mu + \sigma)(\mu + \psi) \\ B_1^1 &= \mu(\gamma + \mu)(\delta + \mu + \sigma)(\mu + \psi)(\Lambda - R_1) \\ B_2^1 &= \mu(\gamma + \mu)(\mu + \alpha)(\delta + \mu + \sigma)(\mu + \psi)(1 - R_1) \\ B_3^1 &= 0 \end{aligned}\right\} \quad (4.5)$$

where

$$R_1 = \frac{Q\beta\rho[\mu^2 + \eta\sigma\psi + \mu(\eta\sigma + \delta\tau + \psi) + \gamma(\mu + (\delta + \sigma)\tau) + \psi]}{\mu(\gamma + \mu)(\delta + \sigma + \mu)(\mu + \psi)} \quad (4.6)$$

is the basic reproductive number for this scenario and

$$\frac{\mu + (\alpha + \mu)\rho}{\mu} = \Lambda \quad (4.7)$$

$\Lambda > 1$ if and only if

$$\rho > \rho^{\dagger} = 0$$

We obtain the following result:

***Proposition 4.1*:**

1. *If $\rho \geq \rho^{\dagger}$, then the state system (4.1) exhibits trans-critical bifurcation.*
2. *If $\rho < \rho^{\dagger}$, then the state system (4.1) exhibits backward bifurcation. That is, there exists $R_c$ in $(0, 1)$ such that*
   - *i. if $1 \leq R_1$ , then the state system has one endemic equilibrium point.*
   - *ii. if $R_c < R_1 < 1$ , then the state system has two endemic equilibrium points.*
   - *iii. if $R_c = R_1$ , then the state system has one endemic equilibrium point.*

*iv. if $R_c > R_1$ , then the state system has no endemic equilibrium points.*

***Proof:***

1. If $\rho \geq \rho^{\dagger}$, then $\Lambda \geq 1$. In this case, we have the following:
   i. If $R_1 > 1$, then $B_2 < 0$. In this case the endemic equilibrium polynomial equation (4.3) has a unique positive solution.
   ii. If $R_1 \leq 1$, then $B_2 \geq 0$ and $B_1 \geq 0$(because $R_1 \leq 1 \leq \sqrt{\Lambda}$ ). This together with $B_0 > 0$ imply that the endemic equilibrium polynomial equation (4.3) has no positive solution.

2. If $\rho < \rho^{\dagger}$, then $\Lambda < 1$. In this case we have
   i. If $R_1 \geq 1$, then $B_2 \leq 0$ which implies that the endemic equilibrium polynomial equation (4.3) has a unique positive solution.
   ii. If $R_1 \leq \sqrt{\Lambda}$, then $B_1 \geq 0$ and $B_2 > 0$. This implies that the endemic equilibrium polynomial equation (4.3) has no positive solution.
   iii. If $\sqrt{\Lambda} < R_1$, we consider the discriminant of (4.3), $\Delta(R_1) \coloneqq B_1^2 - 4B_0B_2$. One can see that $\Delta(\sqrt{\Lambda}) \coloneqq -4B_0B_2$ and $\Delta(1) \coloneqq B_1^2 > 0$. Therefore, there exists $R_c \in (\sqrt{\Lambda}, 1)$ such that $\Delta(R_c) = 0$ and $\Delta(R_1) < 0$ for $R_1 \in (\sqrt{\Lambda}, R_c)$ and $\Delta(R_1) > 0$ for $R_1 \in (R_c, 1)$. In this case we have
      a. if $\sqrt{\Lambda} < R_1 < R_c$ then (4.3) has no positive solution.
      b. if $R_1 = R_c$ then $\Delta = 0$ and $B_1 < 0$. This implies that (4.3) has one positive solution.
      c. if $R_c < R_1 < 1$, then (4.3) has two real solutions which are positive since $B_2 > 0$ and $B_1 < 0$. ■

Proposition 4.1 establishes the existence of two endemic equilibria for $\Lambda$ in $(R_c, 1)$.

### 4.3.2 Susceptible Recruits Only

If there is no recruitment of infected individuals, i.e. $\pi_1 \neq 0, \pi_2 = \pi_3 = 0$, the DFE of the model (4.1) is given by

$$\varepsilon_0 = (S_p^0, S_n^0, I_n^0, I_p^0, A^0) = \left(\frac{(1-\pi_1)Q + \alpha}{\mu}, \frac{Q\pi_1}{\alpha + \mu}, 0, 0, 0\right)$$

while the endemic equilibrium polynomial equation now results in

$$\left.\begin{aligned} B_0 &= \rho(\gamma+\mu)(\delta+\mu+\sigma)(\mu+\psi) \\ B_1^2 &= \mu(\gamma+\mu)(\delta+\mu+\sigma)(\mu+\psi)(\Lambda-R_1) \\ B_2^2 &= \frac{\mu(\gamma+\mu)(\mu+\alpha)(\delta+\mu+\sigma)(\mu+\psi)[(\alpha+\mu)\rho+(1-\rho)\mu\pi_1]}{\rho}(\Omega-R_1) \\ B_3^2 &= 0 \end{aligned}\right\} \quad (4.8)$$

where

$$\Omega = \frac{\rho}{(\alpha+\mu)\rho+(1-\rho)\mu\pi_1} \quad (4.9)$$

Note that this scenario is a generalisation of the preceding one (where $\Omega = 1$). In this case, $\Omega = 1$ if and only if

$$\rho = \frac{\mu\pi_1}{1-\alpha-\mu(1-\pi_1)}$$

Hence, the model exhibits backward bifurcation in the presence of non-productive susceptible recruits.

### 4.3.3 Productive Recruits Only

Assuming there is no recruitment of the non-productive, i.e. $\pi_1 = \pi_2 = 0, \pi_3 \neq 0$, the endemic equilibrium polynomial equation coefficients are then given by

$$\left.\begin{aligned} B_0 &= \rho(\gamma+\mu)(\delta+\mu+\sigma)(\mu+\psi) \\ B_1^3 &= \mu(\gamma+\mu)(\delta+\mu+\sigma)(\mu+\psi)(\Lambda_2-R_1) \\ B_2^3 &= \mu(\gamma+\mu)(\mu+\alpha)(\delta+\mu+\sigma)(\mu+\psi)(\Lambda_3-R_1) \\ B_3^3 &= -Q\beta\mu(\mu+\alpha)(\delta+\mu+\sigma)\big(\gamma\tau+\eta(\mu+\psi)\big)\pi_3 \end{aligned}\right\} \quad (4.10)$$

where

$$\frac{\mu(\gamma+\mu)(\mu+(\alpha+\mu)\rho)(\delta+\mu+\sigma)(\mu+\psi)+F}{\mu(\gamma+\mu)(\delta+\mu+\sigma)(\mu+\psi)} = \Lambda_2$$

$$\frac{\mu(\gamma+\mu)(\alpha+\mu)(\delta+\mu+\sigma)(\mu+\psi)+G}{\mu(\gamma+\mu)(\alpha+\mu)(\delta+\mu+\sigma)(\mu+\psi)} = \Lambda_3 \quad (4.11)$$

$$F = Q\beta\rho\big[\gamma(\mu(1-\tau)+\psi)+(1-\eta)\mu(\mu+\psi)+\delta\big(\mu\tau-\eta(\mu+\psi)\big)\big]\pi_3$$

$$G = Q\beta\big[(\alpha+\mu)\rho\{\mu(1-\tau)+\psi+(1-\eta)\mu(\mu+\psi)+\delta\big(\mu\tau-\eta(\mu+\psi)\big)\}$$
$$-\mu(\delta+\mu+\sigma)\big(\gamma\tau+\eta(\mu+\psi)\big)\big]\pi_3$$

By the Routh-Hurwitz criteria the roots of the endemic equilibrium polynomial equation (4.3) have negative real parts if and only if $B_0 > 0$, $B_2^3 > 0$ and $B_0B_1^3 - B_2^3 > 0$. It is clear from (4.10) that $B_3^3 < 0$, so the disease free equilibrium is unstable. Numerically, we shall show that periodic solutions bifurcate from the endemic equilibrium, implying that the endemic equilibrium is also unstable, Fig 4.2.

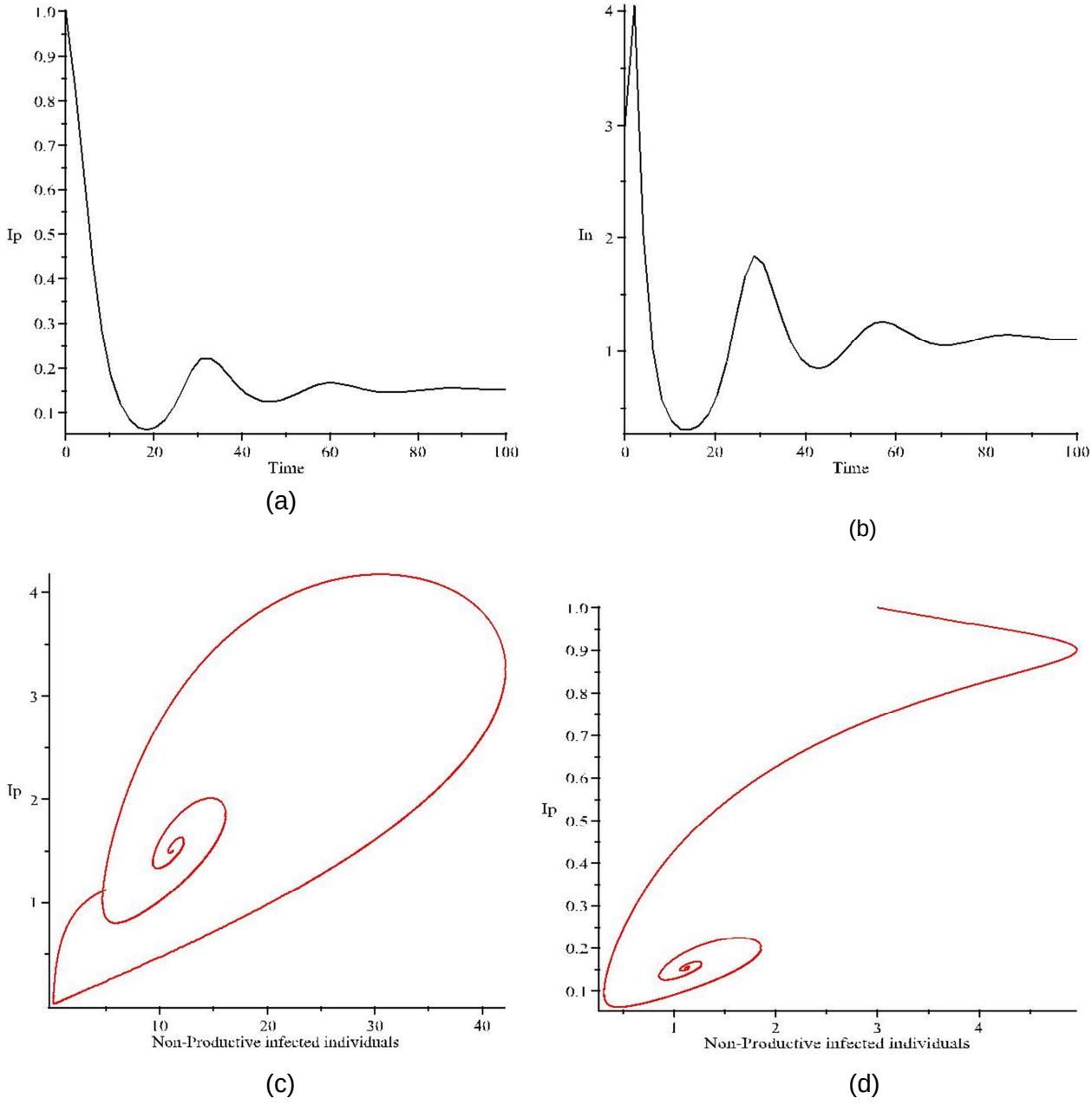



Fig 4.2: Simulations of the state system (4.1) for $Q = 100$, $\mu = 0.04$, $\pi_3 = 0.03$, $\gamma = 0.288$, $\rho = 0.2$, $\sigma = 0.04$, $\delta = 0.8$, $\alpha = 0.81$. (a) $I_p$ versus time $t$ (b) $I_n$ versus time $t$ (c) the projected $I_n - I_p$ phase plane of the phase space (d) $I_n - I_p$ phase plane with $Q = 10$ while all the other parameters remain the same

In Fig 4.3 (b), the endemic equilibrium loses its stability and periodic solutions bifurcate from endemic equilibrium. This is an explicit example of the existence of Hopf bifurcation using $\rho$ as bifurcation parameter and variation of initial values of state variables.

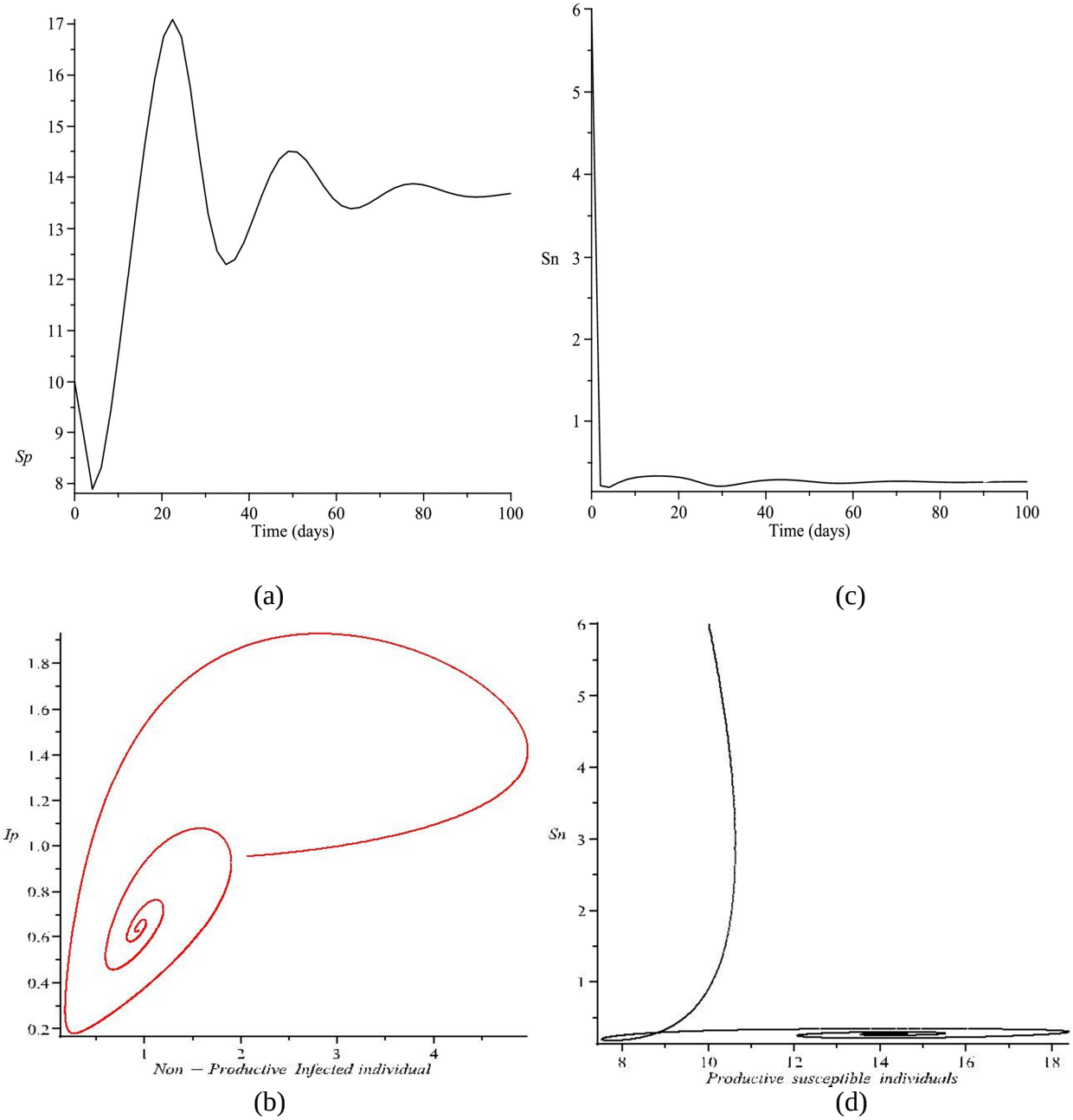



Fig 4.3: Simulations of the state system (4.1) for $Q = 100$, $\mu = 0.04$, $\pi_3 = 0.03$, $\gamma = 0.288$, $\rho = 0.2$, $\sigma = 0.04$, $\delta = 0.8$, $\alpha = 0.81$ (a) $S_p$ versus time $t$ (b) the projected $I_n - I_p$ phase plane (c) $S_n$ versus time $t$ (d) the projected $S_n - S_p$ phase plane of the phase space.

### 4.4 Optimal Control Analysis

We now incorporate time-dependent controls into the model to obtain the following state system:

$$\left.\begin{aligned}
\frac{dS_p}{dt} &= (1 - u_1(\pi_1 + \pi_2 + \pi_3))Q - (1-u_3)\rho\beta\big(I_n + \eta I_p + \tau\mathrm{A}\big)S_p + u_2\alpha S_n - \mu S_p \\
\frac{dS_n}{dt} &= u_1\pi_1 Q - (1-u_3)\beta\big(I_n + \eta I_p + \tau\mathrm{A}\big)S_n - u_2\alpha S_n - \mu S_n \\
\frac{dI_n}{dt} &= u_1\pi_2 Q + (1-u_3)\beta\big(I_n + \eta I_p + \tau\mathrm{A}\big)(\rho S_p + S_n) - u_4\sigma I_n - \delta I_n - \mu I_n \\
\frac{dI_p}{dt} &= u_1\pi_3 Q + u_4\sigma I_n - \gamma I_p - \mu I_p \\
\frac{dA}{dt} &= \delta I_n + \gamma I_p - \psi A - \mu A
\end{aligned}\right\} \quad (4.12)$$

where $u_1$ , $u_2$ , $u_3$ and $u_4$ are time-dependent controls. $u_1$ is the control effort to minimise the recruitment of non-productive and infected individuals (e.g. screening, etc), $u_2$ is the enlightenment/monitoring control on the non-productive susceptible in order to enhance their productivity, $u_3$ is the preventive control measure on susceptible individuals from getting infected with HIV/AIDS and $u_4$ is the treatment strategy on the non-productive infected individuals.

To investigate the optimal level of efforts that would be needed to control the disease and ensure productivity, we wish to minimize the number of the non-productive susceptible and infectious individuals and the cost of applying the controls $\mathrm{u}_1$, $\mathrm{u}_2$, $\mathrm{u}_3$ and $\mathrm{u}_4$ over a finite time interval $[0, T]$. We achieve this by defining an objective functional, $J$, by choosing a quadratic cost on the controls, this is similar with what is in other literature on epidemics control [57, 1, 37, 73, 67].

$$J = \int_0^T (n\mathrm{S_n} + m\mathrm{I_n} + b_1u_1^2 + b_2u_2^2 + b_3u_3^2 + b_4u_4^2)dt, \quad (4.13)$$

where $n$, $m$, $b_1$, $b_2$, $b_3$ and $b_4$ are positive weights. With the given objective functional, $J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3)$, our goal is to minimize the number of carefree susceptibles $\mathrm{S_n}$, while minimizing the cost of controls $\mathrm{u}_1(\mathrm{t})$, $\mathrm{u}_2(\mathrm{t})$, $\mathrm{u}_3(\mathrm{t})$ and $\mathrm{u}_4(\mathrm{t})$. We thus seek an optimal control quadruple $\left(u_1^{\#}, u_2^{\#}, u_3^{\#}, u_4^{\#}\right)$ such that

$$J\left(u_1^{\#}, u_2^{\#}, u_3^{\#}, u_4^{\#}\right) = \min\{J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3, \mathrm{u}_4): (\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3, \mathrm{u}_4) \in \mathcal{U}\}, \quad (4.14)$$

where

$$\mathcal{U} = \{(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3, \mathrm{u}_4): \mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3, \mathrm{u}_4 \text{ are measurable with } 0 \le \mathrm{u_i} \le 1, \mathrm{i} = 1, 2, 3, 4 \text{ for } \mathrm{t} \in [0, \mathrm{T}]\}$$

is the control set. The necessary conditions that an optimal control problem must satisfy come from Pontryagin's Maximum Principle [103]. We use this principle to convert the problem of minimization of the objective functional (4.13) coupled with the state variable

system (4.12) into a problem of minimizing point-wise a Hamiltonian, $H$, with respect to the controls $\mathrm{u}_1$, $\mathrm{u}_2$, $\mathrm{u}_3$ and $\mathrm{u}_4$

$$\begin{aligned} H = {} & n\mathrm{S_n} + m\mathrm{I_n} + b_1u_1^2 + b_2u_2^2 + b_3u_3^2 + b_4u_4^2 \\ & + \lambda_{\mathrm{S_p}}\{(1 - (1-u_1)(\pi_1 + \pi_2 + \pi_3))Q - (1-u_3)\rho\beta(I_n + \eta I_p + \tau\mathrm{A})S_p + u_2\alpha S_n \\ & - \mu S_p\} + \lambda_{\mathrm{S_n}}\{(1-u_1)\pi_1 Q - (1-u_3)\beta(I_n + \eta I_p + \tau\mathrm{A})S_n - u_2\alpha S_n - \mu S_n\} \\ & + \lambda_{\mathrm{I_n}}\{(1-u_1)\pi_2 Q + (1-u_3)\beta(I_n + \eta I_p + \tau\mathrm{A})(\rho S_p + S_n) - u_4\sigma I_n - \delta I_n - \mu I_n\} \\ & + \lambda_{\mathrm{I_p}}\{(1-u_1)\pi_3 Q + u_4\sigma I_n - \gamma I_p - \mu I_p\} + \lambda_A\{\delta I_n + \gamma I_p - \psi A - \mu A\} \end{aligned} \tag{4.15}$$

where $\lambda_{\mathrm{S_p}}, \lambda_{\mathrm{S_n}}, \lambda_{\mathrm{I_n}}, \lambda_{\mathrm{I_p}}$ and $\lambda_A$ are adjoint or co-state variables. By applying Pontryagin's Maximum Principle and the existence result for the optimal control [39], we obtain

***Proposition 4.2***: *For the optimal control quadruple* $(u_1^{\#}, u_2^{\#}, u_3^{\#}, u_4^{\#})$ *that minimizes* $J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3, \mathrm{u}_4)$ *over* $\mathcal{U}$*, there exist adjoint variables* $\lambda_{\mathrm{S_p}}, \lambda_{\mathrm{S_n}}, \lambda_{\mathrm{I_n}}, \lambda_{\mathrm{I_p}}$ and $\lambda_A$ *satisfying the following:*

***(i) Adjoint System***

$$\left.\begin{aligned} \frac{d\lambda_{S_p}}{dt} &= (1-u_3)\rho\beta(I_n + \eta I_p + \tau\mathrm{A})\left(\lambda_{S_p} - \lambda_{I_n}\right) + \mu\lambda_{S_p} \\ \frac{d\lambda_{S_n}}{dt} &= -n + u_2\alpha\left(\lambda_{S_n} - \lambda_{S_p}\right) + (1-u_3)\beta(I_n + \eta I_p + \tau\mathrm{A})(\lambda_{S_n} - \lambda_{I_n}) + \mu\lambda_{S_n} \\ \frac{d\lambda_{I_n}}{dt} &= -m + (1-u_3)\beta\lambda_{SI} + u_4\sigma\left(\lambda_{I_n} - \lambda_{I_p}\right) + \delta(\lambda_{I_n} - \lambda_A) + \mu\lambda_{I_n} \\ \frac{d\lambda_{I_p}}{dt} &= (1-u_3)\beta\eta\left\{\rho S_p\left(\lambda_{S_p} - \lambda_{I_n}\right) + S_n(\lambda_{S_n} - \lambda_{I_n})\right\} + \gamma\left(\lambda_{I_p} - \lambda_A\right) + \mu\lambda_{I_p} \\ \frac{d\lambda_A}{dt} &= (1-u_3)\beta\tau\left\{\rho S_p\left(\lambda_{S_p} - \lambda_{I_n}\right) + S_n(\lambda_{S_n} - \lambda_{I_n})\right\} + (\psi + \mu)\lambda_A \end{aligned}\right\} \textit{(4.16)}$$

*where* $\lambda_{SI} = \rho S_p\left(\lambda_{S_p} - \lambda_{I_n}\right) + S_n(\lambda_{S_n} - \lambda_{I_n})$.

***(ii) Transversality Conditions***

$$\lambda_{\mathrm{S}_p}(T) = \lambda_{\mathrm{S_n}}(T) = \lambda_{\mathrm{I_n}}(T) = \lambda_{\mathrm{I_p}}(T) = \lambda_{\mathrm{A}}(T) = 0 \tag{4.17}$$

***(iii) Stationary Values***

$$\left.\begin{aligned} u_1^{\#} &= max\left\{0, min\left\{1, \frac{Q\left[\pi_1\left(\lambda_{S_n}-\lambda_{S_p}\right)+\pi_2\left(\lambda_{I_n}-\lambda_{S_p}\right)+\pi_3\left(\lambda_{I_p}-\lambda_{S_p}\right)\right]}{2b_1}\right\}\right\} \\ u_2^{\#} &= max\left\{0, min\left\{1, \frac{\alpha S_n\left(\lambda_{S_n}-\lambda_{S_p}\right)}{2b_2}\right\}\right\} \\ u_3^{\#} &= max\left\{0, min\left\{1, \frac{\beta\left(I_n+\eta I_p+\tau A\right)\left[\rho S_p\left(\lambda_{I_n}-\lambda_{S_p}\right)+S_n\left(\lambda_{I_n}-\lambda_{S_n}\right)\right]}{2b_3}\right\}\right\} \\ u_4^{\#} &= max\left\{0, min\left\{1, \frac{\sigma I_n\left(\lambda_{I_n}-\lambda_{I_p}\right)}{2b_4}\right\}\right\} \end{aligned}\right\} \quad (4.18)$$

***Proof***: Corollary 4.1 in [39], gives the existence of an optimal control due to the convexity of the integrand of $J$ with respect to $u_1$, $u_2$, $u_3$, $u_4$ a priori boundedness of the state solutions and the Lipschitz property of the state system with respect to the state variables [39]. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control. In particular

$$\frac{\partial H}{\partial x} = -\frac{dx}{dt}$$

where $x = S_p, S_n, I_n, I_p, A$ establishes the adjoint system. Furthermore, by equating to zero the derivatives of the Hamiltonian with respect to the controls we obtain (see [72])

$$\left.\begin{aligned} \tilde{u}_1 &= \frac{Q\left[\pi_1\left(\lambda_{S_n}-\lambda_{S_p}\right)+\pi_2\left(\lambda_{I_n}-\lambda_{S_p}\right)+\pi_3\left(\lambda_{I_p}-\lambda_{S_p}\right)\right]}{2b_1} \\ \tilde{u}_2 &= \frac{\alpha S_n\left(\lambda_{S_n}-\lambda_{S_p}\right)}{2b_2} \\ \tilde{u}_3 &= \frac{\beta\left(I_n+\eta I_p+\tau A\right)\left[\rho S_p\left(\lambda_{I_n}-\lambda_{S_p}\right)+S_n\left(\lambda_{I_n}-\lambda_{S_n}\right)\right]}{2b_3} \\ \tilde{u}_4 &= \frac{\sigma I_n\left(\lambda_{I_n}-\lambda_{I_p}\right)}{2b_4} \end{aligned}\right\} \quad (4.19)$$

Standard control arguments involving the bounds on the controls

$$u_i^{\#} = \begin{cases} 0, if\ \tilde{u}_i \le 0 \\ \tilde{u}_{i\,,}\ if\ 0 < \tilde{u}_i < 1 \\ 1, if\ \tilde{u}_i \ge 1 \end{cases} \quad (4.20)$$

provide the stationary values.

Due to the a priori 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 $T$. The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of the state system (4.12) and adjoint system (4.16) with characterization (4.18). There is a restriction on the length of the time interval in order to guarantee the uniqueness of the optimality system. This smallness restriction of the length on the time is due to the opposite time orientations of the state and adjoint systems; the state problem (4.12) has initial values and the adjoint problem (4.16) has final values (4.17). This restriction is very common in control problems (see [57, 37, 74, 67]). ■

### 4.5 Numerical Results and Discussion

In this section, we examine a deterministic model with non-productive susceptibles and we study numerically the effects of prevention, enlightenment and HAART treatments on the spread of HIV/AIDS. The optimal control is obtained by solving the optimality system, consisting of the state and adjoint systems. An iterative scheme is used for solving the optimality system. We start to solve the state equations with a guess for the controls over the simulated time using the fourth order Runge-Kutta scheme. Because of the transversality conditions (4.17), the adjoint equations (4.16) are solved by a backward fourth order Runge-Kutta scheme using the current iteration's solutions of the state system (4.12). Then the controls are updated by using a convex combination of the previous controls and the value from the stationarity characterizations (4.18). This process is repeated and iterations stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iterations [72].

We explore a simple model with screening, prevention, enlightenment and treatment as control measures to study the effects of control practices and transmission of HIV using various combinations of the controls: four, three and two controls at a time. This is done under the following scenarios to compare numerical results:

• Strategy A: Using screening ($u_1$) and enlightenment ($u_2$) without prevention ($u_3 = 0$) and no treatment of infectives ($u_4 = 0$)
• Strategy B: Using screening ($u_1$) and treatment of infectives ($u_4$) without enlightenment ($u_2 = 0$) and no prevention ($u_3 = 0$)
• Strategy C: Using screening ($u_1$) and prevention ($u_3$) without enlightenment ($u_2 = 0$) and no treatment of infectives ($u_4 = 0$)

• Strategy D: Using enlightenment ($u_2$) and prevention ($u_3$) without screening ($u_1 = 0$) and no treatment of infectives ($u_4 = 0$)

• Strategy E: Using enlightenment ($u_2$) and treatment of infectives ($u_4$) without screening ($u_1 = 0$) and no prevention ($u_3 = 0$)

• Strategy F: Using prevention ($u_3$) and treatment of infectives ($u_4$) without screening ($u_1 = 0$) and no enlightenment ($u_2 = 0$)

• Strategy G: Using screening ($u_1$), enlightenment ($u_2$) and prevention ($u_3$) with no treatment of infectives ($u_4 = 0$)

• Strategy H: Using screening ($u_1$), enlightenment ($u_2$) and treatment of infectives ($u_4$) with no prevention ($u_3 = 0$)

• Strategy I: Using screening ($u_1$), prevention ($u_3$) and treatment of infectives ($u_4$) with no enlightenment ($u_2 = 0$)

• Strategy J: Using enlightenment ($u_2$), prevention ($u_3$) and treatment of infectives ($u_4$) with no screening ($u_1 = 0$)

• Strategy K: Using all four control measures ($u_1$, $u_2$, $u_3$ and $u_4$)

### 4.5.1 Strategy A

The control profiles suggest that control $u_1$ be kept at the upper bound for the entire period while $u_2$ should be at the upper bound for the first two years before dropping gradually to the lower bound. Shadow prices indicate the negative impact of the non-productive and the infected.

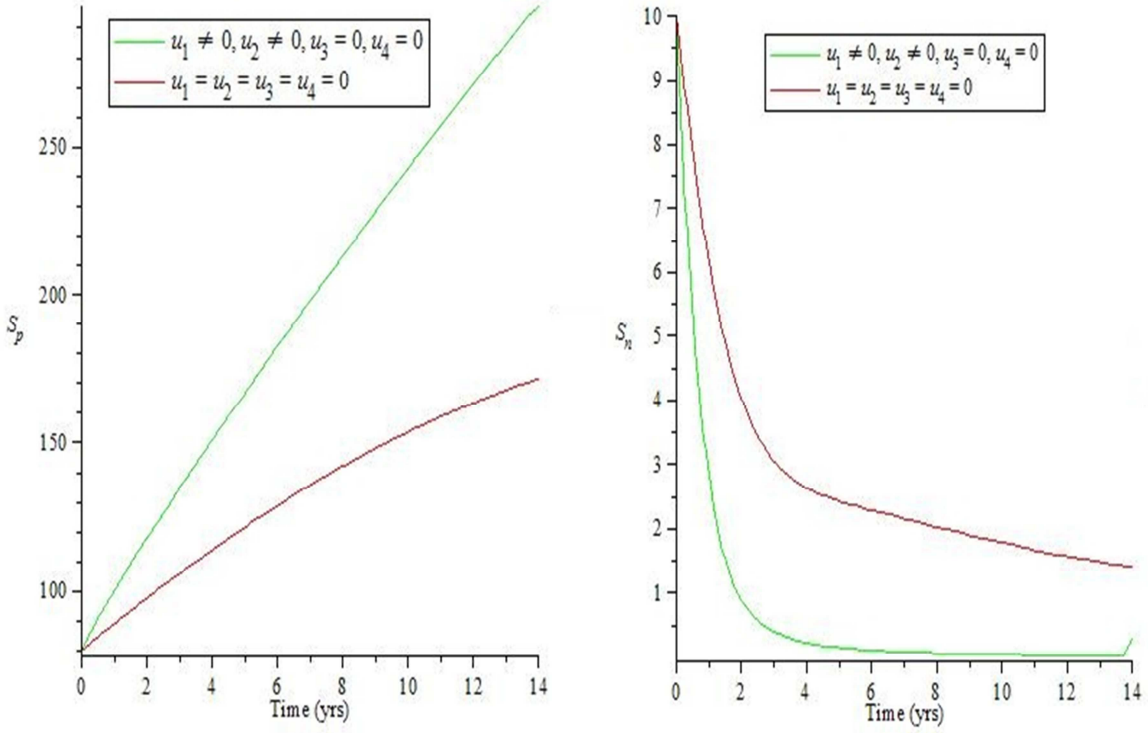



Fig 4.4 (a): Simulations of the model showing the effect of control strategy A on susceptibles

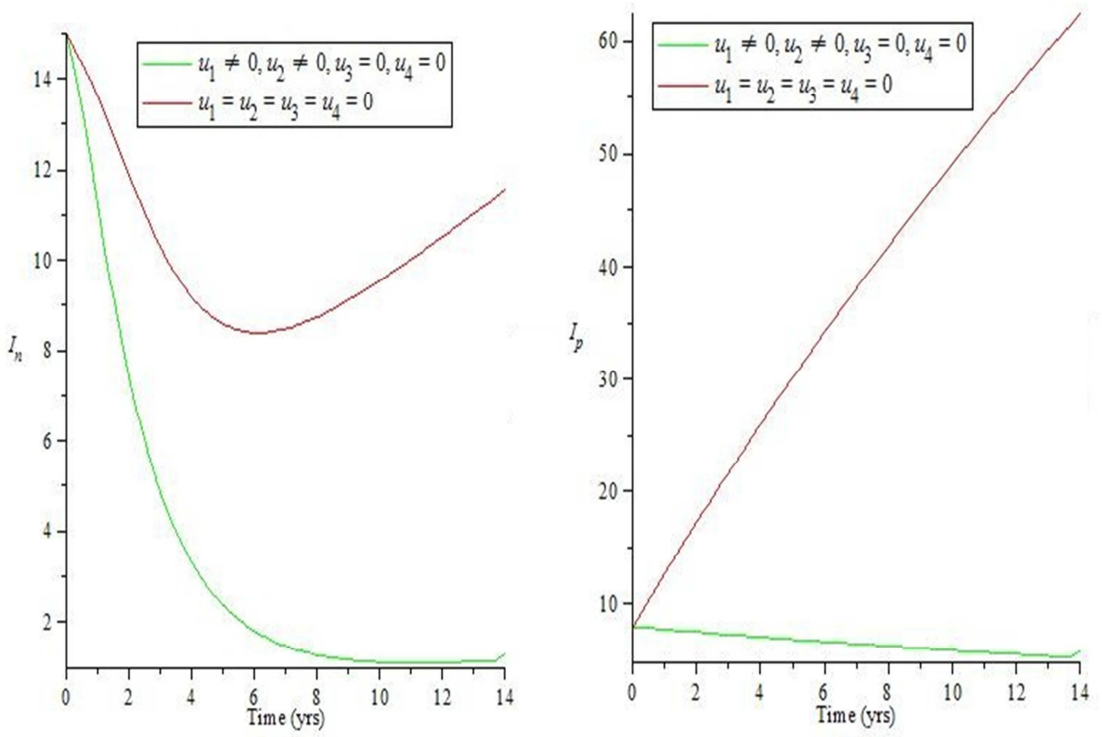



Fig 4.4 (b): Simulations of the model showing the effect of control strategy A on infectives

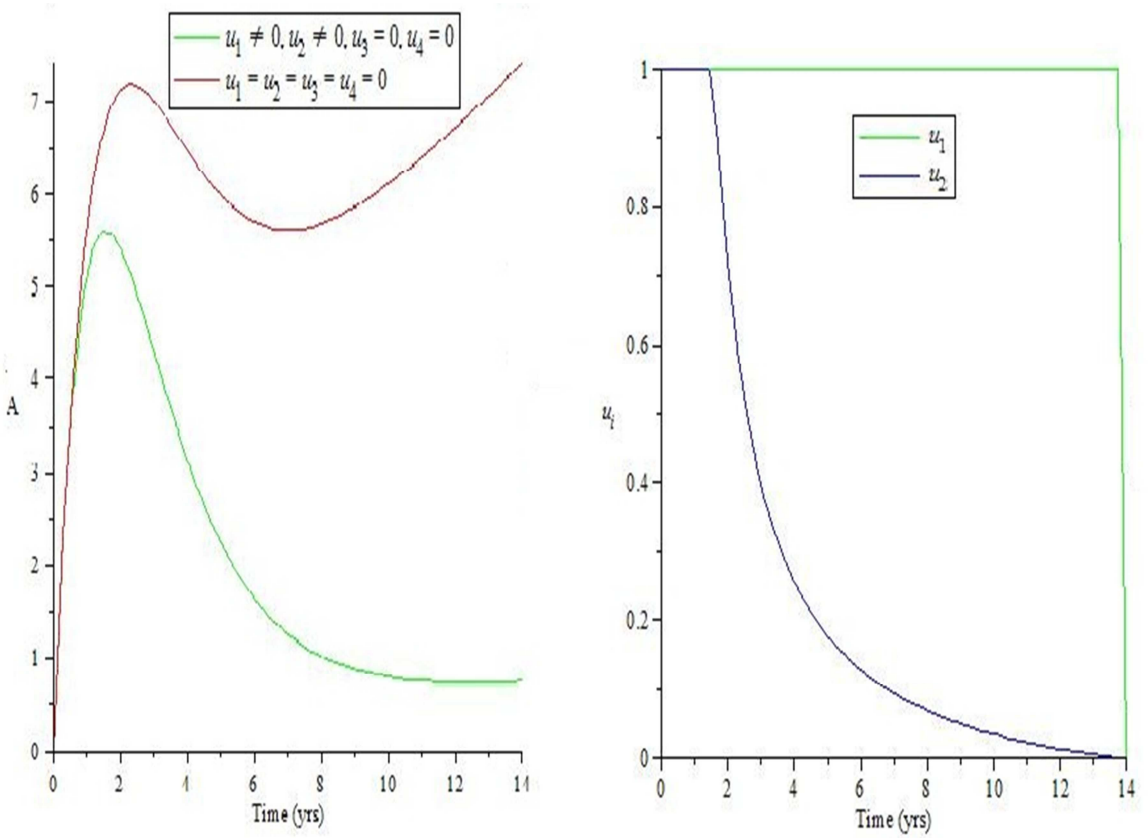



Fig 4.4 (c): Simulations of the model showing the effect of control strategy A on AIDS individuals and controls

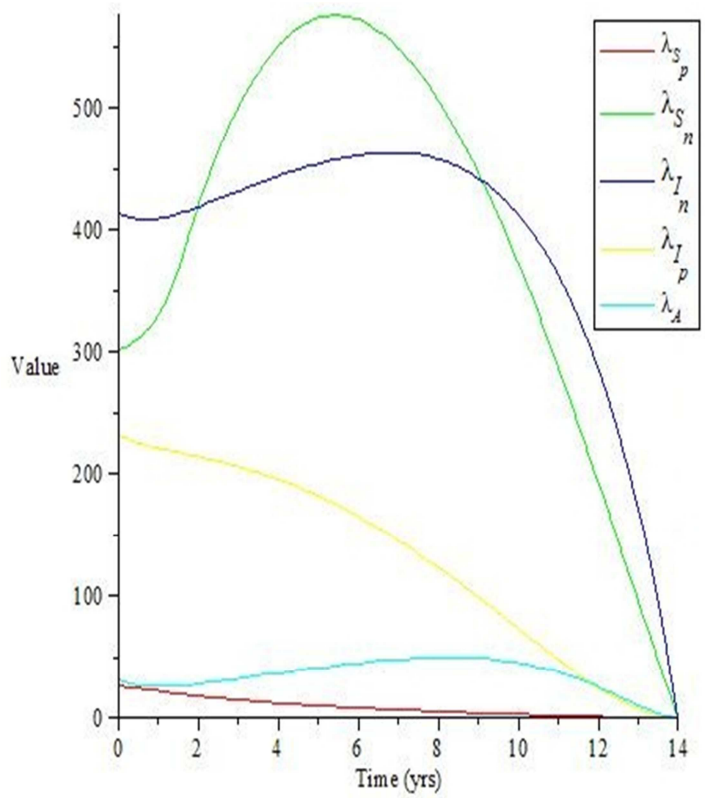



Fig 4.4 (d): Simulations of the model showing the effect of control strategy A on co-state variables

### 4.5.2 Strategy B

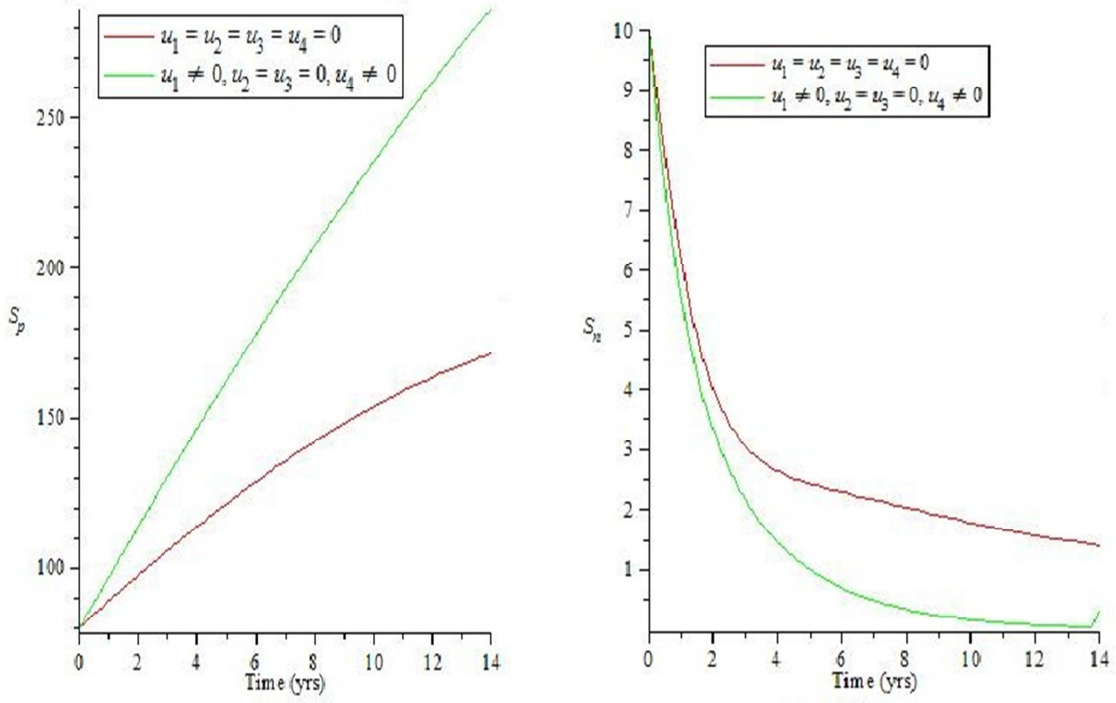



Fig 4.5 (a): Simulations of the model showing the effect of control strategy B on susceptibles

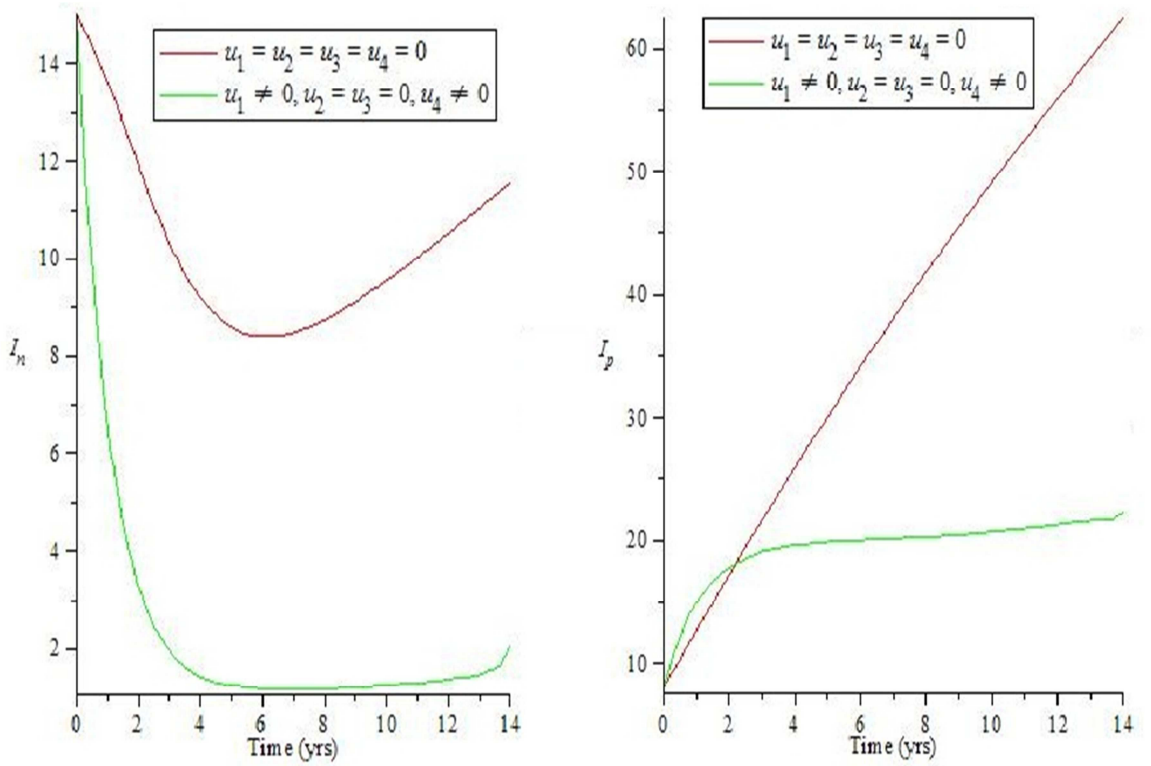



Fig 4.5 (b): Simulations of the model showing the effect of control strategy B on infectives

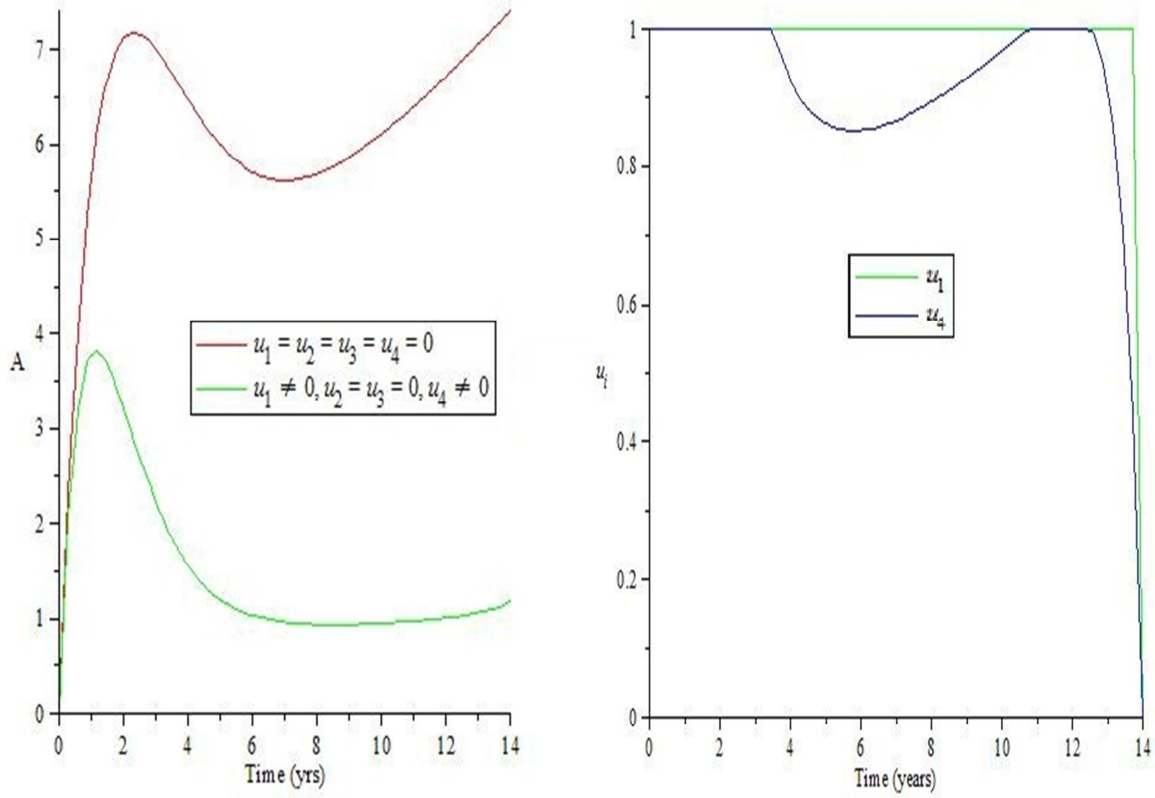



Fig 4.5 (c): Simulations of the model showing the effect of control strategy B on AIDS individuals and controls

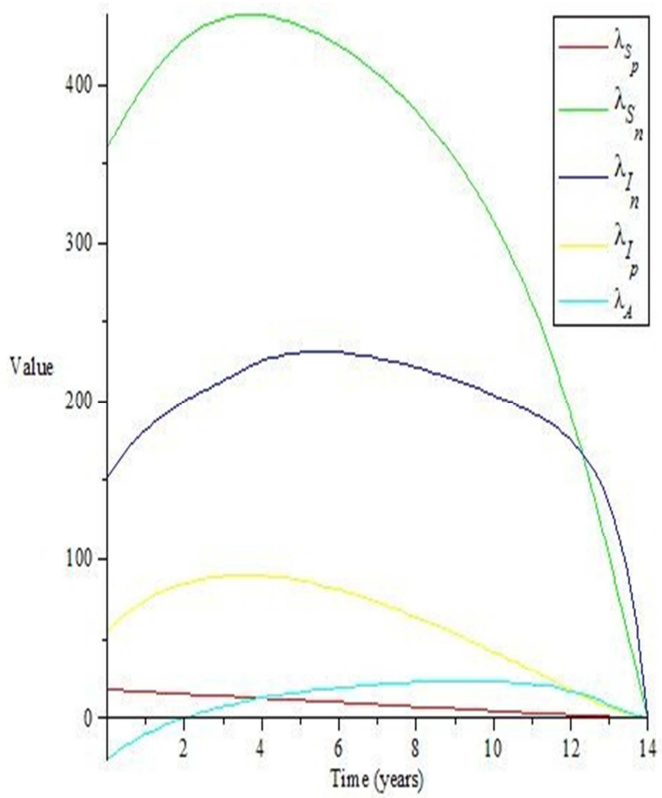



Fig 4.5 (d): Simulations of the model showing the effect of control strategy B on adjoints

The control profiles suggest that the control $u_1$ must be kept at the upper bound throughout the intervention period whilst the control $u_4$ must be maintained at the upper bound for about four years, dropping slightly to about 0.8 before rising again to the upper bound between the tenth and twelfth years then dropping sharply to the lower bound during the last two years. Shadow prices for the non-productive and the infected are quite significant.

### 4.5.3 Strategy C

Plots show significant drops in the non-productive and the number of AIDS individuals despite the fall in the number of the productive infected. However, shadow prices for the non-productive and the infected are quite significant.

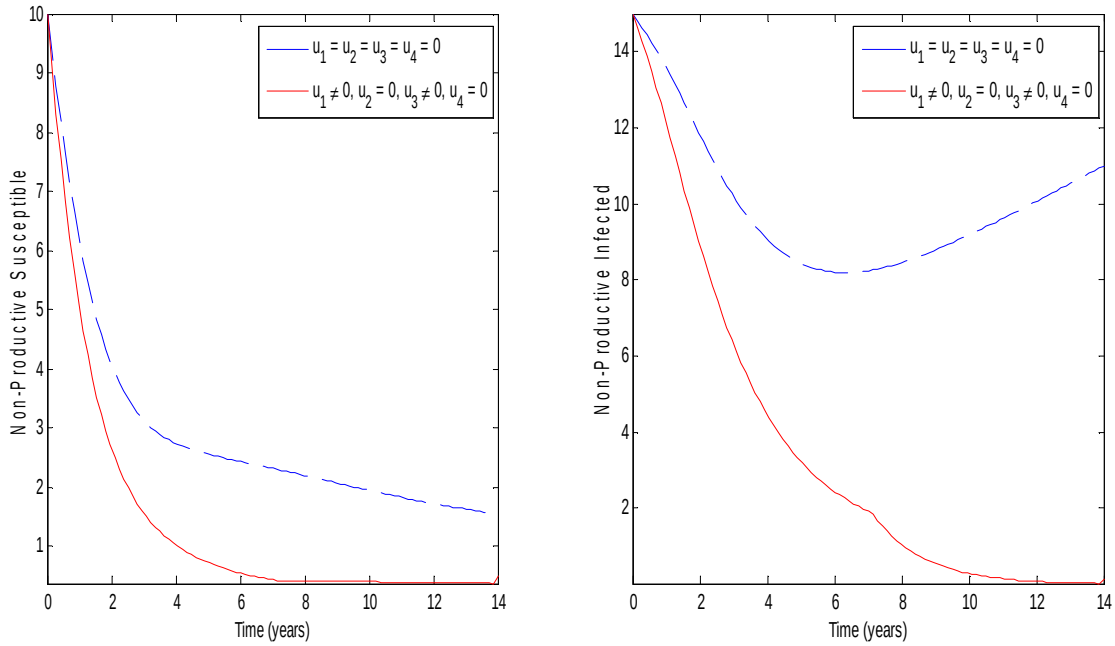



Fig 4.6 (a): Simulations of the model showing the effect of strategy C on the non-productive

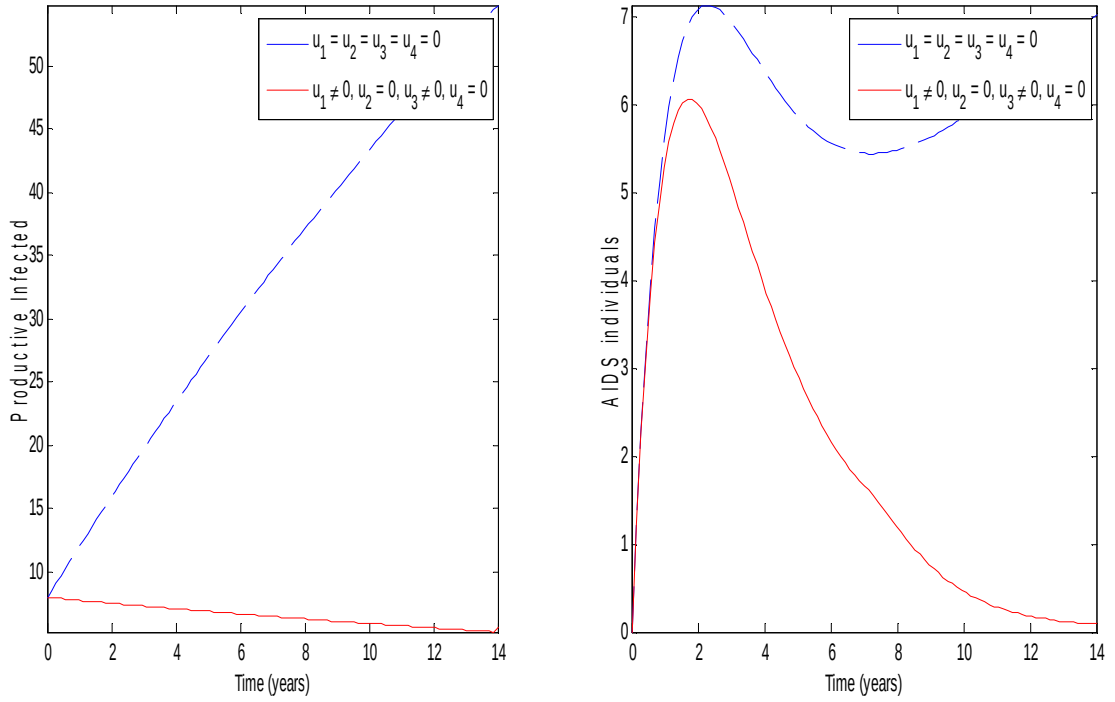



Fig 4.6 (b): Simulations of the model showing the effect of strategy C on productive infectives and AIDS individuals

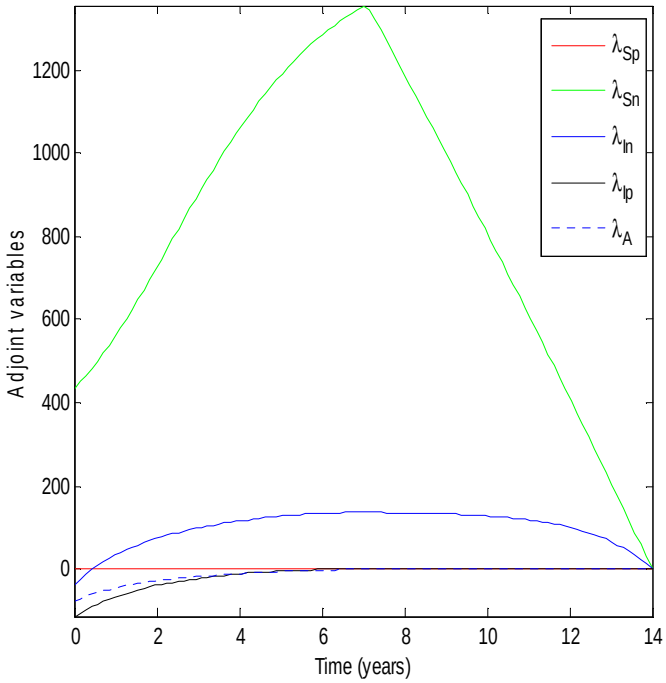



Fig 4.6 (c): Simulations of the model showing the effect of strategy C on co-state variables

### 4.5.4 Strategy D

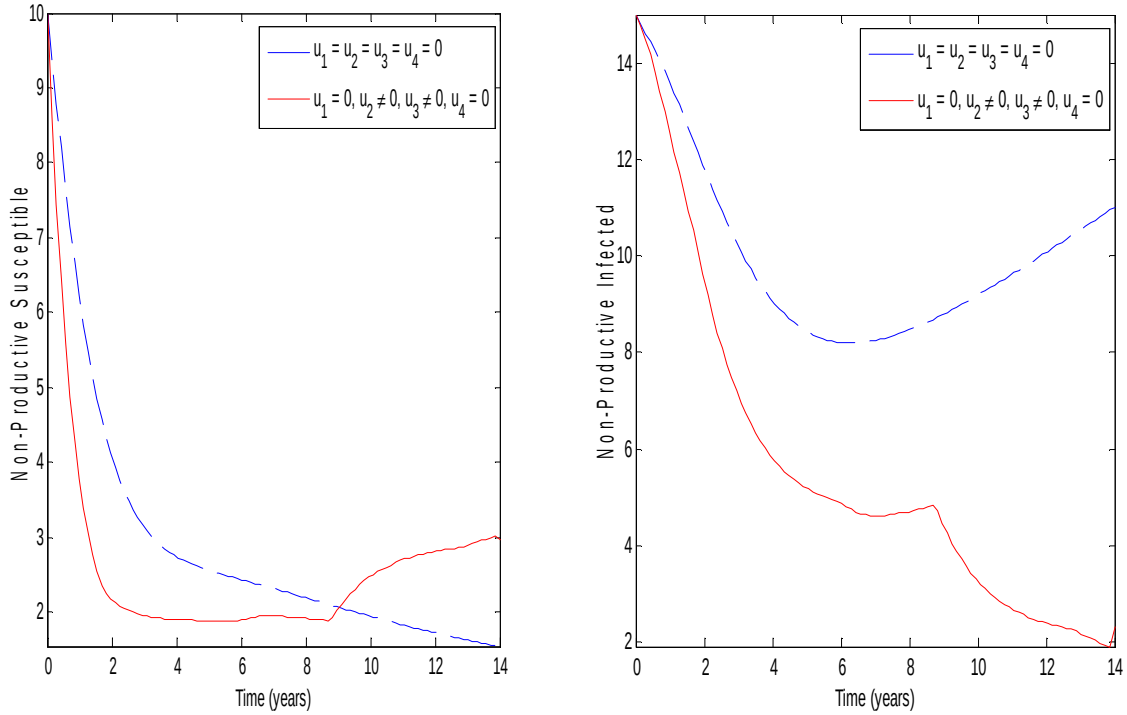



Fig 4.7 (a): Simulations showing the effect of strategy D on the spread of the non-productive

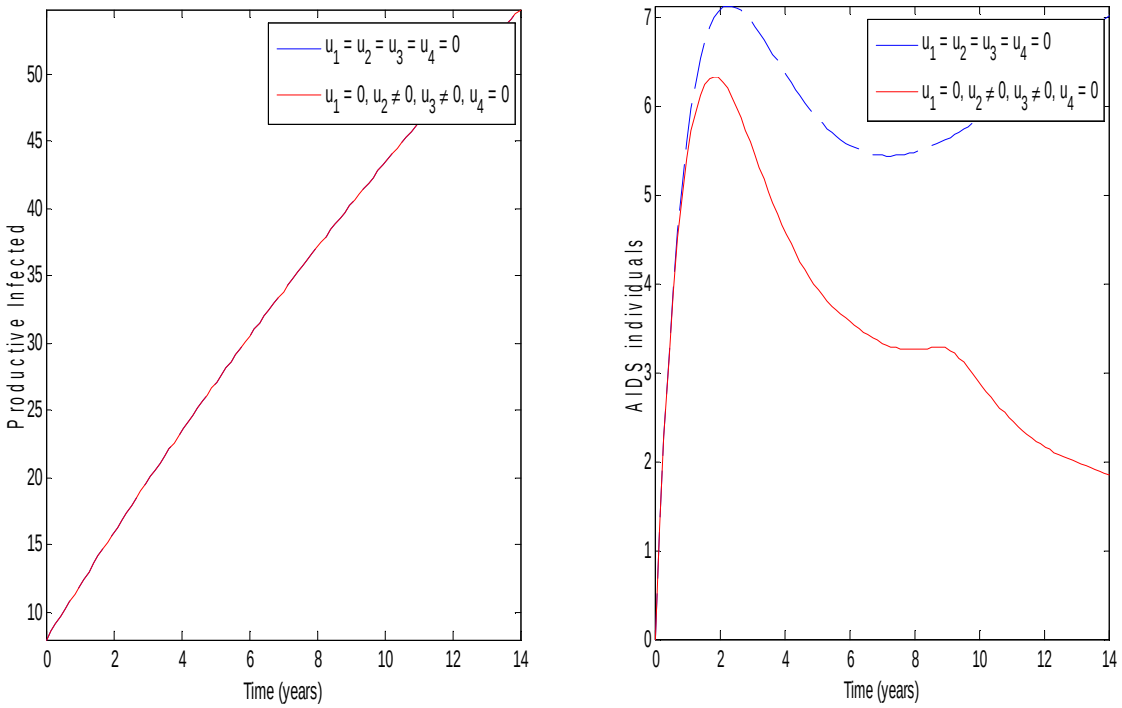



Fig 4.7 (b): Simulations showing the effect of strategy D on productive infectives and AIDS individuals

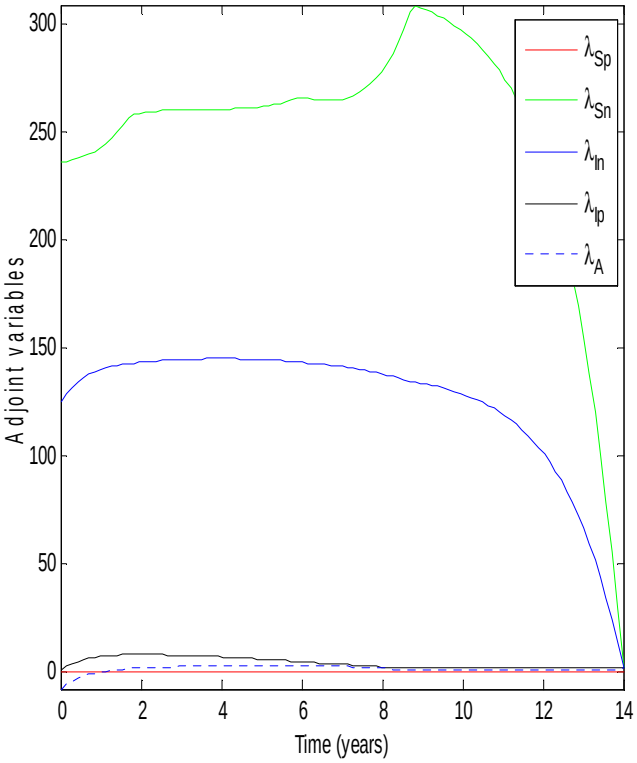



Fig 4.7 (c): Simulations showing the effect of strategy D on adjoint variables

Simulations show marked declines in the non-productive infected and AIDS sub-classes. Shadow prices for the non-productive dominate.

### 4.5.5 Strategy E

The control profiles suggest that the control $u_2$ must be at the upper bound for the first two years before dropping gradually to the lower bound while the control $u_4$ should be maintained at the upper bound throughout the intervention period.

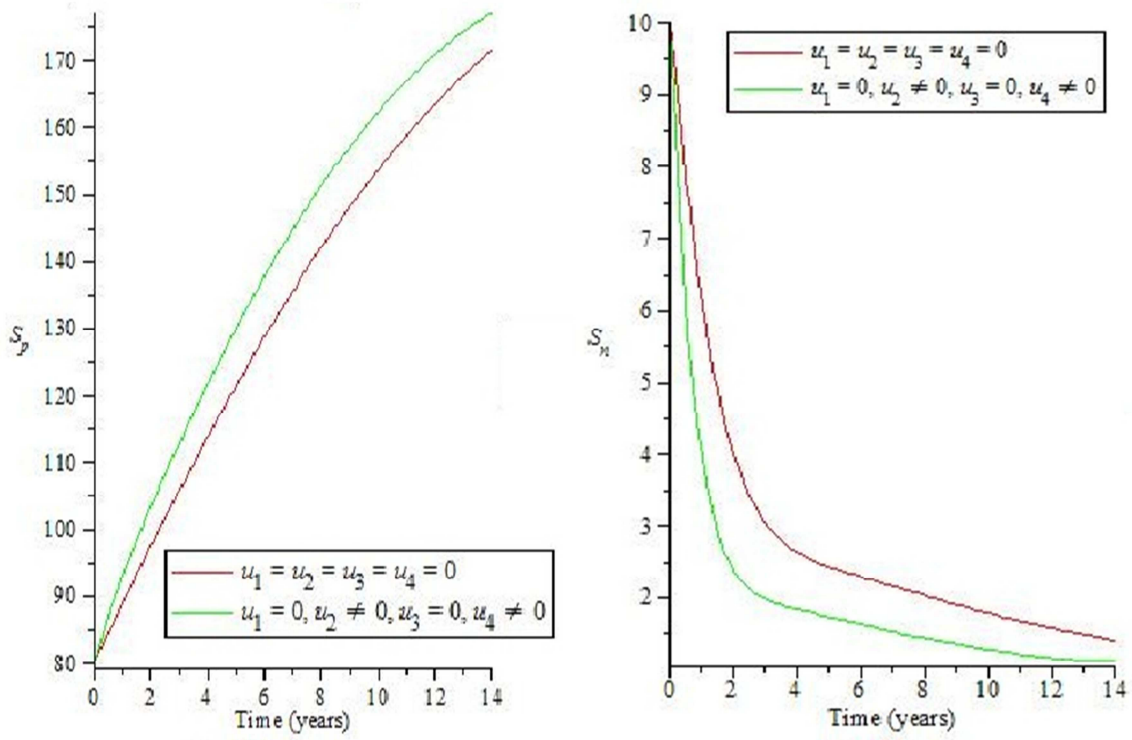



Fig 4.8 (a): Simulations showing the effect of strategy E on susceptibles

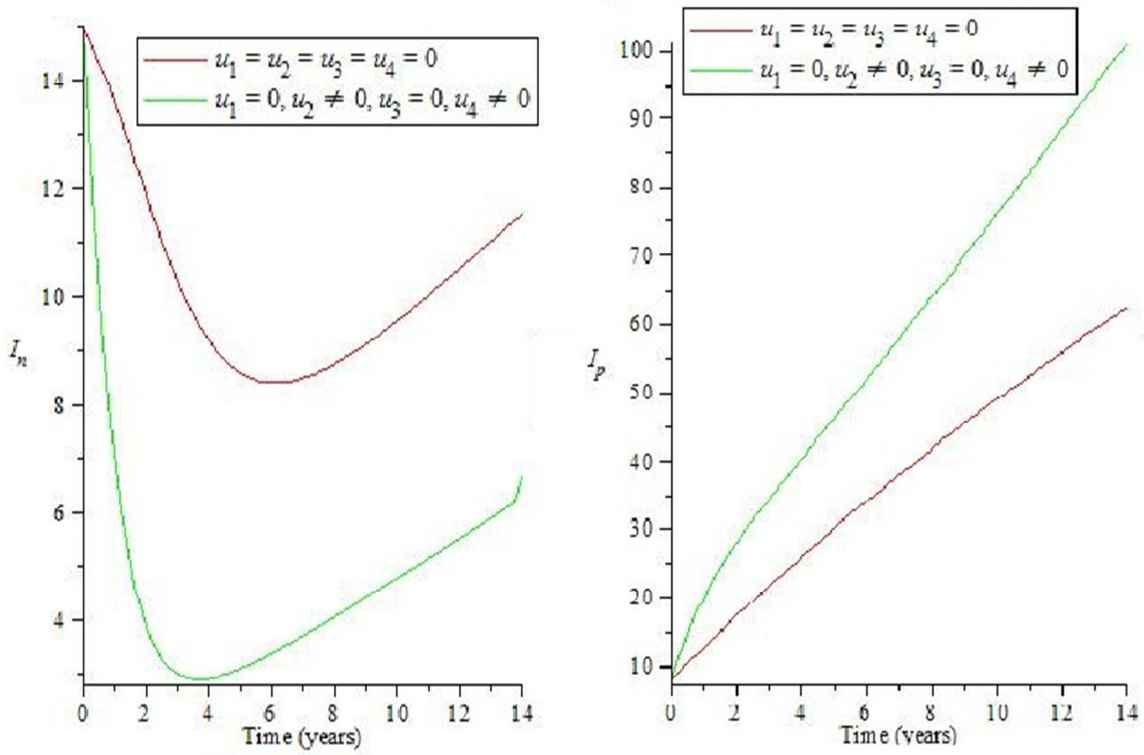



Fig 4.8 (b): Simulations showing the effect of strategy E on infectives

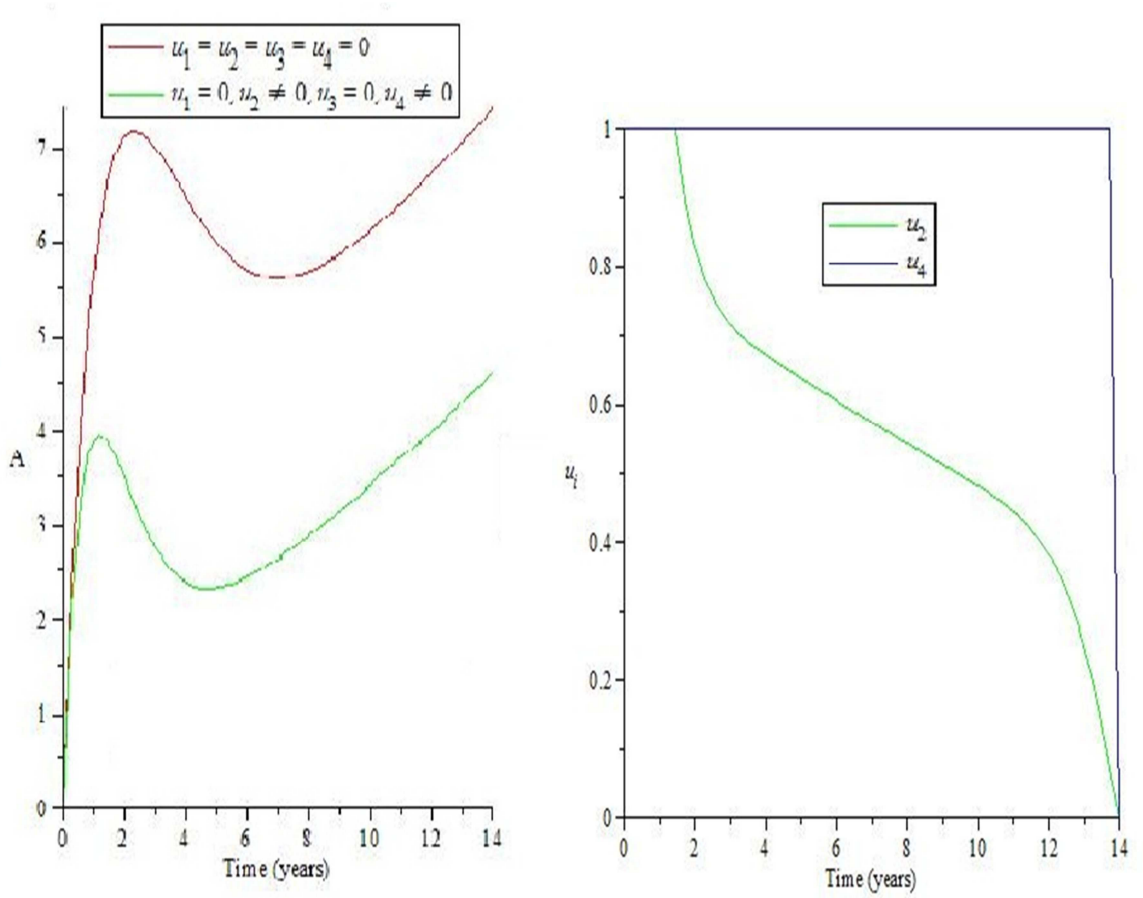



Fig 4.8 (c): Simulations showing the effect of strategy E on AIDS individuals and controls

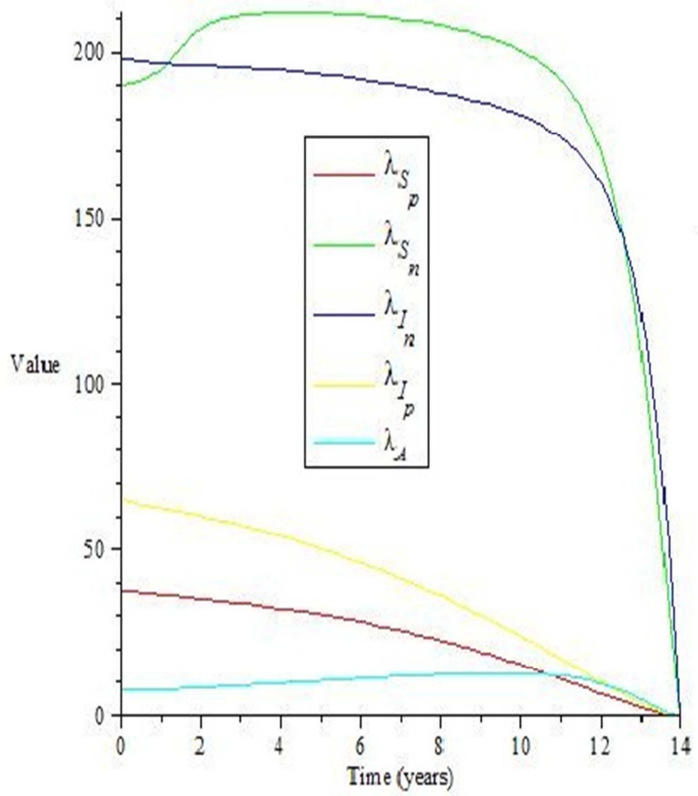



Fig 4.8 (d): Simulations showing the effect of strategy E on shadow prices

### 4.5.6 Strategy F

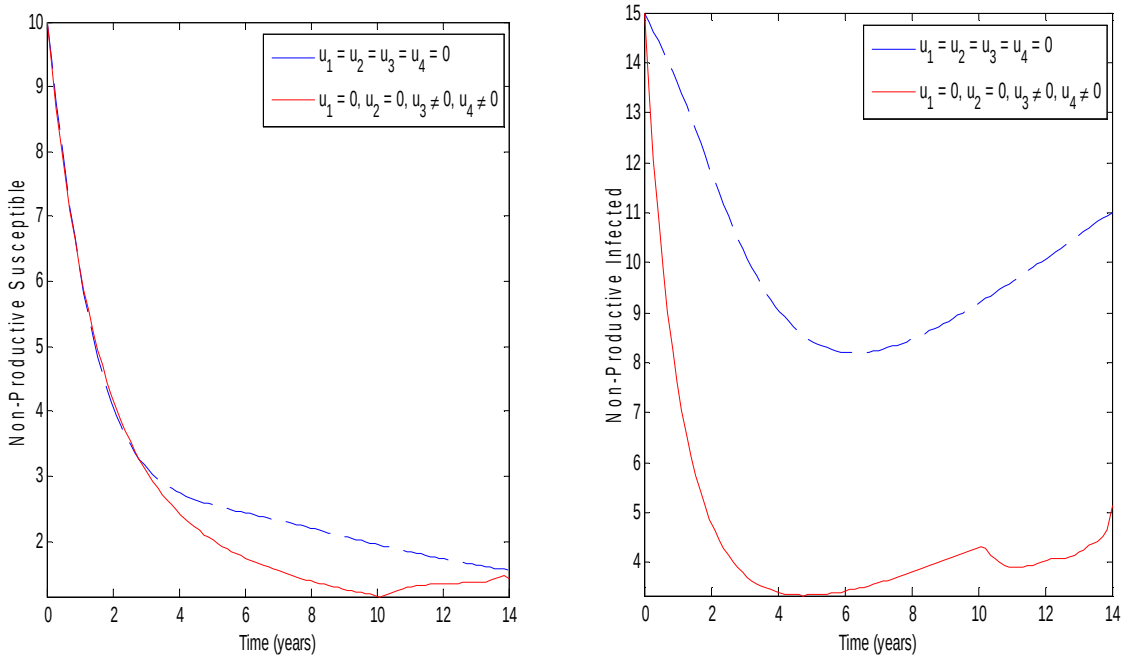



Fig 4.9 (a): Simulations showing the effect of strategy F on the non-productive

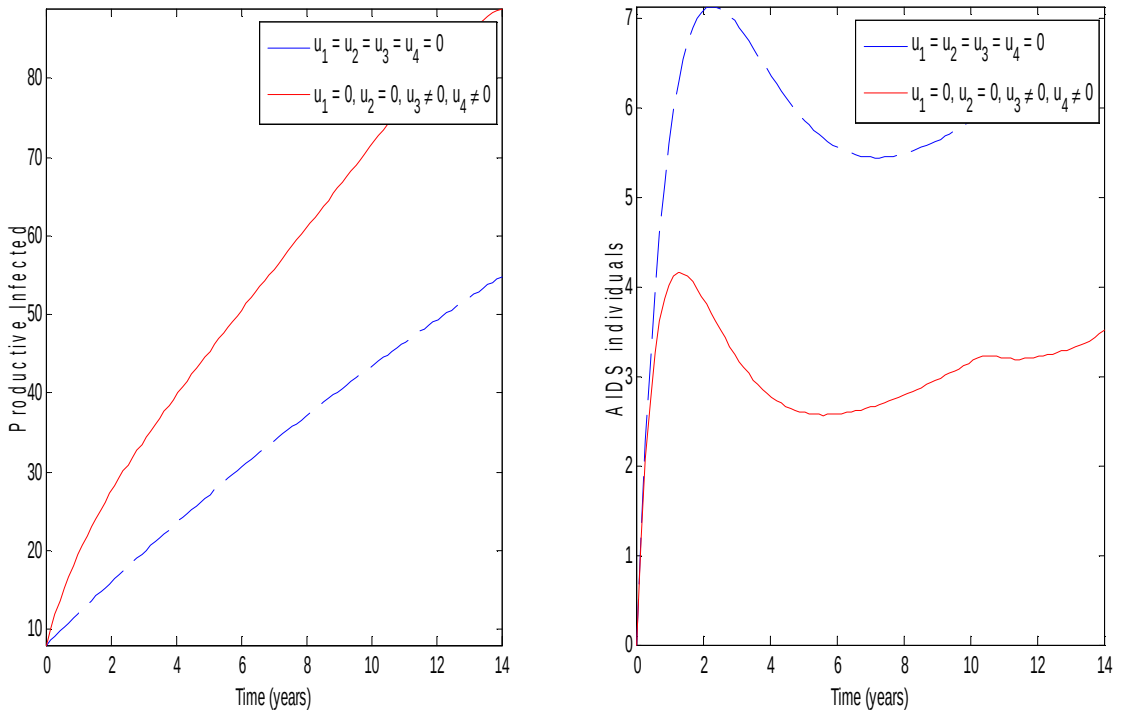



Fig 4.9 (b): Simulations showing the effect of strategy F on productive infectives and AIDS individuals

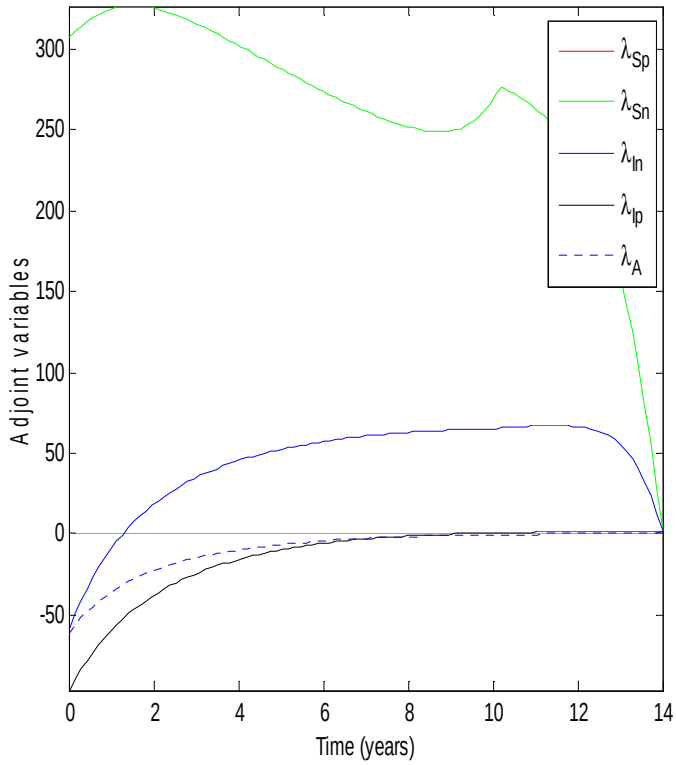



Fig 4.9 (c): Simulations showing the effect of strategy F on adjoints

Simulations show a significant reduction in the non-productive infected and the number of individuals with AIDS coupled with marked improvements in the productive infected. Shadow prices for the non-productive still stand out.

### 4.5.7 Strategy G

Results show considerable reductions in the non-productive classes including the AIDS class, despite reductions in the productive infected. Shadow prices for the non-productive are quite significant.

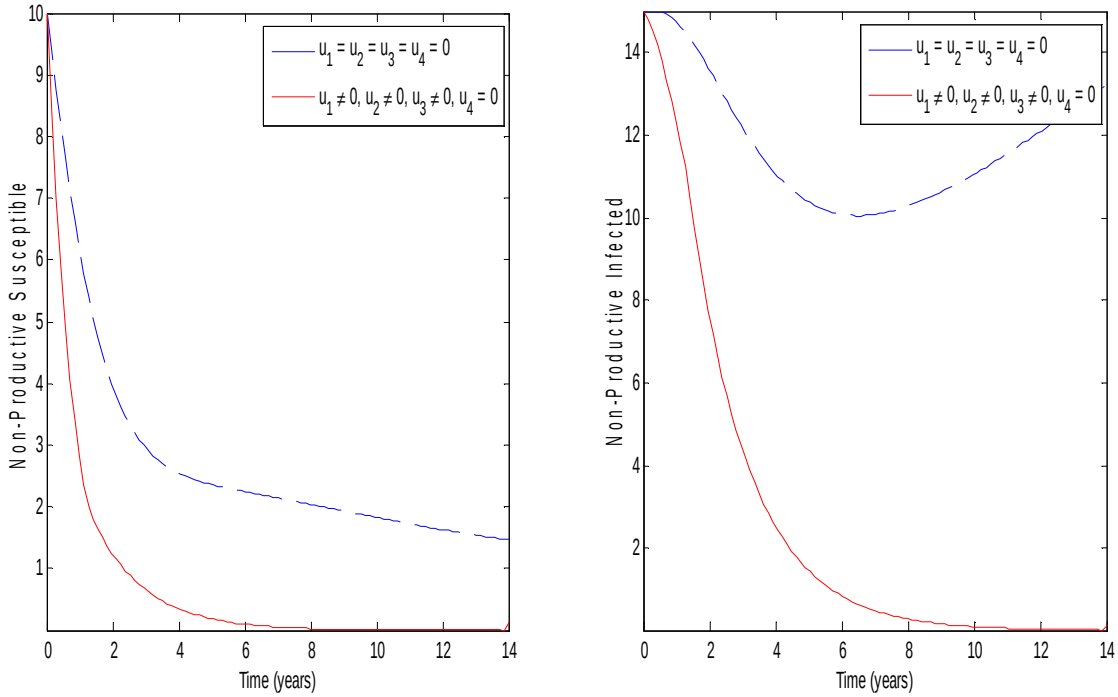



Fig 4.10 (a): Simulation results showing the effect of strategy G on the non-productive

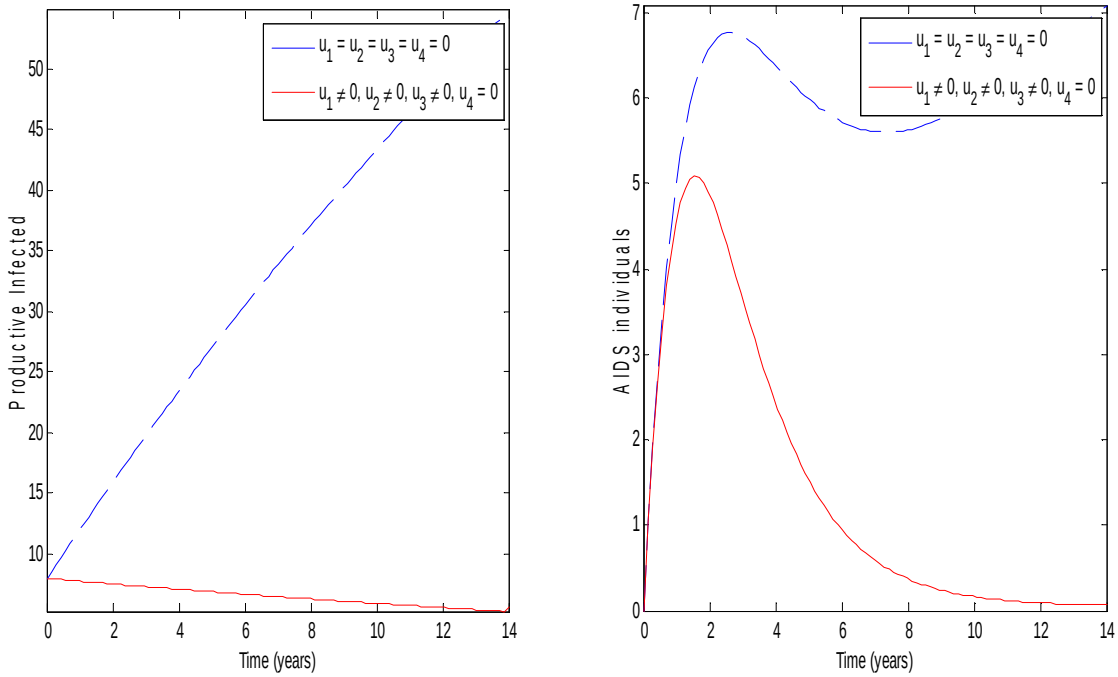



Fig 4.10 (b): Simulation results showing the effect of strategy G on productive infectives and AIDS individuals

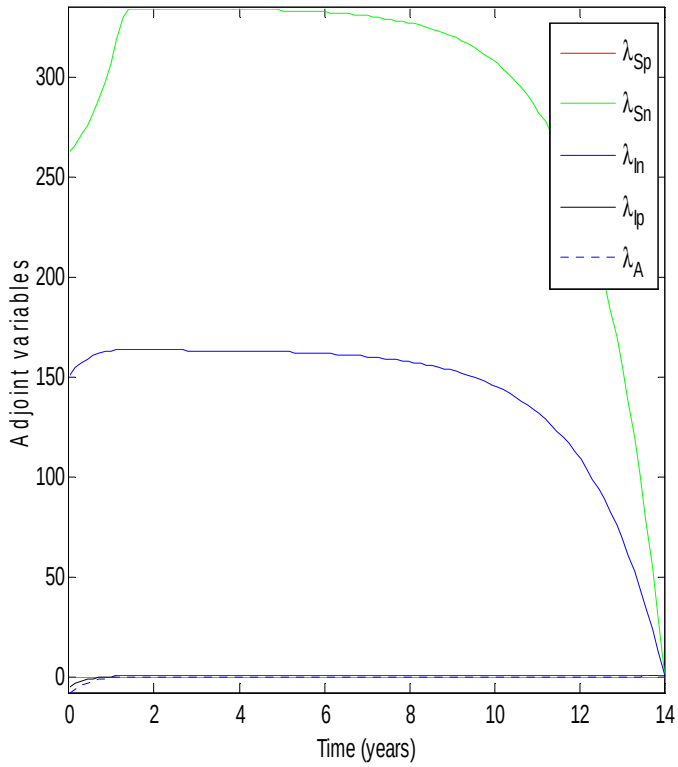



Fig 4.10 (c): Simulation results showing the effect of strategy G on shadow prices

### 4.5.8 Strategy H

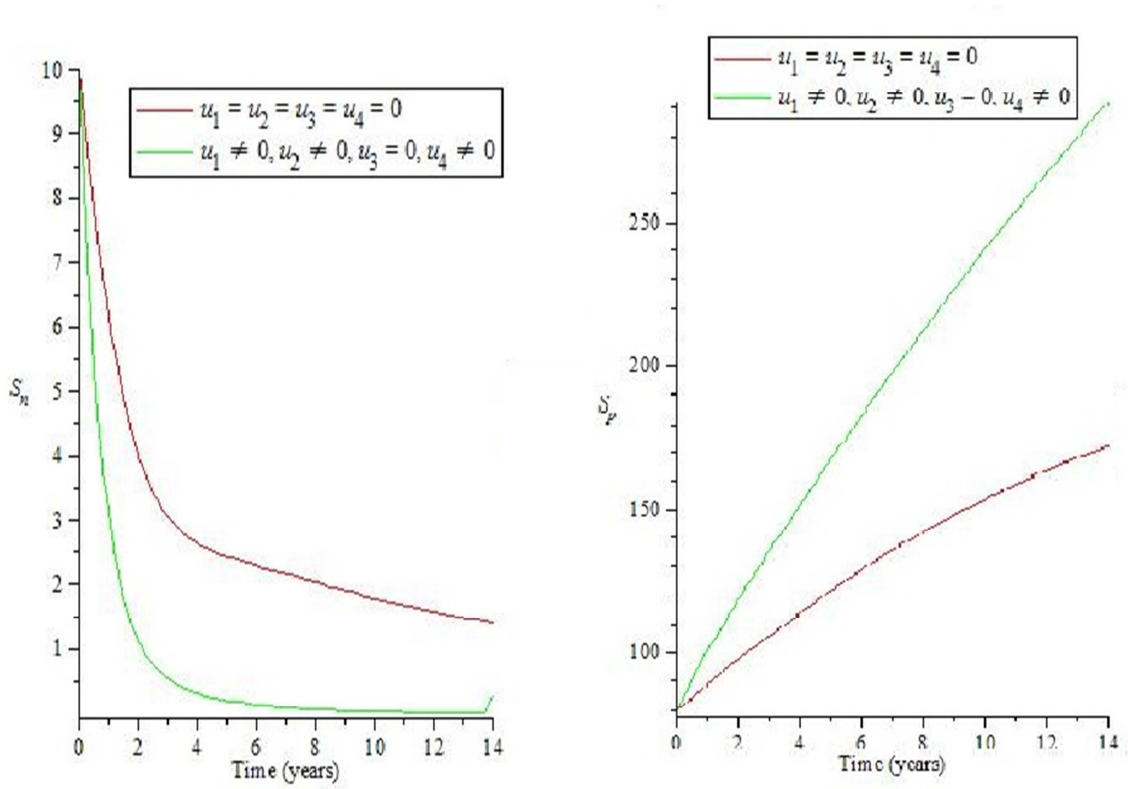



Fig 4.11 (a): Simulations showing the effect of strategy H on susceptibles

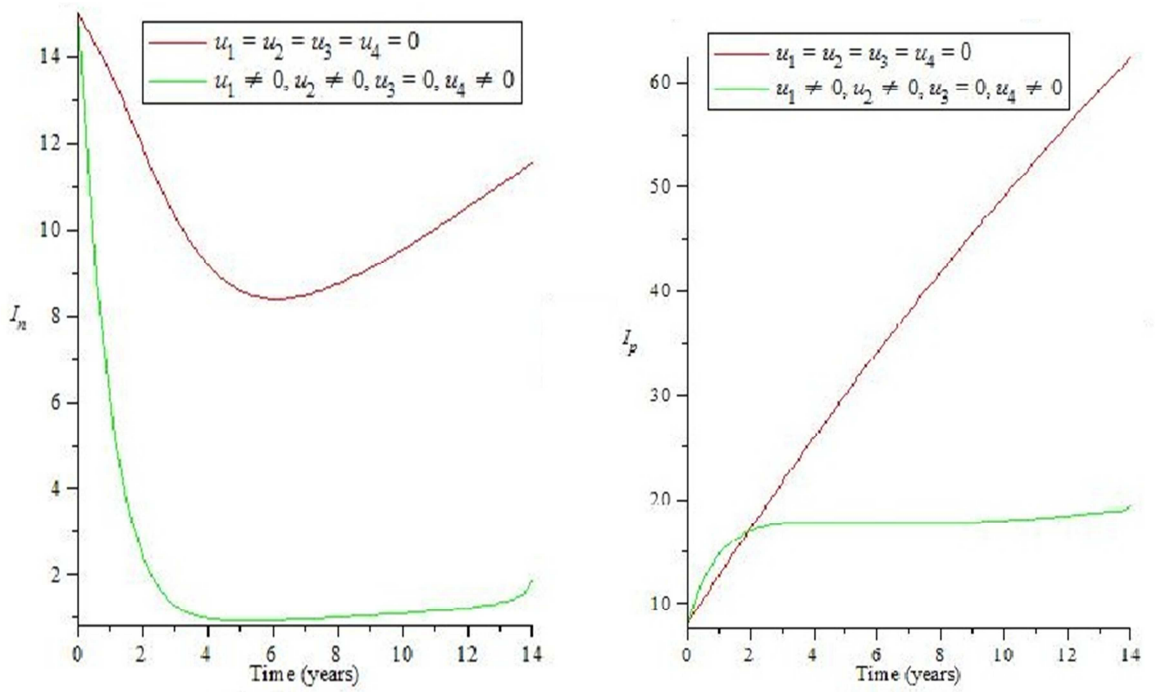



Fig 4.11 (b): Simulations showing the effect of strategy H on infectives

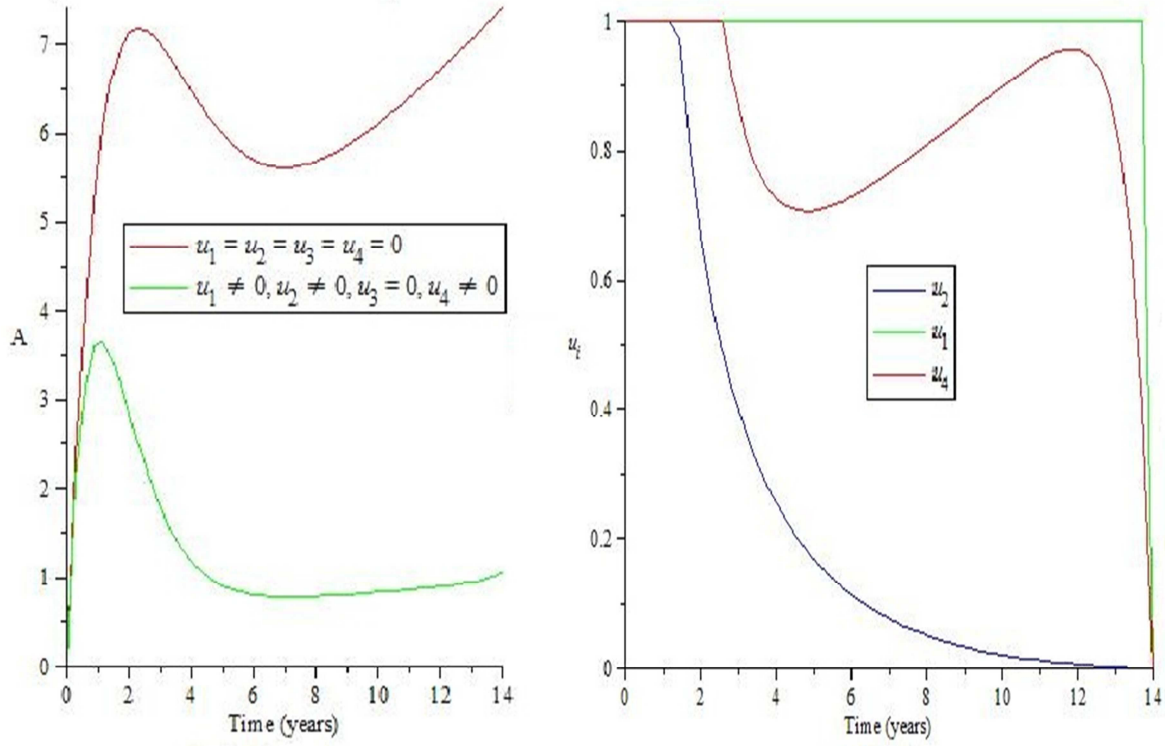



Fig 4.11 (c): Simulations showing the effect of strategy H on AIDS individuals and controls

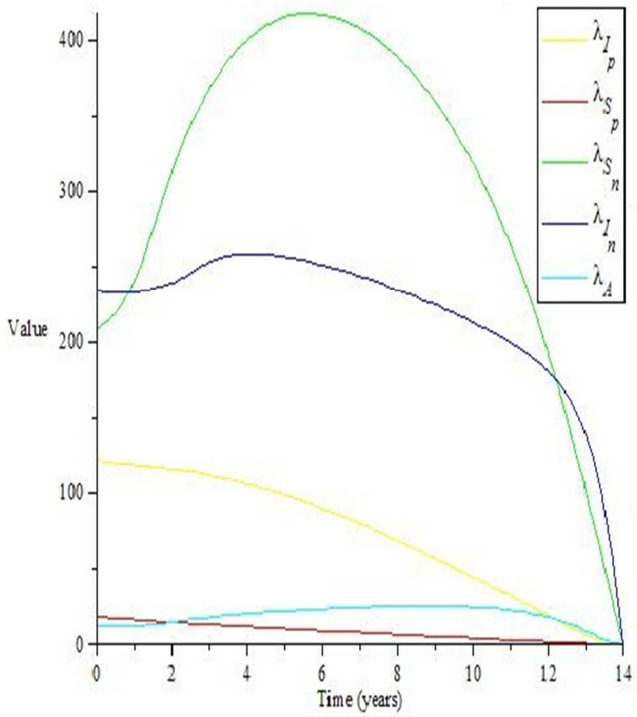



Fig 4.11 (d): Simulations showing the effect of strategy H on co-state variables

The control profiles suggest that the control $u_1$ must be maintained at the upper bound for the whole intervention period while $u_2$ should be kept at the upper bound only for the first two years then gradually reducing to the lower bound. $u_4$ should be at the upper bound for the first three years before dropping gradually to about 0.7 then rising again to just above 0.9 by the twelfth year and finally reducing to the lower bound in the last two years of intervention.

### 4.5.9 Strategy I

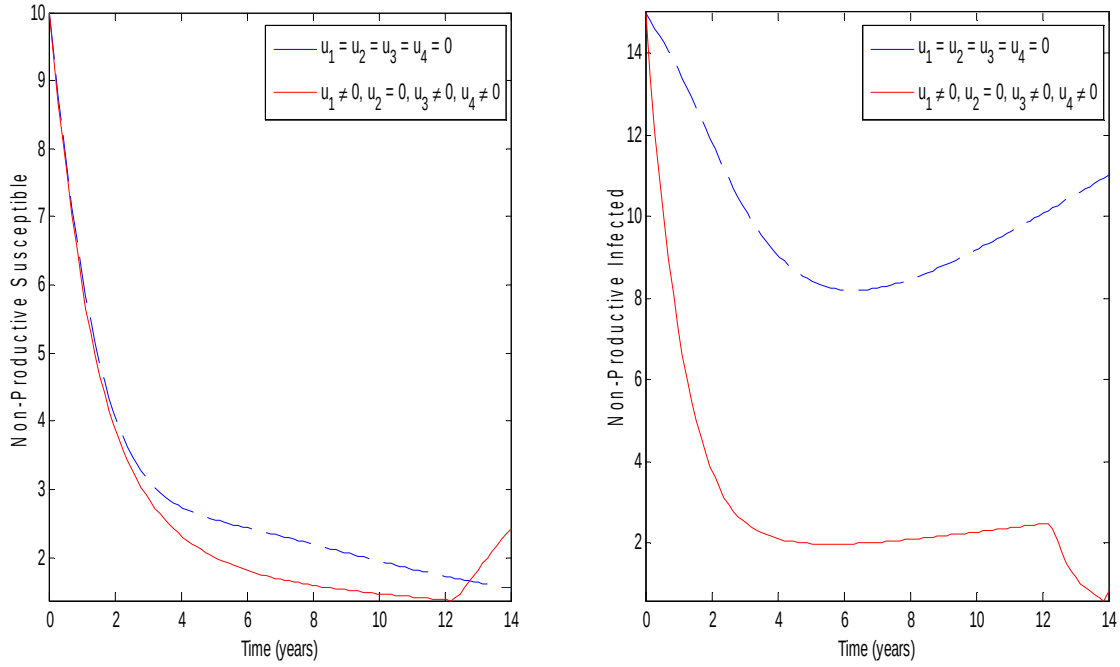



Fig 4.12 (a): Simulations showing the effect of strategy I on the non-productive

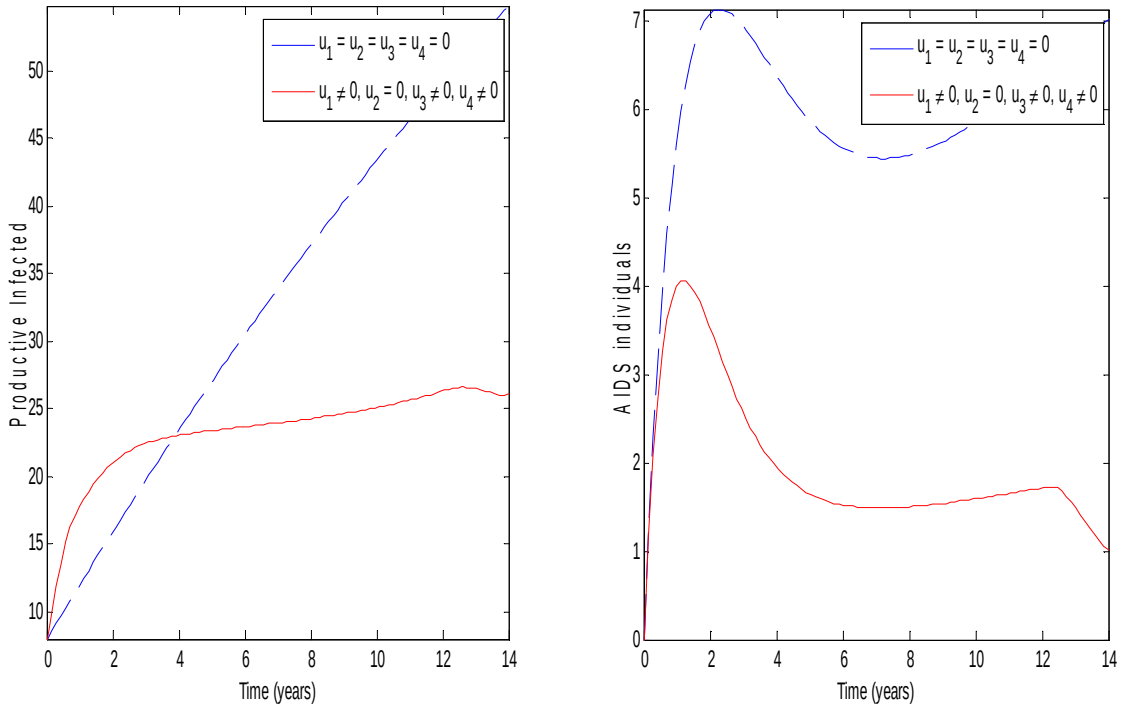



Fig 4.12 (b): Simulations showing the effect of strategy I on productive infectives and AIDS individuals

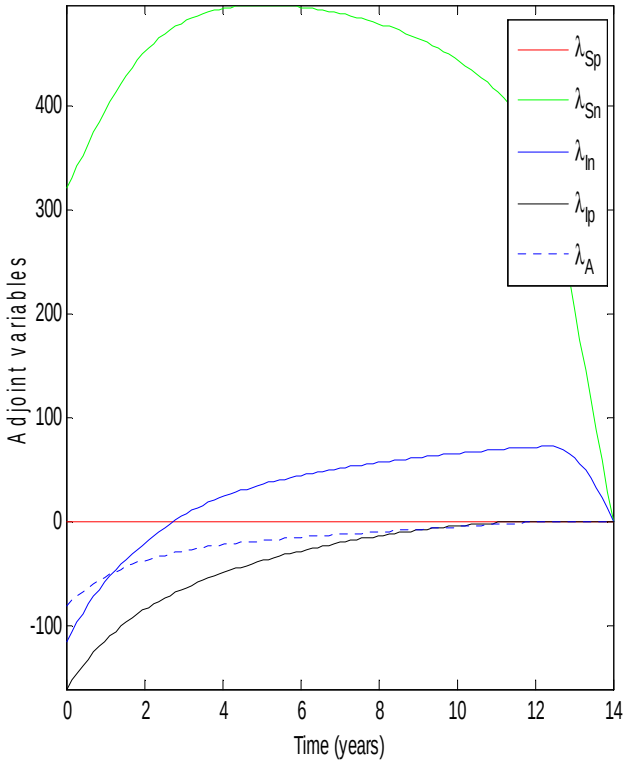



Fig 4.12 (c): Simulations showing the effect of strategy I on adjoints

Significant reductions in the non-productive infected and AIDS cases are evident. Once more, non-productive co-state variables dominate.

### 4.5.10 Strategy J

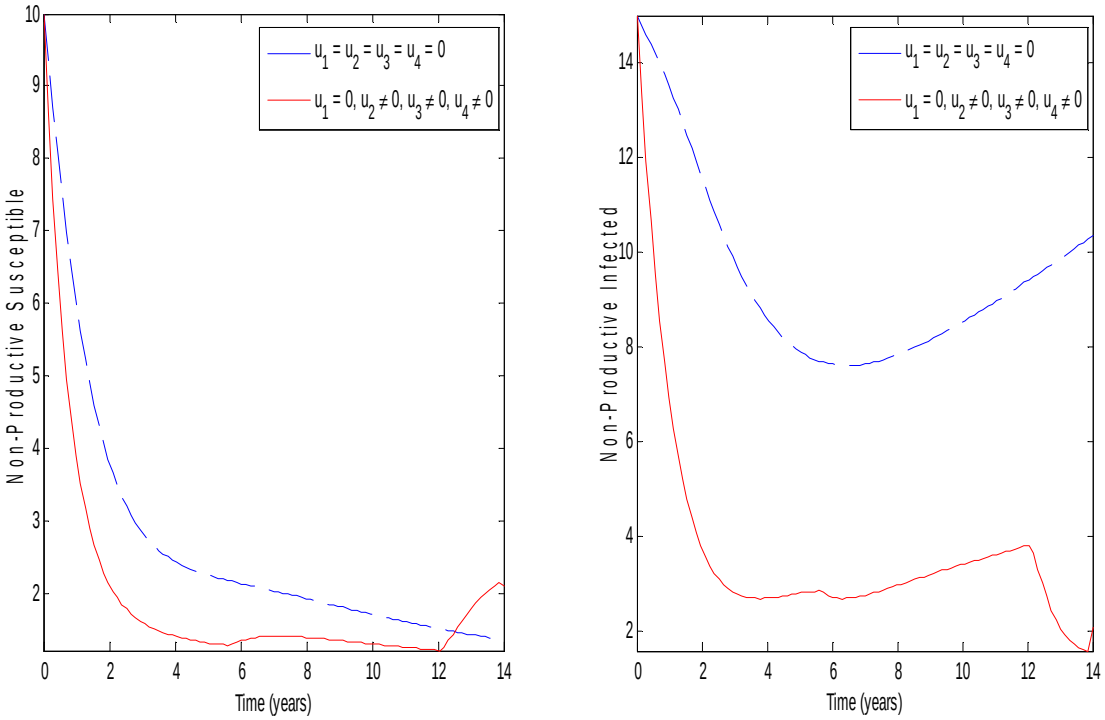



Fig 4.13 (a): Simulations showing the effect of strategy J on the non-productive

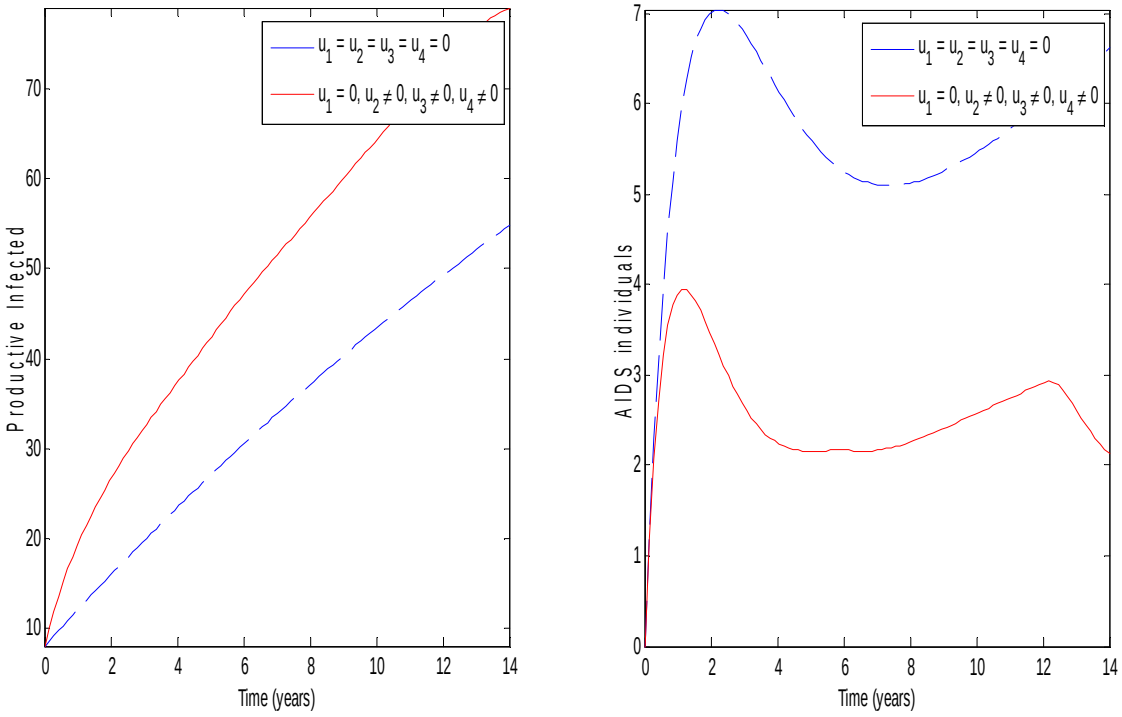



Fig 4.13 (b): Simulations showing the effect of strategy J on productive infectives and AIDS individuals

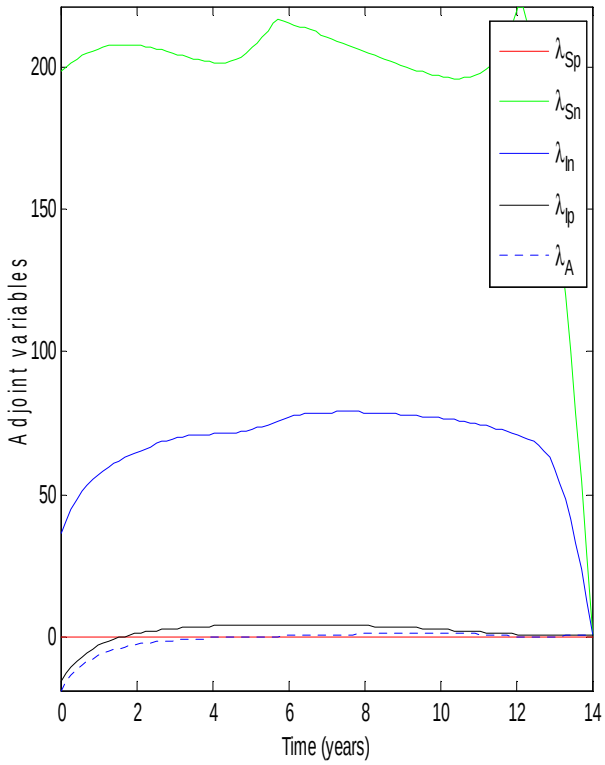



Fig 4.13 (c): Simulations showing the effect of strategy J on adjoints

Results show significant declines in the number of the non-productive infected and the AIDS population coupled with increases in the productive infected. Non-productive adjoint variables are significant.

### 4.5.11 Strategy K

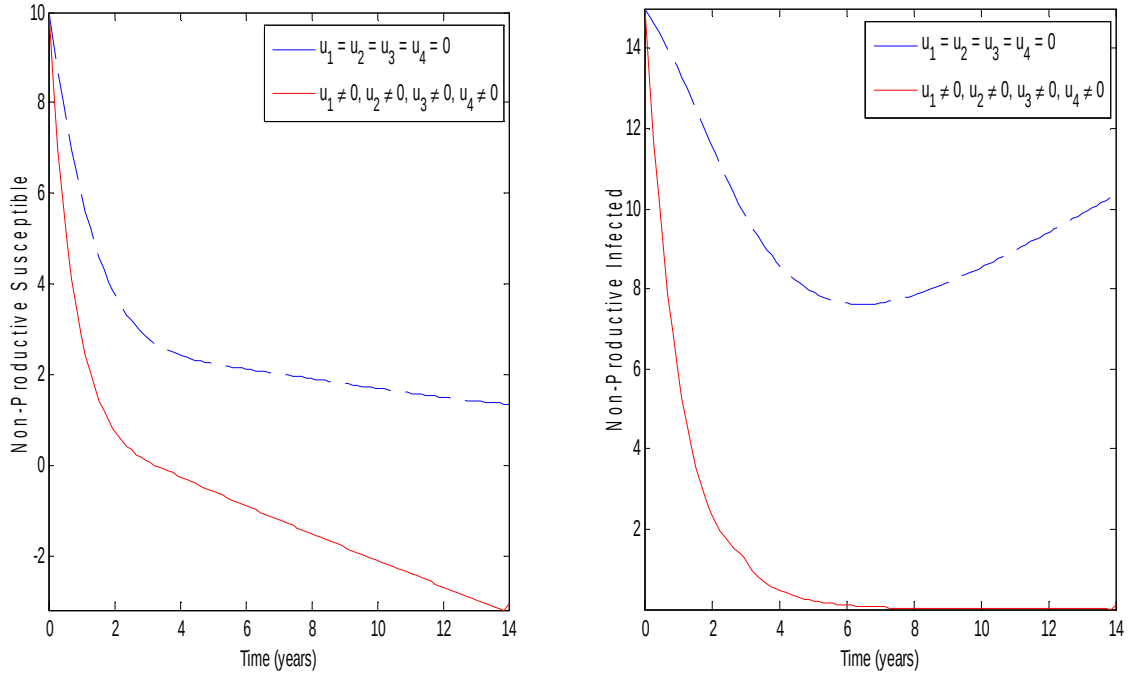



Fig 4.14 (a): Simulations showing the effect of strategy K on the non-productive

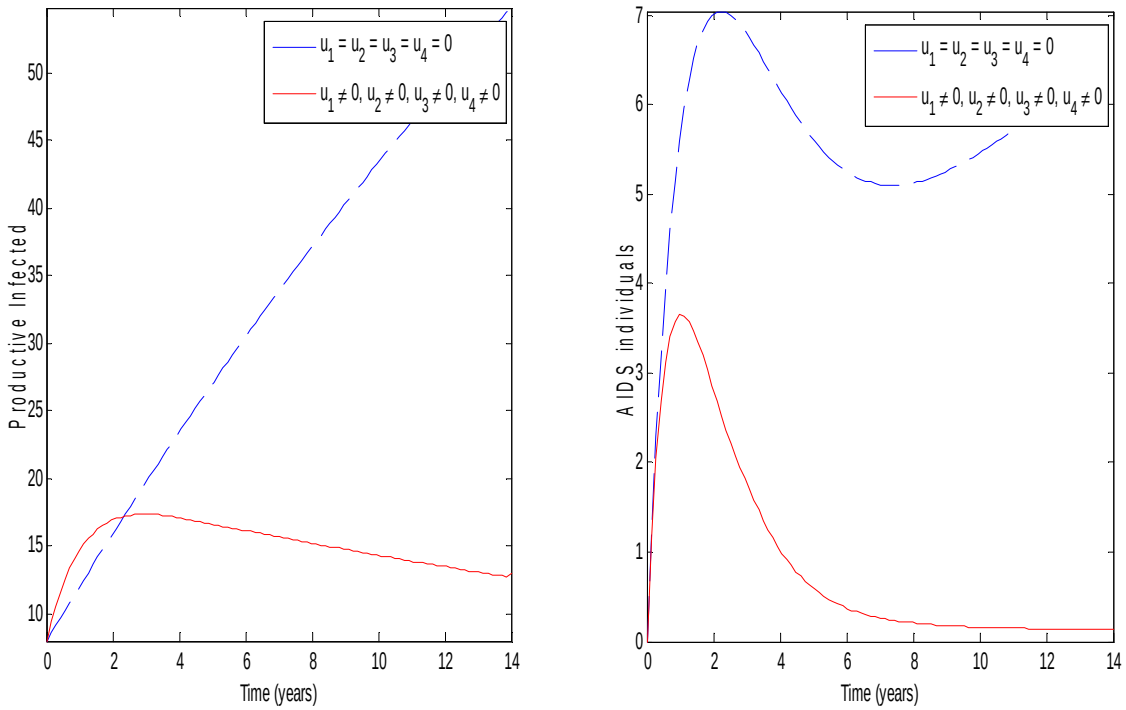



Fig 4.14 (b): Simulations showing the effect of strategy K on productive infectives and AIDS individuals

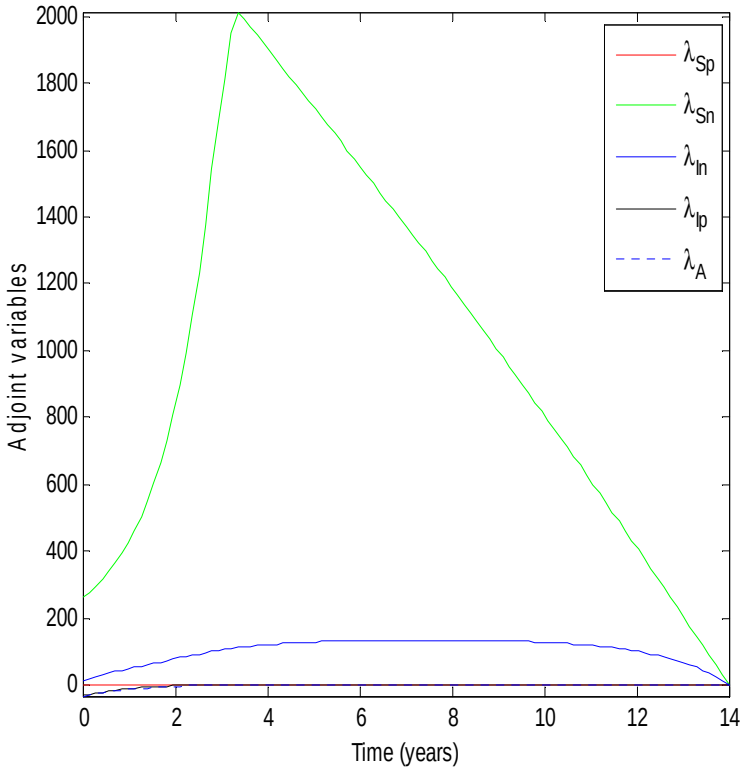



Fig 4.14 (c): Simulations showing the effect of strategy K on the adjoints

Results show significant declines in the number of the non-productive and the AIDS population coupled with increases in the productive infected. Non-productive adjoint variables are significant

From the numerical simulations, Figs. 4.4 – 4.14, we can see that one cannot easily conclude which control strategy gives optimal results. Most of the strategies produce almost similar patterns and effects, therefore we need to further ascertain which of these four most effective strategies is the most cost-effective and efficient. In the next section, we carry out the cost-effectiveness analysis.

### 4.6 Cost Effective Analysis

To quantify the cost-effectiveness of the control measures, we examine the cost effectiveness ratios of the strategies, so that we can draw our conclusions. We assume that the costs are directly proportional to the number of controls deployed. This assumption is based on the understanding that the primary goal of providing preventive measures, enlightenment programs and treatment of infective individuals is to reduce infection. We obtained the total number of cases averted by calculating the difference between the non-productive individuals without control and the non-productive individuals with control according to the specified strategies making use of the following parameter values: $\beta = 0.0344$, $\mu = 0.02$, $\psi = 1$, $\gamma = 0.01$, $\eta = 0.4$, $\alpha = 0.61$, $\delta = 0.53$, $\sigma = 0.72$, $\rho = 0.02$, $\tau = 0.75$, $Q = 20$, $\pi_1 = 0.1$, $\pi_2 = 0.05$, $\pi_3 = 0.25$, $T = 14$, $n = 210, m = 90$, $b_1 = 55$,$b_2 = 150$, $b_3 = 35$ and $b_4 = 75$and initial state variables $S_p(0) = 800$, $S_n(0) = 40, I_n(0) = 45$, $I_p(0) = 30$ and $A(0) = 0$ to illustrate the effect of different optimal control strategies on the spread of HIV/AIDS in a population.

The cases averted and the costs of implementation for all the strategies are as tabled below:

| Strategy | Cases Averted | Costs |
|---|---|---|
| A | 989 | 112 530 |
| B | 724 | 80 486 |
| C | 801 | 131 910 |
| D | 473 | 40 891 |
| E | 612 | 36 811 |
| F | 590 | 36 931 |
| G | 1 120 | 89 903 |
| H | 1 159 | 98 024 |
| I | 739 | 32 272 |
| J | 656 | 37 020 |
| K | 1 165 | 188 350 |

Table 4.1: Cases averted and associated costs for intervention strategies

For the purpose of our study, we consider the incremental cost-effectiveness ratios (ICER). Based on the model simulation results, we conduct the analysis by ranking the strategies in order of increasing effectiveness.

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| D | 473 | 40 891 | 86.45 |
| F | 590 | 36 931 | -33.85 |

The ICER is calculated as follows:

$$ICER(D) = \frac{40\,891}{473} = 86.45$$

$$ICER(F) = \frac{36\,931 - 40\,891}{590 - 473} = -33.85$$

The comparison between strategies D and F shows a cost saving of $33.85 per additional case averted for strategy F over strategy D. The negative ICER for strategy F indicates that strategy D is “dominated”. That is, strategy D is more costly and less effective than strategy F. Therefore, strategy D is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies F and E

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| F | 590 | 36 931 | 62.49 |
| E | 612 | 36 811 | -5.45 |

The comparison between strategies F and E shows a cost saving of $5.45 per additional case averted for strategy E over strategy F. Similarly, the negative ICER for strategy E indicates that strategy F is “dominated”. That is, strategy F is more costly and less effective than strategy E. Therefore, strategy F is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies E and J

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| E | 612 | 36 811 | 60.15 |
| J | 656 | 37 020 | 4.75 |

The comparison between strategies E and J shows an additional cost of $4.75 per additional case averted for strategy J over strategy E. The positive ICER for strategy J indicates that strategy E “dominates”. That is, strategy J is more costly than strategy E. Therefore, strategy J is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies E and B

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| E | 612 | 36 811 | 60.15 |
| B | 724 | 80 486 | 389.96 |

The comparison between strategies E and B shows an additional cost of $389.96 per additional case averted for strategy B over strategy E. The positive ICER for strategy B indicates that strategy E “strongly dominates”. That is, strategy B is more costly than strategy E. Therefore, strategy B is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies E and I

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| E | 612 | 36 811 | 60.15 |
| I | 739 | 32 272 | -35.74 |

The comparison between strategies E and I shows a cost saving of $35.74 per additional case averted for strategy I over strategy E. Similarly, the negative ICER for strategy I indicates that strategy E is “dominated”. That is, strategy E is more costly and less effective than strategy I. Therefore, strategy E is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies I and C

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| I | 739 | 32 272 | 43.67 |
| C | 801 | 131 910 | 1 607.07 |

The comparison between strategies I and C shows an additional cost of $1 607.07 per additional case averted for strategy C over strategy I. Similarly, the positive ICER for strategy C indicates that strategy I “strongly dominates”. That is, strategy C is more costly than strategy I. Therefore, strategy C is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies I and A

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| I | 739 | 32 272 | 43.67 |
| A | 989 | 112 530 | 321.03 |

The comparison between strategies I and A shows an additional cost of $321.03 per additional case averted for strategy A over strategy I. Similarly, the positive ICER for strategy A indicates that strategy I “strongly dominates”. That is, strategy A is more costly than strategy I. Therefore, strategy A is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies I and G

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| I | 739 | 32 272 | 43.67 |
| G | 1 120 | 89 903 | 151.26 |

The comparison between strategies I and G shows an additional cost of $151.26 per additional case averted for strategy G over strategy I. Similarly, the positive ICER for strategy G indicates that strategy I “strongly dominates”. That is, strategy G is more costly than strategy I. Therefore, strategy G is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies I and H

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| I | 739 | 32 272 | 43.67 |
| H | 1 159 | 98 024 | 156.55 |

The comparison between strategies I and H shows an additional cost of $156.55 per additional case averted for strategy H over strategy I. Similarly, the positive ICER for strategy H indicates that strategy I “strongly dominates”. That is, strategy H is more costly than strategy I. Therefore, strategy H is excluded from the set of alternatives so it does not consume limited resources.

We recalculate ICERs for strategies I and K

| Strategy | Cases Averted | Costs | ICER |
|---|---|---|---|
| I | 739 | 32 272 | 43.67 |
| K | 1 165 | 188 350 | 366.38 |

The comparison between strategies I and K shows an additional cost of $366.38 per additional case averted for strategy K over strategy I. Similarly, the positive ICER for strategy K indicates that strategy I “strongly dominates”. That is, strategy K is more costly than strategy I. Therefore, strategy K is excluded from the set of alternatives so it does not consume limited resources.

With this result, we conclude that strategy I (combination of screening, prevention and treatment measures) has the least ICER and therefore is the most cost-effective strategy.

### 4.7 Conclusion

In this chapter, we derived and analyzed a deterministic model for the transmission of HIV/AIDS disease to examine the recruitment effect of the following: non-productive susceptible individuals, non-productive infected individuals, productive susceptible individuals and productive infected individuals into an organizational workforce. We carried out the stability analysis of the equilibrium and found that the model exhibits backward and Hopf bifurcation under different scenarios respectively. Furthermore, we also performed optimal control analysis of the model by using Pontryagin's Maximum Principle to derive and analyze the conditions for optimal control of the disease with effective screening, prevention, HAART treatment regime and enlightenment of non-productive susceptible and infectious individuals. The results suggest that the effective recruitment strategy must include screening and prevention for the susceptible and treatment of the infected towards reducing the non-productivity of employees thereby ensuring productivity. However, deliberate budgetary provisions need to be put in place so that enlightenment/monitoring of employees may be included observing as it has a significant impact in reducing the non-productivity of employees (labour force) in the presence of HIV/AIDS.

# CHAPTER FIVE

# IMPACT OF OPTIMAL CONTROL ON THE TREATMENT OF HIV/AIDS AND SCREENING OF UNAWARE INFECTIVES

*In this chapter, we study the impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives on the transmission dynamics of the disease in a homogeneous population with constant immigration of susceptibles. We modify the model of [113] by incorporating use of condoms, treatment and screening of unaware infectives as time dependent control measures. We first consider the constant control case, calculate the basic reproduction number and investigate the existence and stability of equilibria. The model is found to exhibit trans-critical bifurcation. Formulating the appropriate optimal control problem, we investigate the necessary conditions for the disease control in order to determine the role of unaware infectives in the spread of HIV/AIDS. We found that unawareness by infectives has a great cost impact on the community. Secondly, we investigate the impact of a combination of these strategies in the control of HIV/AIDS. The costs associated with these strategies are investigated through the formulation of the costs function problem. We then used a Maximum Principle to solve the resulting optimal control problem and determine optimal strategies for controlling the spread of the disease. Carrying out cost-effectiveness analysis, we found that the most cost-effective strategy is the combination of all the control strategies.*

## 5.1 Introduction

Infection with the human immunodeficiency virus (HIV) is generally fatal if left untreated and uncontrolled. Worldwide, HIV is now the major cause of years of potential life lost and the most common cause of death attributed to an infectious disease. Just in 2005 alone, 3.1 million people died from AIDS (acquired immunodeficiency syndrome) globally, and 4.9 million people became infected with HIV, leading to 40.3 million people living with the virus across the world [116].

Almost three decades since the first HIV case was reported, it has not been possible to effectively control the spread of the disease, so the need to re-examine the control approach is desirable. The difficulties arise from lack of adequate medical facilities and personnel, unwillingness of people to strictly adhere to preventive measures. To successfully control the spread of HIV, susceptible individuals must be protected from being infected and the already infected individuals must be rendered less infectious. However, at present there is no cure for the disease and so various strategies to control its spread in order to protect susceptible individuals are very important. The other major challenge is that in most parts of Sub-Saharan Africa and Asia, many people who are infected are not even aware of the disease

due to illiteracy, scarcity of medical equipment and other factors and those who are aware of their infection do not always take necessary precautions deliberately while having sexual interactions [20, 14].

The present modes of controlling the disease include abstinence, use of condoms, treatment of infections and blood screening. It is important to note that to effectively control the spread of HIV, the susceptible individuals must be protected from being infected and the already infected individuals must be adequately informed of available measures in ensuring that they do not spread the disease any further. However, at present there is no cure for the disease and hence examining various strategies for controlling the spread of HIV/AIDS in order to minimize the disease prevalence is very important.

This work is motivated by the large number of cases of unaware infectives reported worldwide, which has now become a global concern. For example in France, it was found that roughly 40 000 of the estimated 106 000 - 134 000 HIV infected people throughout the entire country remain unaware of their infection [128]. Findings from a survey carried out by US Center for Disease Control and Prevention in 2008 on HIV among men who have sex with other men indicated that among the 8 153 men tested, 1 562 tested positive for HIV and of these 1 562, the number of persons that were unaware of their infection was 680, amounting to about 44% of the infected cases. The study further revealed that the proportion of those who were unaware of their infection was highest among blacks and lowest among whites and this also decreased with increased education and income [20]. Also, the United Kingdom Health Protection Agency reported that over 22 000 people were unaware that they have the HIV virus [10]. According to the Taipei Times report of 2004, 90% of the Chinese HIV-AIDS cases were unaware of their infection status. Despite the effort, the total number of people tested for HIV globally remains low with an estimated 90% of people who are HIV-infected worldwide unaware of their status [122]. The challenge posed by the number of cases of unaware infectives calls for urgent need for a better understanding of the important parameters in the disease transmission, and to develop effective and optimal strategies for prevention and control of the spread of HIV/AIDS disease.

Having pointed out that the screening of unaware infectives has substantial effect on the spread of AIDS [113], it is therefore desirable to promote the voluntary or random screening of infectives who do not know that they are infected by targeting especially the high risk groups. After being detected, the individual may be motivated to change their behaviour and to take preventive measures like condom use so that the risk of spreading the infection is reduced. To the best of our knowledge, very little attention has been paid to models to study this aspect which may be helpful in reducing the spread of the disease.

The model we consider in this chapter is an extension of the model in [113] by the inclusion of time dependent control parameters (use of condoms, screening of unaware infectives and treatment of infectives) with the assumption that the AIDS individuals can also transmit the disease recklessly. In this study, we analyze and apply optimal control to the improved model and determine the possible impact of condom use, optimal screening of unaware infectives and treatment on the spread of HIV. We carry out a detailed qualitative optimal control analysis of the resulting model and we find the necessary conditions for optimal control of the disease using Pontryagin's Maximum Principle in order to determine optimal strategies for controlling the spread of the disease.

Our main goals are: firstly, to investigate the model under the assumption that the control measures are constants (condom use, screening of unaware infectives and treatment of infectives) and secondly, to set up an optimal control problem relative to the model. In order to do this, we use the following control parameters, use of condoms ($u_1$), screening of unaware infectives ($\theta$) and treatment rate of HIV individuals ($\pi$) as time dependent variables. Hence, we investigate the role of optimal screening of unaware infectives through medical screening, educational preventive campaigns and treatment of HIV and AIDS on the spread of HIV/AIDS.

### 5.2 Model Formulation

The model sub-divides the total human population at time $t$, denoted by $N(t)$, into the following sub-populations of susceptible individuals $S(t)$, individuals who have contracted the infection but are not aware that they are infected $I_1(t)$, HIV positive individuals who know that they are infected $I_2(t)$ and that of the AIDS population $A(t)$, so that

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

The susceptibles are individuals that have not contracted the infection but may be infected through sexual contacts with either type of infectives. The infected population who are aware of their status comprise of individuals that have contracted the virus and are known to be infected after being detected by a screening method (i.e. by way of medical screening or otherwise). We use standard incidence to model the disease transmission.

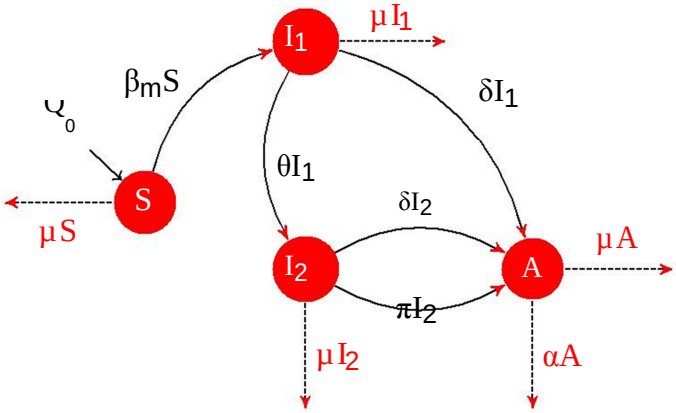



Fig 5.1: Flow diagram for HIV/AIDS disease transmission model

Here $\beta_i$ $(i = 1, 2, 3)$ are the per capita contact rates for susceptible individuals with unaware infectives, infectives that are already aware of their status and AIDS individuals respectively. Control $u_1 \in [0,1]$ is the successful use of condoms by susceptibles to protect themselves. The variable $\theta$ measures the rate at which unaware infectives are detected by a screening method to become aware infectives, the variable $\pi$ measures the progression rate at which the already aware infective individuals on treatment move to the $A$ class in each time period. Here, $\delta$ is the rate by which both types of infectives not on treatment develop AIDS $(\pi < \delta)$. $\mu$ is the natural mortality rate unrelated to HIV/AIDS disease and $\alpha$ is the AIDS related death rate. It is assumed that the rate of contact of susceptibles with AIDS individuals is much less than that with aware infectives which in turn is much less than that with unaware infectives $(\beta_3 \ll \beta_2 \ll \beta_1)$. This is so because on becoming aware of their infection, the infected persons may choose to use preventive measures and change their behavior and thus may contribute little in spreading the infection. However, in some cases, the aware infectives may also contribute to spreading of infection due to lack of taking necessary precautions or the decreased fear of the disease. We assume also that individuals in the $A$ class are less sexually active.

The resulting system of equations is as shown below:

$$\left.\begin{aligned} \frac{dS}{dt} &= Q_0 - \beta_m S - \mu S \\ \frac{dI_1}{dt} &= \beta_m S - (\theta + \delta + \mu) I_1 \\ \frac{dI_2}{dt} &= \theta I_1 - (\delta + \mu + \pi) I_2 \\ \frac{dA}{dt} &= \delta I_1 + \delta I_2 - (\alpha + \mu) A \end{aligned}\right\} \qquad (5.1)$$

where

$$\beta_m = \frac{(1-u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N} \tag{5.2}$$

The terms $c_i$ $(i = 1, 2, 3)$ are the number of sexual partners of susceptibles with individuals from the $I_1$, $I_2$ and $A$ classes respectively in each time period.

### 5.3 Mathematical Analysis of the HIV/AIDS model

#### 5.3.1 Positivity and Boundedness of Solutions

For the HIV/AIDS transmission model to be epidemiologically meaningful, it is important to prove that all solutions with non-negative initial data will remain non-negative for all time.

***Theorem 5.1***: *If* $S(0)$, $I_1(0)$, $I_2(0)$ and $A(0)$ *are non-negative, then so are* $S(t)$, $I_1(t)$, $I_2(t)$ and $A(t)$ *for all time* $t > 0$. *Moreover,*

$$\lim_{t \to \infty} N(t) \leq \frac{Q_0}{\mu}. \tag{5.3}$$

*Furthermore, if* $N(0) \leq \frac{Q_0}{\mu}$, *then* $N(t) \leq \frac{Q_0}{\mu}$ .

The feasible region for the system is therefore given by

$$D = D_1 \subset \mathbb{R}_+^4 \tag{5.4}$$

where

$$D_1 = \left\{(S, I_1, I_2, A) \in \mathbb{R}_+^4 : S + I_1 + I_2 + A \leq \frac{Q_0}{\mu}\right\}. \tag{5.5}$$

$D$ is positively invariant (see [113]) .

#### 5.3.2 Stability of the Disease-Free Equilibrium

The disease-free equilibrium (DFE) of the HIV/AIDS model (5.1) exists only when $u_1$ and $\theta$ are constant, it is given by

$$\xi_0 = (S^0, I_1^0, I_2^0, A^0) = \left(\frac{Q_0}{\mu}, 0, 0, 0\right).$$

The basic reproduction number of the model with condom use and screening of unaware infective individuals is given by

$$R = \frac{(1-u_1)\{\beta_1 c_1(\delta+\mu+\pi)(\alpha+\mu)+\beta_2 c_2\theta(\alpha+\mu)+\beta_3 c_3[\theta(\delta+\mu)+\delta(\delta+\mu+\pi)]\}}{(\theta+\delta+\mu)(\delta+\mu+\pi)(\alpha+\mu)} \quad (5.6)$$

while the basic reproduction number of the model without condom use and screening of unaware infective individuals is then given by

$$R_0 = \frac{\beta_1 c_1(\delta+\mu+\pi)(\alpha+\mu)+\beta_3 c_3\delta(\delta+\mu+\pi)}{(\delta+\mu)(\delta+\mu+\pi)(\alpha+\mu)} \quad (5.7)$$

We use Theorem 2 of van den Driessche and Watmough [120] to establish the following result:

***Proposition 5.1***: *The DFE of the HIV/AIDS model is locally asymptotically stable if* $R < 1$ *and unstable if* $R > 1$.

The basic reproduction number, $R$, measures the average number of new infections generated by a single infected individual in a completely susceptible population. Thus, Proposition 5.1 implies that the disease can be eliminated from the community when $R < 1$. Next, we calculate the endemic steady states.

### 5.3.3 Existence of Endemic Equilibrium

Solving the HIV/AIDS model equations in terms of $\beta_m^*$, we calculate the endemic equilibrium point to obtain

$$\left.\begin{aligned} S^* &= \frac{Q_0}{\beta_m^*+\mu} \\ I_1^* &= \frac{\beta_m^* Q_0}{(\beta_m^*+\mu)(\theta+\delta+\mu)} \\ I_2^* &= \frac{\theta\beta_m^* Q_0}{(\beta_m^*+\mu)(\theta+\delta+\mu)(\delta+\mu+\pi)} \\ A^* &= \frac{\beta_m^* Q_0[\delta(\delta+\mu+\pi)+\theta(\delta+\pi)]}{(\beta_m^*+\mu)(\theta+\delta+\mu)(\delta+\mu+\pi)(\alpha+\mu)} \\ N^* &= \frac{Q_0-\alpha A^*}{\mu} \end{aligned}\right\} \quad (5.8)$$

By solving the model system (5.1) at equilibrium we obtain $\beta_m^* = 0$ (which corresponds to the DFE) or

$$B_1\beta_m^* + B_0 = 0 \tag{5.9}$$

where

$$\left.\begin{aligned} B_1 &= (\delta+\alpha+\mu)(\theta+\delta+\mu)+\pi(\alpha+\delta+\theta+\mu) \\ B_0 &= (\alpha+\mu)(\pi+\delta+\mu)(\delta+\theta+\mu)(1-R) \end{aligned}\right\} \tag{5.10}$$

$B_1 > 0$ and $B_0 \geq 0$ whenever $R < 1$ or $\theta > \theta^*$, so that $\beta_m^* = -\frac{B_0}{B_1} \leq 0$. Therefore the HIV/AIDS model has no endemic equilibrium whenever $\theta > \theta^*$ where the critical screening coverage $\theta^*$ is given by

$$\theta^* = \frac{(\pi+\delta+\mu)\big((1-u_1)c_3\delta\beta_3 + (\alpha+\mu)(1-u_1)c_1\beta_1 - (\alpha+\mu)(\delta+\mu)\big)}{(1-u_1)\big((\alpha+\mu)c_2\beta_2 + (\pi+\delta)c_3\beta_3\big) - (\alpha+\mu)(\pi+\delta+\mu)}$$

***Proposition 5.2****: The HIV model has a unique endemic equilibrium if and only if* $R > 1$*.*

The above result suggests the impossibility of backward bifurcation in the HIV/AIDS model, since no endemic equilibrium exists when $R < 1$ or $\theta > \theta^*$.

### 5.4 Modified Model

We now modify the model (5.1) by sub-dividing the total human population at any time $t$, denoted by $N(t)$, into the following sub-populations: susceptible individuals ($S(t)$), unaware infective individuals ($I_1(t)$), screened and already aware infective individuals who are not yet on treatment ($I_2(t)$), HIV positive individuals who are on treatment ($H(t)$) and that of the AIDS population ($A(t)$), so that

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

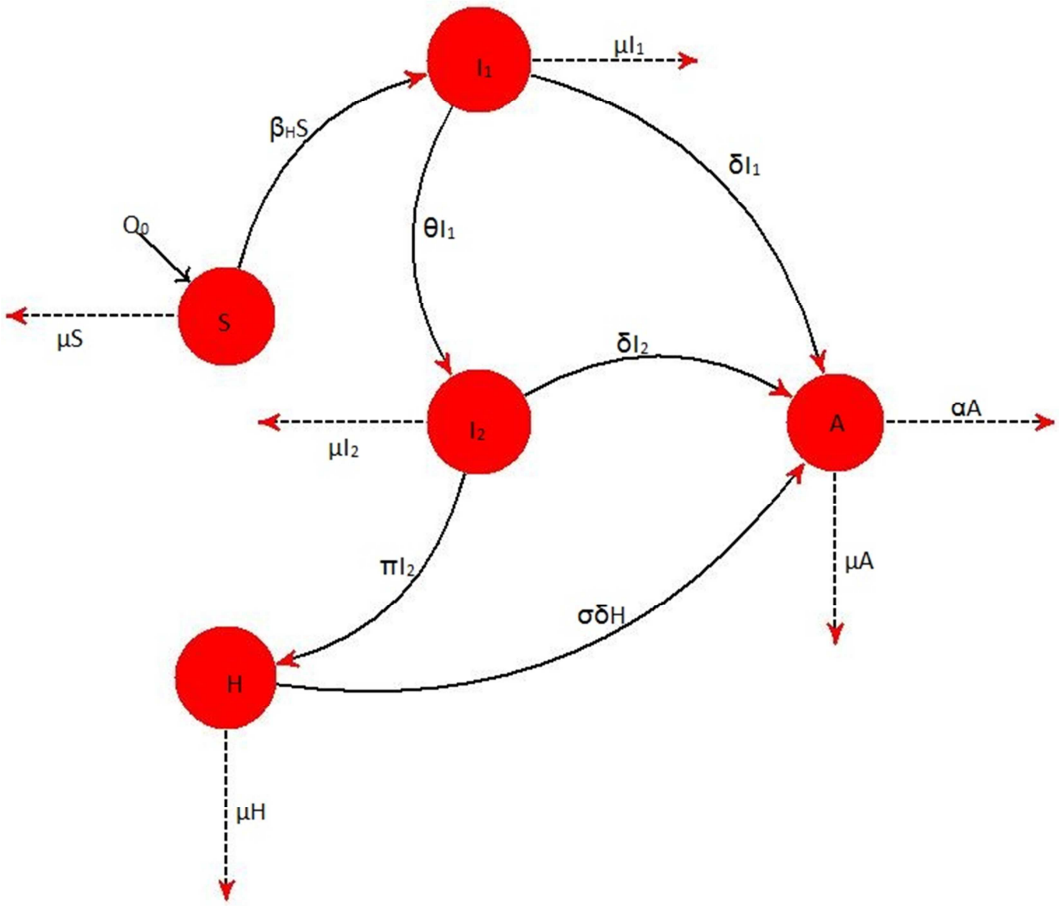



Fig 5.2: Flow diagram for the modified HIV/AIDS disease transmission model

The resulting system of equations is the following:

$$\left.\begin{aligned}
\frac{dS}{dt} &= Q_0 - \beta_H S - \mu S \\
\frac{dI_1}{dt} &= \beta_H S - (\theta + \delta + \mu) I_1 \\
\frac{dI_2}{dt} &= \theta I_1 - (\delta + \mu + \pi) I_2 \\
\frac{dH}{dt} &= \pi I_2 - (\sigma\delta + \mu) H \\
\frac{dA}{dt} &= \delta I_1 + \delta I_2 + \sigma\delta H - (\alpha + \mu) A
\end{aligned}\right\} \qquad (5.11)$$

Here

$$\beta_H = \frac{(1-u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A + \beta_h c_h H)}{N} \qquad (5.12)$$

where $\beta_h$ is the per capita contact rate for susceptible individuals with HIV positive individuals on treatment and $c_h$ is the number of sexual partners of susceptibles with HIV positive individuals on treatment. Here $\sigma\delta$ is the rate of progression of HIV positive individuals on treatment to the AIDS population, where $\sigma$ is the modification parameter due to treatment.

### 5.4.1 Stability of the Disease-Free Equilibrium

The disease-free equilibrium (DFE) of the modified model (5.11) also exists only when $u_1$ and $\theta$ are constant and it is given by

$$\xi_0 = (S^0, I_1^0, I_2^0, H^0, A^0) = \left(\frac{Q_0}{\mu}, 0, 0, 0, 0\right)$$

The basic reproduction number for the modified model with condom use and screening of unaware infective individuals is given by the linear stability of $\xi_0$ established by using the next generation operator method [119]. The matrices $F$ and $V$, for the new infection terms and the remaining transfer terms are, respectively, given by

$$F = (1-u_1)\begin{bmatrix} \varphi_1 & \varphi_2 & \varphi_h & \varphi_3 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

where

$\varphi_i = \frac{c_i\beta_i}{N}$, $i = 1, 2, 3, h$ and

$$V = \begin{bmatrix} \theta+\delta+\mu & 0 & 0 & 0 \\ -\theta & \delta+\pi+\mu & 0 & 0 \\ -\pi & 0 & \sigma\delta+\mu & 0 \\ -\delta & -\delta & -\sigma\delta & \alpha+\mu \end{bmatrix}$$

It follows that the reproduction number is given by

$$R_h = \frac{(1-u_1)\{\Omega + \delta[(\theta+\delta+\mu)+\pi(\sigma(\delta+\theta)+\mu)]\beta_3 c_3 + \pi\theta(\alpha+\mu)\beta_h c_h\}}{(\theta+\delta+\mu)(\delta+\mu+\pi)(\alpha+\mu)(\sigma\delta+\mu)} \tag{5.13}$$

$$\Omega = (\sigma\delta+\mu)\{(\delta+\mu+\pi)(\alpha+\mu)\beta_1 c_1 + \theta(\alpha+\mu)\beta_2 c_2\}$$

while the basic reproduction number of the modified model without condom use and screening of unaware infective individuals is then given by

$$R_{0h} = \frac{(\alpha+\mu)\beta_1 c_1 + \delta\beta_3 c_3}{(\theta+\delta+\mu)(\alpha+\mu)} \tag{5.14}$$

We use Theorem 2 of [119] to establish the following result. The critical condom use coverage $u_1^0$ that would be required to contain HIV/AIDS can be calculated by setting $R_h = 1$, to obtain

$$u_1^0 = 1 - \frac{1}{R_{0h}}$$

$R_h \geq 1$ if and only if $u_1 \leq u_1^0$. Hence when $u_1 < u_1^0$, then the disease will persist, but when $u_1 > u_1^0$, the disease may be eradicated if DFE is globally asymptotically stable.

***Proposition 5.3***: *The DFE of the modified HIV/AIDS model is locally asymptotically stable if* $R_h < 1$ *and unstable if* $R_h > 1$.

Thus, Proposition 5.3 also implies that the disease can be eliminated from the community when $R_h < 1$. Next we calculate the endemic steady states of the modified model.

### 5.4.2 Existence of Endemic Equilibrium

Solving the HIV/AIDS model equation in terms of $\beta_H^*$, we calculate the endemic equilibrium point and obtain

$$\left.\begin{aligned}
S^* &= \frac{Q_0}{\beta_H^* + \mu} \\
I_1^* &= \frac{\beta_H^* Q_0}{(\beta_H^* + \mu)(\theta + \delta + \mu)} \\
I_2^* &= \frac{\theta \beta_H^* Q_0}{(\beta_H^* + \mu)(\theta + \delta + \mu)(\delta + \mu + \pi)} \\
H^* &= \frac{\pi\theta \beta_H^* Q_0}{(\beta_H^* + \mu)(\theta + \delta + \mu)(\delta + \mu + \pi)(\sigma\delta + \mu)} \\
A^* &= \frac{\delta \beta_H^* Q_0 [(\sigma\delta + \mu)(\delta + \mu + \pi) + \pi(\mu + \sigma(\delta + \theta)]}{(\beta_H^* + \mu)(\theta + \delta + \mu)(\delta + \mu + \pi)(\alpha + \mu)(\sigma\delta + \mu)} \\
N^* &= \frac{Q_0 - \alpha A^*}{\mu}
\end{aligned}\right\} \quad (5.15)$$

By solving the modified system at equilibrium we obtain $\beta_H^* = 0$ (which corresponds to the DFE) or

$$P_1 \beta_H^* + P_0 = 0 \quad (5.16)$$

where

$$\left.\begin{aligned}
P_1 &= (\theta + \delta + \mu)(\delta + \alpha + \mu)(\sigma\delta + \mu) + \pi\{(\theta + \delta + \mu)(\sigma\delta + \mu) + \alpha(\theta + \mu + \sigma\delta)\} \\
P_0 &= (\theta + \delta + \mu)(\delta + \mu + \pi)(\alpha + \mu)(\sigma\delta + \mu)(1 - R_h)
\end{aligned}\right\} \quad (5.17)$$

It is clear that $P_1 > 0$ and $P_0 \geq 0$ whenever $R_h < 1$ or $\theta > \theta_h^*$, so that $\beta_H^* = -\frac{P_0}{P_1} \leq 0$. Therefore the modified HIV/AIDS model has no endemic equilibrium whenever $\theta > \theta_h^*$ where the critical screening coverage is given by

$$\theta_h^* = \frac{(\delta+\mu+\pi)(\sigma\delta+\mu)\{\delta(1-u_1)\beta_3 c_3 + (\alpha+\mu)(1-u_1)\beta_1 c_1 - (\alpha+\mu)(\delta+\mu)\}}{(1-u_1)\{(\alpha+\mu)(\sigma\delta+\mu)\beta_2 c_2 + \delta\big(\mu+\sigma(\pi+\delta)\big)\beta_3 c_3 + \pi(\alpha+\mu)\beta_h c_h\} - \chi}$$

where $\chi = (\delta+\mu+\pi)(\sigma\delta+\mu)(\alpha+\mu)$.

***Theorem 5.2****: The DFE is locally asymptotically stable if $R_h < 1$ and unstable if $R_h > 1$.*

***Proof:***. We evaluate the Jacobian matrix of the model at the disease-free equilibrium and we obtain

$$J_s = \begin{bmatrix} -G-\mu & 0 & 0 & J_1 & J_2 \\ 0 & -B+J_3 & J_4 & -J_1 & -J_2 \\ 0 & \theta & -C & 0 & 0 \\ 0 & 0 & \pi & -D & 0 \\ 0 & \delta & \delta & \delta\sigma & -E \end{bmatrix}$$

where

$B = \theta + \delta + \mu$, $C = \delta + \pi + \mu$, $D = \sigma\delta + \mu$, $E = \alpha + \mu$,

$$G = \frac{(N^* - S^*)(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2}$$

$$J_1 = \frac{Sc_h\beta_h(1-u_1)}{N} + \frac{S(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2}$$

$$J_2 = \frac{Sc_3\beta_3(1-u_1)}{N} + \frac{S(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2}$$

$$J_3 = \frac{Sc_1\beta_1(1-u_1)}{N} + \frac{S(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2}$$

$$J_4 = \frac{Sc_2\beta_2(1-u_1)}{N} + \frac{S(1-u_1)(c_1\beta_1 I_1^* + c_2\beta_2 I_2^* + c_3\beta_3 A^* + c_h\beta_h H^*)}{N^2}$$

Then, the local stability of the DFE is determined by the eigenvalues of the matrix

$$J_s = \begin{bmatrix} -\mu & 0 & 0 & -\vartheta_h & -\vartheta_3 \\ 0 & -B + \vartheta_1 & \vartheta_2 & \vartheta_h & \vartheta_3 \\ 0 & \theta & -C & 0 & 0 \\ 0 & 0 & \pi & -D & 0 \\ 0 & \delta & \delta & \delta\sigma & -E \end{bmatrix}$$

where

$\vartheta_1 = c_1\beta_1(1-u_1)$, $\vartheta_2 = c_2\beta_2(1-u_1)$, $\vartheta_3 = c_3\beta_3(1-u_1)$ and $\vartheta_h = c_h\beta_h(1-u_1)$.

It is clear that the first column has diagonal entry, so, this diagonal entry $-\mu$ is an eigenvalue. Hence, removing this column and the row corresponding to it, the Jacobian matrix ($J_s$) is then reduced to the following:

$$J_{as} = \begin{bmatrix} -B + \vartheta_1 & \vartheta_2 & \vartheta_h & \vartheta_3 \\ \theta & -C & 0 & 0 \\ 0 & \pi & -D & 0 \\ \delta & \delta & \delta\sigma & -E \end{bmatrix}$$

We therefore calculate the eigenvalues of the reduced matrix. Solving the eigenvalues of $J_{as}$, requires that

$$det(J_{as} - \Lambda) = 0$$

which leads to the following characteristic equation:

$\Lambda^4 + a_1\Lambda^3 + a_2\Lambda^2 + a_3\Lambda + a_4 = 0.$

Here

$a_1 = (B + C + D + E) - (1 - u_1)c_1\beta_1$

$$a_2 = BC + BD + CD + (B + C + D)E - (1 - u_1)\big((C + D + E)c_1\beta_1 + \theta c_2\beta_2 + \delta c_3\beta_3\big) \quad (5.18)$$

$$\begin{aligned} a_3 = {} & BCD + CDE + BE(D + C) \\ & - (1 - u_1)\Big(\big(DE + C(D + E)\big)c_1\beta_1 + (D + E)\theta c_2\beta_2 + \delta(C + D + \theta)c_3\beta_3 \\ & + \pi\theta c_h\beta_h\Big) \end{aligned}$$

$$\begin{aligned} a_4 = {} & BCDE - (1 - u_1)(CDEc_1\beta_1 + DE\theta c_2\beta_2 + \delta(D(C + \theta) + \pi\theta\sigma)c_3\beta_3 + E\pi\theta c_h\beta_h) \\ & = BCDE(1 - R_H) \end{aligned}$$

By applying the Routh–Hurwitz stability conditions, we establish the following for the characteristic equation: $a_1 > 0$, $a_2 > 0$, $a_3 > 0$, $a_4 > 0$ and

$$H_1 = a_1 > 0,\ H_2 = \begin{vmatrix} a_1 & 1 \\ a_3 & a_2 \end{vmatrix} > 0,\ H_3 = \begin{vmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & a_4 & a_3 \end{vmatrix} > 0,\ H_4 = \begin{vmatrix} a_1 & 1 & 0 & 0 \\ a_3 & a_2 & a_1 & 1 \\ 0 & a_4 & a_3 & a_2 \\ 0 & 0 & 0 & a_4 \end{vmatrix} > 0$$

The steady state is stable (that is, $Re < 0$) for all $\lambda$ if and only if $\det H_j \geq 0$ for $j = 1, 2, 3, 4$. Furthermore, we only need to prove that $H_2 > 0$, $H_3 > 0$, $H_4 > 0$.

$H_2 = a_1 a_2 - a_3$, $H_3 = a_3(a_1 a_2 - a_3) - a_4 {a_1}^2$ and $H_4 = a_4 H_3$

Using Mathematica 5.0, we found that

$$\begin{aligned} H_2 = {} & (C + D)(C + E)(D + E) + B^2(C + D + E) + B(C + D + E)^2 \\ & + c_1\beta_1(1 - u_1)^2\big((C + D + E)c_1\beta_1 + \theta c_2\beta_2 + \delta c_3\beta_3\big) \\ & - (1 - u_1)\big((2B + C + D + E)(C + D + E)c_1\beta_1 + \theta(B + C)c_2\beta_2 \\ & + \delta(B + E - \theta)c_3\beta_3 - \pi\theta c_h\beta_h\big) \end{aligned} \tag{5.19}$$

$H_3 = a_3 H_2 - a_4 {a_1}^2$

$H_4 = a_4 H_3$

Consequently, having $H_2 > 0$, $H_3 > 0$ and $H_4 > 0$ shows that the eigenvalues of the Jacobian matrix, $J_{as}$, all have negative real parts whenever $R_h < 1$. But if $R_h > 1$, then clearly we can see that $a_4 < 0$. Moreover, having $a_1 > 0$, $a_2 > 0$, $a_3 > 0$ and $a_4 > 0$ shows that not all the roots of the polynomial will have negative real parts. This means that whenever $R_h > 1$, the disease-free equilibrium point is unstable.

***Proposition 5.4***: *The modified HIV model has a unique endemic equilibrium if and only if* $R_h > 1$.

The above result suggests the impossibility of backward bifurcation in the HIV/AIDS model, since no endemic equilibrium exists when $R_h < 1$ or $\theta > \theta_h^*$. We now investigate the global stability property of the endemic equilibrium of the modified HIV/AIDS model for a special case.

### 5.4.3 Global Stability of the Endemic Equilibrium for $\alpha = 0$

Considering the model (5.11) with $\alpha = 0$, we get

$$\left.\begin{aligned}
\frac{dS}{dt} &= Q_0 - \beta_H S - \mu S \\
\frac{dI_1}{dt} &= \beta_H S - (\theta + \delta + \mu) I_1 \\
\frac{dI_2}{dt} &= \theta I_1 - (\delta + \mu + \pi) I_2 \\
\frac{dH}{dt} &= \pi I_2 - (\sigma\delta + \mu) H \\
\frac{dA}{dt} &= \delta I_1 + \delta I_2 + \sigma\delta H - \mu A
\end{aligned}\right\} \tag{5.20}$$

It is obvious from (5.15) that there is no change in the endemic equilibrium. Let,

$$D_2 = \{(S, I_1, I_2, H, A) \in \mathbb{R}_+^5 : I_1 = I_2 = H = A = 0\} \text{ and } R_{h1} = R_h|_{\alpha=0} \tag{5.21}$$

We then claim the following:

***Theorem 5.3***: *The endemic equilibrium of the HIV model (5.20) is globally asymptotically stable (GAS) in* $D_1\, D_2$ *whenever* $R_{h1} > 1$.

***Proof***: It can be shown, as for the case of Proposition 5.2, that the unique endemic equilibrium for this special case exists only if $R_{h1} > 1$. Further, $N = \frac{Q_0}{\mu}$ as $t \to \infty$. Thus, using $S = \frac{Q_0}{\mu} - I_1 - I_2 - H - A$ and substituting in (5.20) gives the following limiting system:

$$\left.\begin{aligned}
\frac{dI_1}{dt} &= \beta_H \left(\frac{Q_0}{\mu} - I_1 - I_2 - H - A\right) - (\theta + \delta + \mu) I_1 \\
\frac{dI_2}{dt} &= \theta I_1 - (\delta + \mu + \pi) I_2 \\
\frac{dH}{dt} &= \pi I_2 - (\sigma\delta + \mu) H \\
\frac{dA}{dt} &= \delta I_1 + \delta I_2 + \sigma\delta H - \mu A
\end{aligned}\right\} \tag{5.22}$$

Using the Dulacs multiplier $\frac{1}{I_1 A}$, (see [89]), it follows that

$$\frac{\partial}{\partial A}\left[\frac{\delta}{I_2 HA} + \frac{\delta}{I_1 HA} + \frac{\delta\sigma}{I_1 I_2 A} - \frac{\mu}{I_1 I_2 H}\right] + \frac{\partial}{\partial I_1}\left[\frac{(1-u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A + \beta_h c_h H)}{I_1 I_2 HAQ_0/\mu}\left(\frac{Q_0}{\mu} - I_1 - I_2 - H - A\right) - \frac{(\theta+\delta+\mu)}{I_2 HA}\right]$$

$$= -\frac{Q_0AH+\delta I_2H}{{I_2}^2H^2A^2} - \frac{\delta I_2H}{{I_1}^2H^2A^2} - \frac{\sigma\delta I_1I_2}{{I_1}^2{I_2}^2A^2} - \frac{c_1\beta_1\mu}{Q_0I_2HA} - \frac{c_2\beta_2}{{I_1}^2AH}\left(1-\frac{(I_2+H+A)}{Q_0/\mu}\right) - \frac{c_3\beta_3}{{I_1}^2I_2H}\left(1-\frac{(I_2+H+A)}{Q_0/\mu}\right) - \frac{c_h\beta_h}{{I_1}^2I_2A}\left(1-\frac{(I_2+H+A)}{Q_0/\mu}\right) < 0, \quad (5.23)$$

since $I_2 + H + A < Q_0/\mu$ in $D_1$. Hence, by Dulacs criterion, there are no periodic orbits in $D_1\ D_2$. Since $D_1$ is positively invariant and the endemic equilibrium exists whenever $R_{h1} > 1$, then it follows from the Poincare–Bendixson Theorem [98] that all solutions of the limiting system originating in $D_1$ remain in $D_1$ for all $t$. Further, the absence of periodic orbits in $D_1$ implies that the unique endemic equilibrium of the special case of the HIV/AIDS model is GAS whenever $R_{h1} > 1$. ■

The HIV/AIDS model has a locally-asymptotically stable disease-free equilibrium whenever $R_h \leq 1$, and a unique endemic equilibrium whenever $R_h > 1$. The unique endemic equilibrium is globally-asymptotically stable for the case $\alpha = 0$ if $R_{h1} > 1$. In Fig 5.3 we show the contour plot of the reproductive number $R_h$ as a function of $\theta$ and $\pi$ when there is condom use and the case without condom use.

In the next section, we apply the optimal control method using Pontryagin's Maximum Principle to determine the necessary conditions for the optimal control of screening of unaware infectives and use of condom on the spread of HIV.

### 5.5 Optimal Control Analysis

From the previous section, we show that effective control of the disease may be too costly when constant controls are considered as it requires treatment at higher levels for all time. For effective control to be achievable in a finite time, we need to consider time dependent controls. When the control is time dependent the disease-free equilibrium no longer exists [95]. We then proceed by applying Pontryagin's Maximum Principle to determine the conditions for effective control in finite time. We introduce into the modified model, condom use control ($u_1$), screening control of unaware infectives ($u_2$) and treatment control ($u_3$) as time dependent controls to curtail the spread of HIV/AIDS. The modified model (5.11) becomes

$$\left.\begin{aligned}
\frac{dS}{dt} &= Q_0 - \beta_H S - \mu S \\
\frac{dI_1}{dt} &= \beta_H S - (u_2\theta + \delta + \mu)I_1 \\
\frac{dI_2}{dt} &= u_2\theta I_1 - (\delta + \mu + u_3\pi)I_2 \\
\frac{dH}{dt} &= u_3\pi I_2 - (\sigma\delta + \mu)H \\
\frac{dA}{dt} &= \delta I_1 + \delta I_2 + \sigma\delta H - (\alpha + \mu)A
\end{aligned}\right\} \quad (5.24)$$

with

$$\beta_H = \frac{(1-u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A + \beta_h c_h H)}{N} \quad (5.25)$$

where $0 \leq u_1 \leq 1$ models the control on condom use, $0 \leq u_2 \leq 1$ is the control on screening of unaware infectives and $0 \leq u_3 \leq 1$ is the control on treatment. To investigate the optimal level of efforts that would be needed to control the disease, we give the objective functional $J$, which is to minimize the number of unaware infectives and the cost of applying the controls $u_1$, $u_2$ and $u_3$.

$$J = \int_0^T (aI_1 + b_1 u_1^2 + b_2 u_2^2 + b_3 u_3^2)dt, \quad (5.26)$$

where $a$, $b_1$, $b_2$, and $b_3$ are positive weights. The terms $b_1 u_1^2$, $b_2 u_2^2$ and $b_3 u_3^2$ are the costs associated with condom use, screening of unaware infectives and treatment respectively. We choose a quadractic cost on the controls, in keeping with what is in other literature on epidemics control [1, 37, 56, 74, 67].

With the given objective functional, $J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3)$, our goal is to minimize the number of unaware infectives $I_1$, while minimizing the cost of controls $\mathrm{u}_1(\mathrm{t})$, $\mathrm{u}_2(\mathrm{t})$ and $\mathrm{u}_3(\mathrm{t})$. We thus seek an optimal control triple $(u_1^*, u_2^*, u_3^*)$ such that

$$J(u_1^*, u_2^*, u_3^*) = \min\{J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3): (\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3) \in \mathcal{U}\}, \quad (5.27)$$

where

$$\mathcal{U} = \{(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3): \mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3 \text{ are measurable with } 0 \leq \mathrm{u}_\mathrm{i} \leq 1, \mathrm{i} = 1, 2, 3 \text{ for } \mathrm{t} \in [0, \mathrm{T}]\}$$

is the control set. The necessary conditions that an optimal control problem must satisfy come from Pontryagin's Maximum Principle [103]. We use this principle to convert the

problem of minimization of the objective functional (5.26) coupled with the state variable system (5.24) into a problem of minimizing point-wise a Hamiltonian, $H_m$, with respect to the controls $\mathrm{u}_1$, $\mathrm{u}_2$ and $\mathrm{u}_3$. The Hamiltonian is defined by

$$H_m = aI_1 + b_1u_1^2 + b_2u_2^2 + b_3u_3^2 + \lambda_S\frac{dS}{dt} + \lambda_{I_1}\frac{dI_1}{dt} + \lambda_{I_2}\frac{dI_2}{dt} + \lambda_H\frac{dH}{dt} + \lambda_A\frac{dA}{dt}, \qquad (5.28)$$

where the $\lambda_S$, $\lambda_{I_1}$, $\lambda_{I_2}$, $\lambda_H$ and $\lambda_A$ are the adjoint variables or co-state variables. By applying Pontryagin's Maximum Principle [103] and the existence result for the optimal control from [39], we obtain

***Proposition 5.5***: *For the optimal control triple* $(u_1^*, u_2^*, u_3^*)$ *that minimizes* $J(\mathrm{u}_1, \mathrm{u}_2, \mathrm{u}_3)$ *over* $\mathcal{U}$, *there exist adjoint variables* $\lambda_S$, $\lambda_{I_1}$, $\lambda_{I_2}$, $\lambda_H$ and $\lambda_A$ *satisfying:*

### *(i) Adjoint System*

$$\left.\begin{aligned}
\frac{d\lambda_S}{dt} &= (1-u_1)\left(\frac{\beta_1c_1I_1+\beta_2c_2I_2+\beta_3c_3A+\beta_hc_hH}{N} - \frac{K_S}{N^2}\right)(\lambda_S - \lambda_{I_1}) + \mu\lambda_S \\
\frac{d\lambda_{I_1}}{dt} &= -a + (1-u_1)\left(\frac{\beta_1c_1S}{N} - \frac{K_S}{N^2}\right)(\lambda_S - \lambda_{I_1}) + (u_2\theta + \delta + \mu)\lambda_{I_1} - u_2\theta\lambda_{I_2} - \delta\lambda_A \\
\frac{d\lambda_{I_2}}{dt} &= (1-u_1)\left(\frac{\beta_2c_2S}{N} - \frac{K_S}{N^2}\right)(\lambda_S - \lambda_{I_1}) + (u_3\pi + \delta + \mu)\lambda_{I_2} - u_3\pi\lambda_H - \delta\lambda_A \\
\frac{d\lambda_H}{dt} &= (1-u_1)\left(\frac{\beta_hc_hS}{N} - \frac{K_S}{N^2}\right)(\lambda_S - \lambda_{I_1}) + (\sigma\delta + \mu)\lambda_H - \sigma\delta\lambda_A \\
\frac{d\lambda_A}{dt} &= (1-u_1)\left(\frac{\beta_3c_3S}{N} - \frac{K_S}{N^2}\right)(\lambda_S - \lambda_{I_1}) + (\alpha + \mu)\lambda_A
\end{aligned}\right\} \qquad (5.29)$$

*where* $K_S = S(\beta_1c_1I_1 + \beta_2c_2I_2 + \beta_3c_3A + \beta_hc_hH)$.

### *(ii) Transversality Conditions*

$$\lambda_S(T) = \lambda_{I_1}(T) = \lambda_{I_2}(T) = \lambda_H(T) = \lambda_A(T) = 0 \qquad (5.30)$$

### *(iii) Stationary Values*

$$\left.\begin{aligned}
u_1^* &= max\left(0, min\left(1, \frac{(\lambda_{I_1}-\lambda_S)S(\beta_1c_1I_1+\beta_2c_2I_2+\beta_3c_3A+\beta_hc_hH)}{2b_1}\right)\right) \\
u_2^* &= max\left(0, min\left(1, \frac{\theta(\lambda_{I_1}-\lambda_{I_2})I_1}{2b_2}\right)\right) \\
u_3^* &= max\left(0, min\left(1, \frac{\pi(\lambda_{I_2}-\lambda_H)I_2}{2b_3}\right)\right)
\end{aligned}\right\} \qquad (5.31)$$

***Proof***: Corollary 4.1 of [39] gives the existence of an optimal control due to the convexity of the integrand of $J$ with respect to $u_1$, $u_2$ and $u_3$, a priori boundedness of the state solutions, and the Lipschitz property of the state system with respect to the state variables. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control.

Due to the a priori 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 $T$. The uniqueness of the optimal control follows from the uniqueness of the optimality system, which consists of (5.29) and (5.30) with characterization (5.31). There is a restriction on the length of the time interval in order to guarantee the uniqueness of the optimality system. This smallness restriction of the length of time is due to the opposite time orientations of (5.24) and (5.29); the state problem has initial values whereas the adjoint problem has final values. This restriction is very common in control problems (see [37, 56, 74, 67, 81]). ■

### 5.6 Numerical Results and Discussion

In this section, we examine the modified deterministic HIV/AIDS model and study the effects of condom use, screening of unaware infectives and treatment on the transmission dynamics of the disease. We carry out numerical simulations and discuss results. The optimal control set is obtained by solving the optimality system, consisting of the state and adjoint systems. An iterative scheme is used for solving the optimality system. We start to solve the state equations (5.24) with a guess for the controls over the simulated time using the fourth order Runge-Kutta scheme. Because of the transversality conditions (5.30), the adjoint equations (5.29) are solved by a backward fourth order Runge-Kutta scheme using the current iteration's solutions of the state equations. Then the controls are updated by using a convex combination of the previous controls and the value from the characterizations (5.31). This process is repeated and iterations are stopped if the values of the unknowns at the previous iteration are very close to the ones at the present iteration [72].

We investigate and compare numerical results in the following scenarios (i) when control efforts on screening ($u_2$) and treatment ($u_3$) are optimized while the control on condom use ($u_1$) is set to zero (ii) when control efforts on screening ($u_2$) and condom use ($u_1$) are optimized while the treatment control ($u_3$) is set to zero (iii) when control efforts on treatment ($u_3$) and condom use ($u_1$) are optimized while the control on screening ($u_2$) is set to zero (iv) when all controls are optimized.

We assume that the weight factor, $b_1$, associated with control $u_1$ is lower than $b_2$ and $b_3$ which are associated with controls $u_2$ and $u_3$. This assumption is based on the facts that the

cost associated with $u_2$ will include the cost of screening and the cost associated with treatment, $u_3$, will include the cost of drugs, medical examinations and hospitalization. We have chosen the same set of the weight factors, $a = 800$, $b_1 = 35$, $b_2 = 55$ and $b_3 = 75$ with initial state variables $S(0) = 800$, $I_1(0) = 40$, $I_2(0) = 45$, $H(0) = 30$, and $A(0) = 0$ to illustrate the effect of different optimal control strategies on the spread of HIV/AIDS in a population.

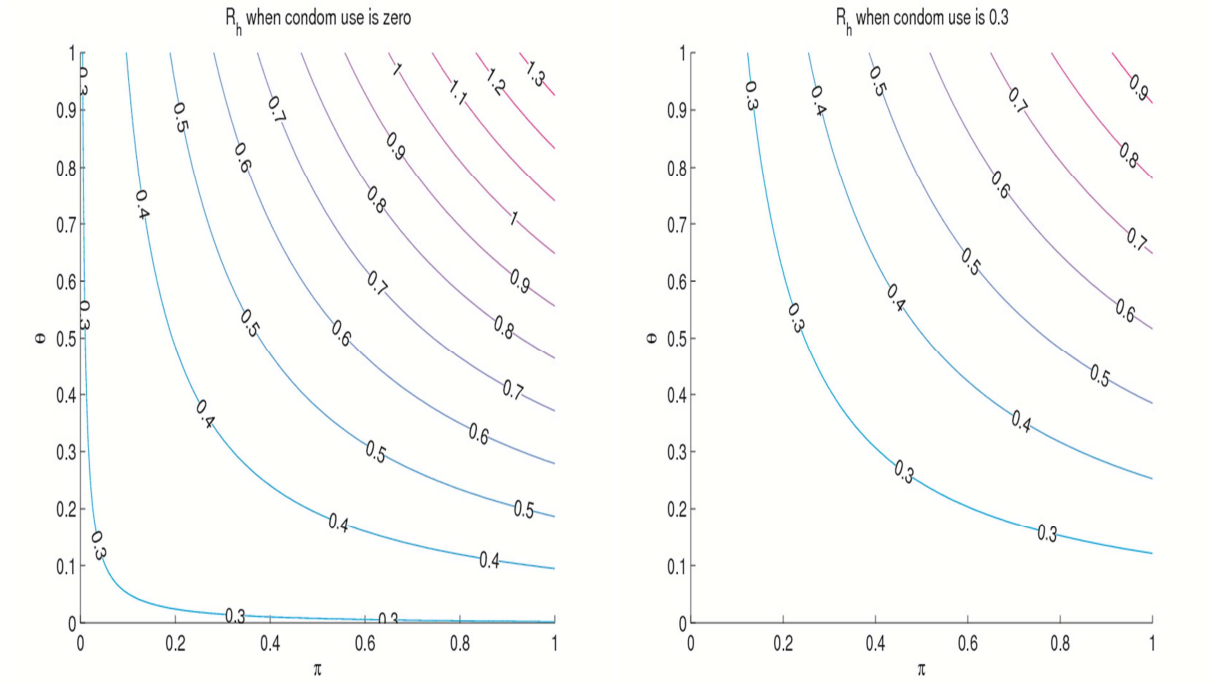



Fig 5.3: Simulation of the model (5.11) showing contour plots of the reproduction number $R_h$ as a function of $\theta$ and $\pi$ at steady state.

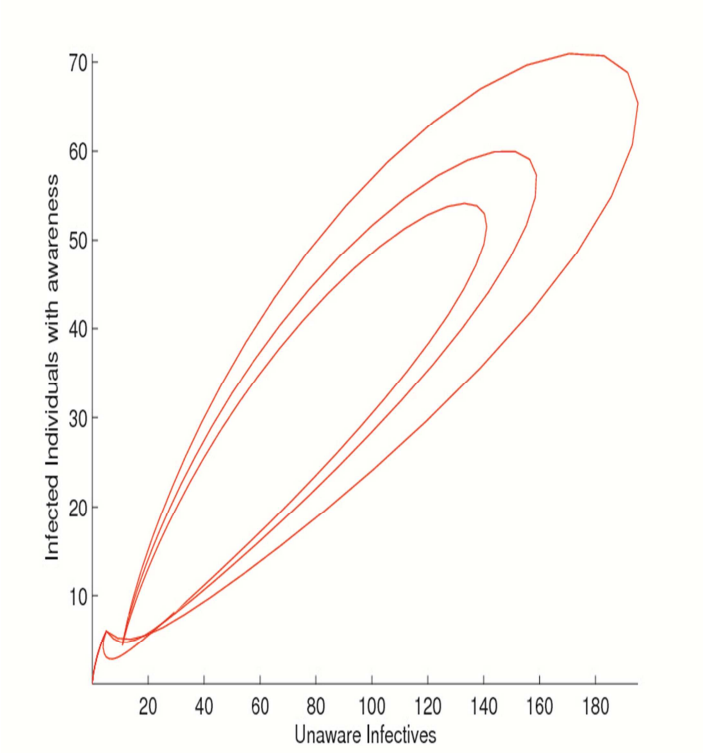



Fig 5.4: The projected $I_1 - I_2$ phase plane of the phase space

The parameter values used are as given in Table 5.1, the following:

| Parameter | Value | Reference |
|---|---|---|
| $\beta_1$ | 0.20 | Assumed |
| $\beta_2$ | 0.15 | [113] |
| $\beta_3$ | 0.12 | [113] |
| $\beta_h$ | 0.15 | Assumed |
| $\mu$ | 0.02 | [113] |
| $\alpha$ | 1.0 | [113] |
| $Q_0$ | 2 000 | [113] |
| $\delta$ | 0.1 | [113] |
| $\sigma$ | 0.002 | Assumed |
| $\theta$ | 0.02 | Assumed |
| $\pi$ | 0.6 | Assumed |

Table 5.1: HIV/AIDS model parameter values

### 5.6.1 Screening and Treatment Only

With this strategy, the screening control $u_2$ and the treatment control $u_3$ are both used to optimize the objective function $J$ while the condom use control $u_1$ is set to zero. In Fig 5.5, we observe that this control strategy results in a significant decrease in the number of unaware infectives ($I_1$) and AIDS cases ($A$) compared with the case without control. The total averted cases of unaware infectives and AIDS are 6100 and 7900 respectively. Also this control strategy results in a significant increase in the number of HIV positive individuals on treatment which stabilizes at 250. The control profiles show that $u_2$ is at the upper bound for 98 days before dropping to the lower bound at the final time and $u_3$ remains at the upper bound till the final time.

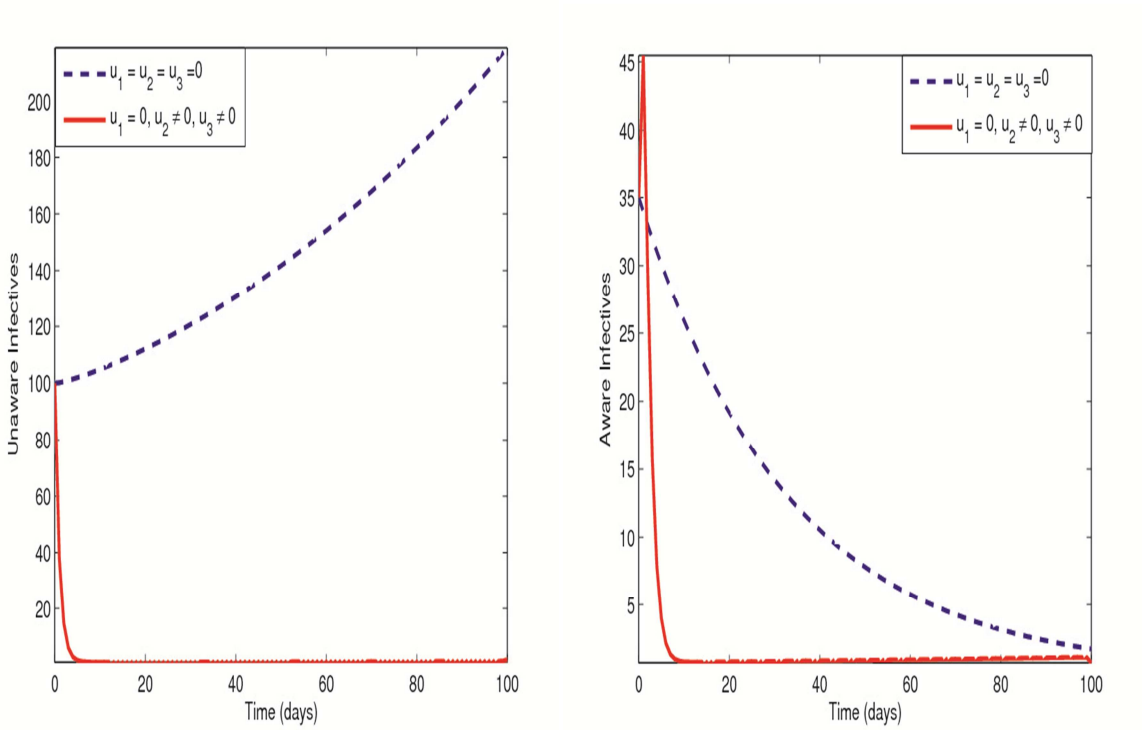



Fig 5.5 (a): Simulations showing the effect of screening and treatment on infectives

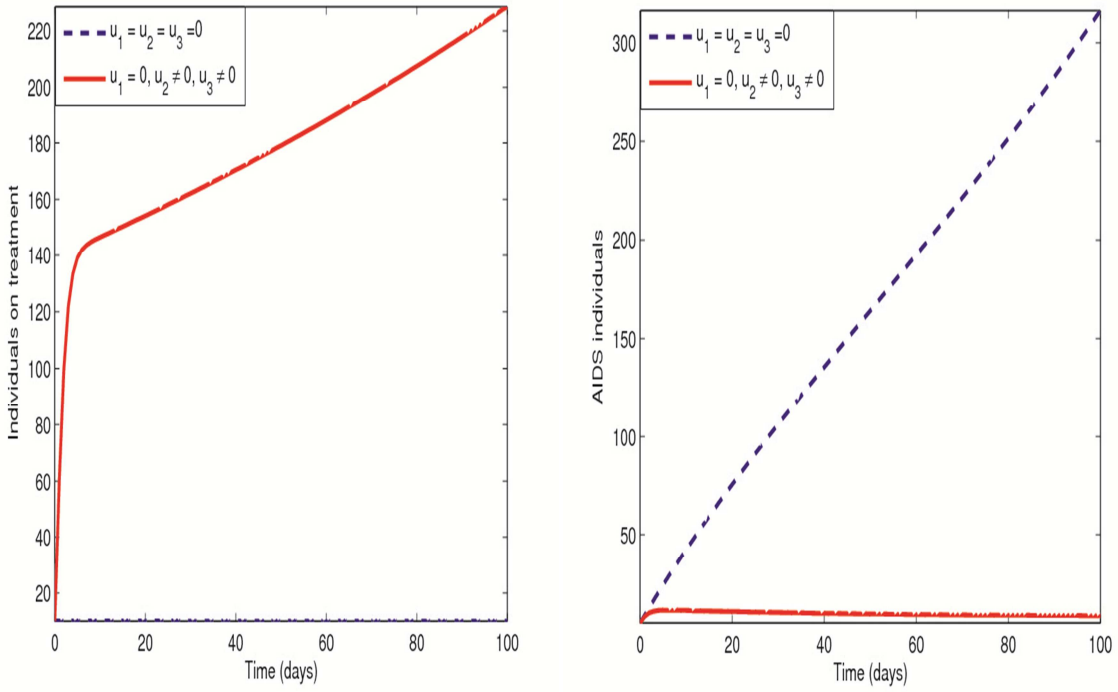



Fig 5.5 (b): Simulations showing the effect of screening and treatment on the treated and AIDS individuals

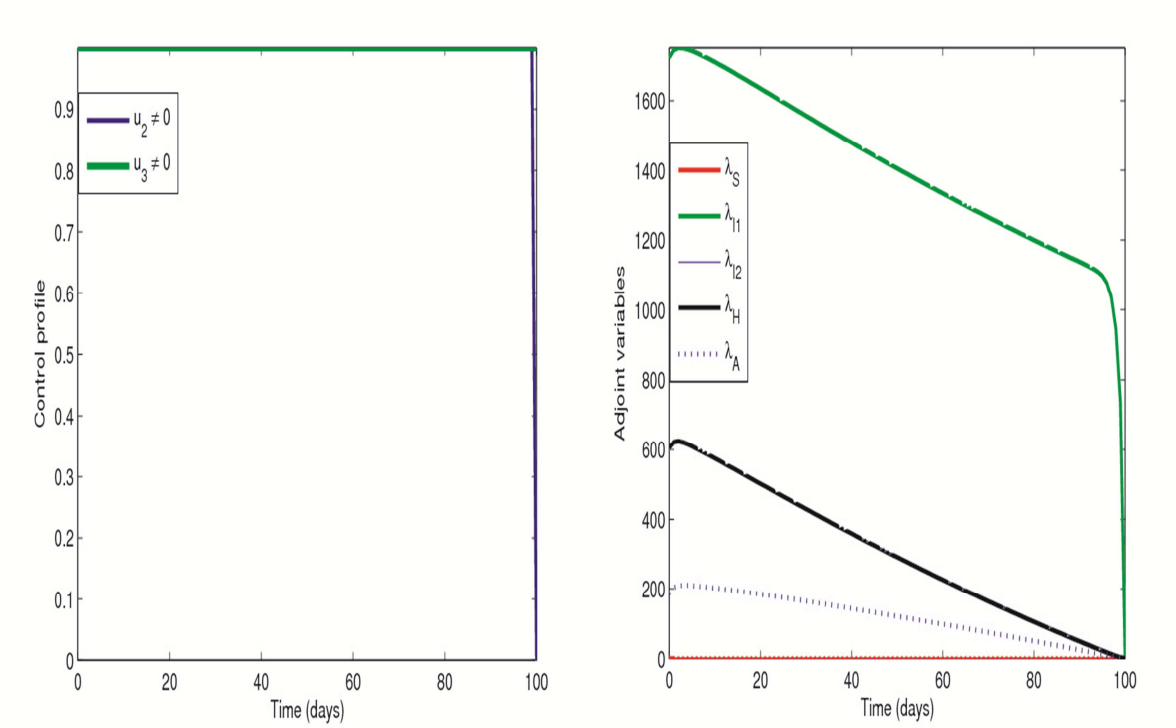



Fig 5.5 (c): Simulations showing control profiles and the effect of screening and treatment on adjoints

### 5.6.2 Screening and Condom Use Only

With this strategy, the screening control $u_2$ and the condom use control $u_1$ are both used to optimize the objective function $J$ while the treatment control $u_3$ is set to zero. In Fig 5.6, we observe that this control strategy also results in a significant decrease in the number of unaware infectives ($I_1$) and AIDS cases ($A$) compared with the case without control. Here, the total averted cases of unaware infectives and AIDS are 6100 and 7800 respectively. The control profiles show that $u_2$ is at the upper bound for 18 days before dropping to the lower bound at the final time and $u_1$ remains at the upper bound till the final time.

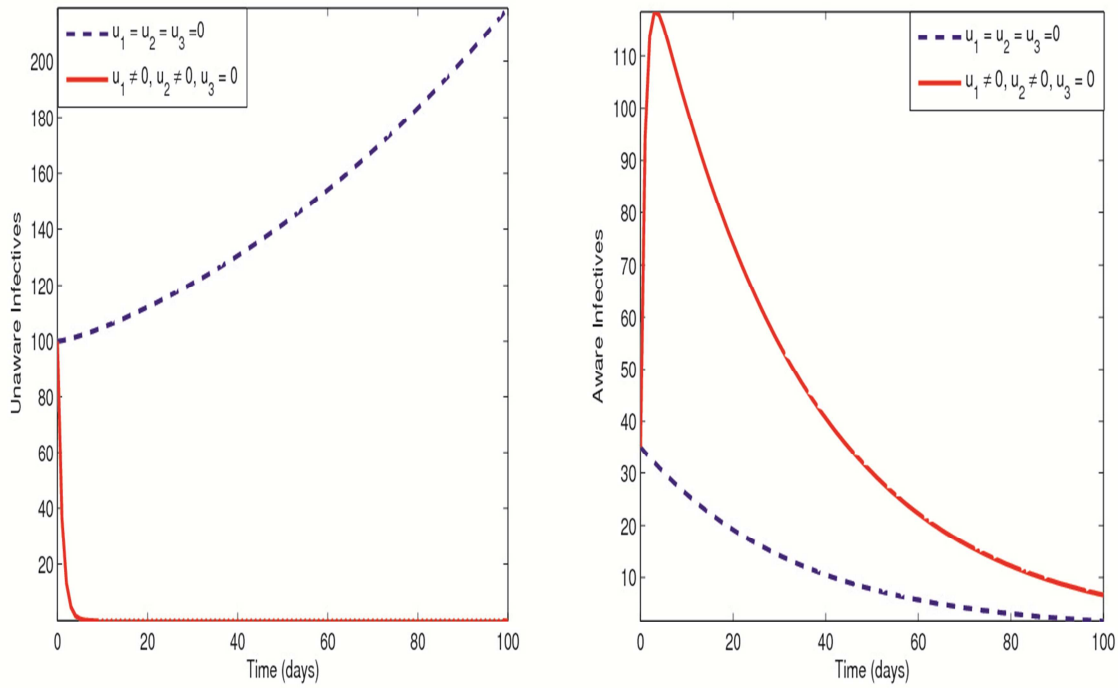



Fig 5.6 (a): Simulations showing the effect of condom use and screening on infectives

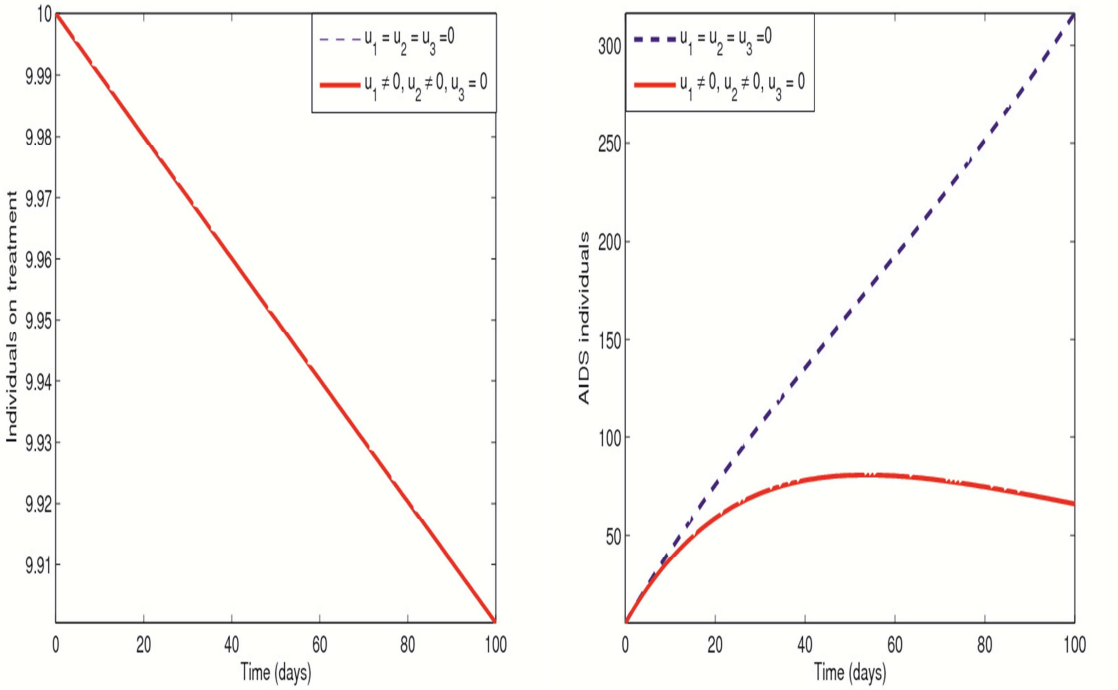



Fig 5.6 (b): Simulations showing the effect of condom use and screening on individuals on the treated and AIDS individuals

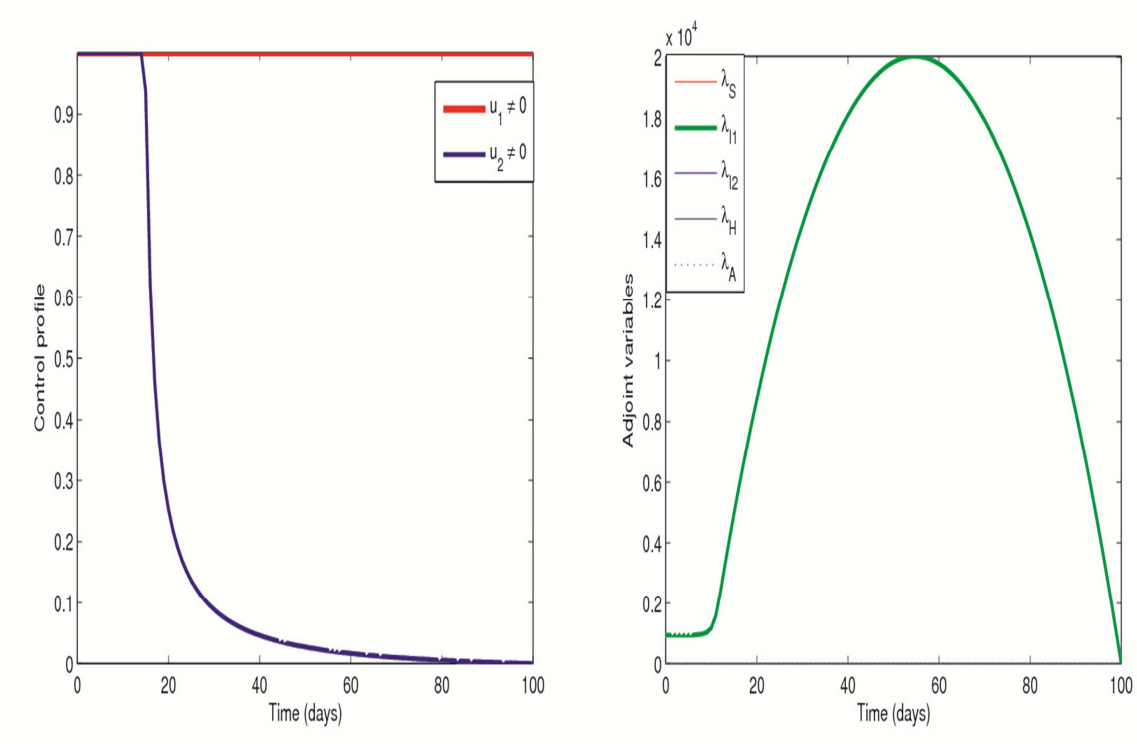



Fig 5.6 (c): Simulations showing control profiles and the effect of condom use and screening on adjoints

### 5.6.3 Condom Use and Treatment Only

With this strategy, the control on treatment $u_3$ and the condom use control $u_1$ are both used to optimize the objective function $J$ while the screening control $u_2$ is set to zero.

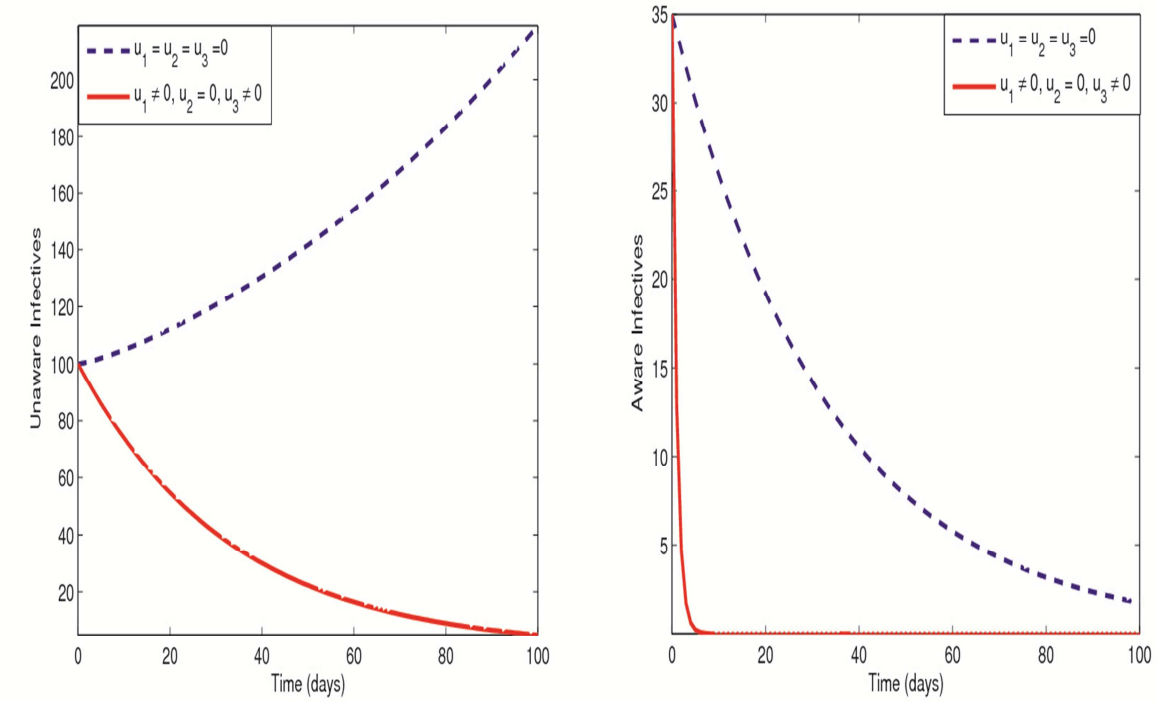



Fig 5.7 (a): Simulations showing the effect of condom use and treatment on infectives

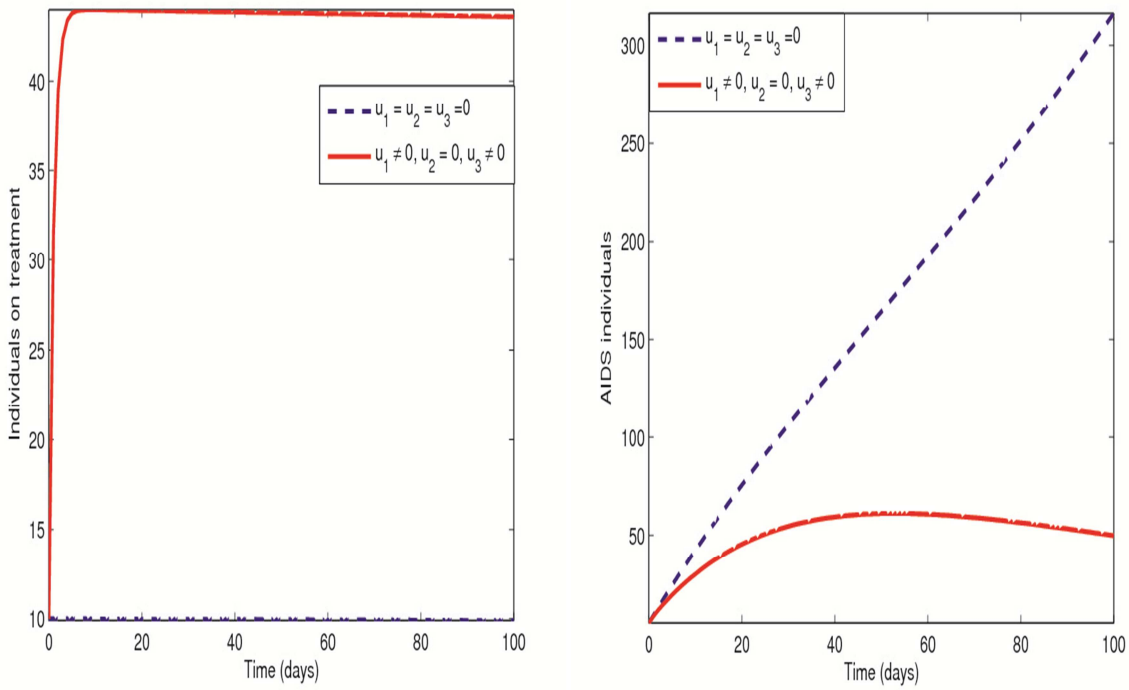



Fig 5.7 (b): Simulations showing the effect of condom use and treatment on the treated and AIDS individuals

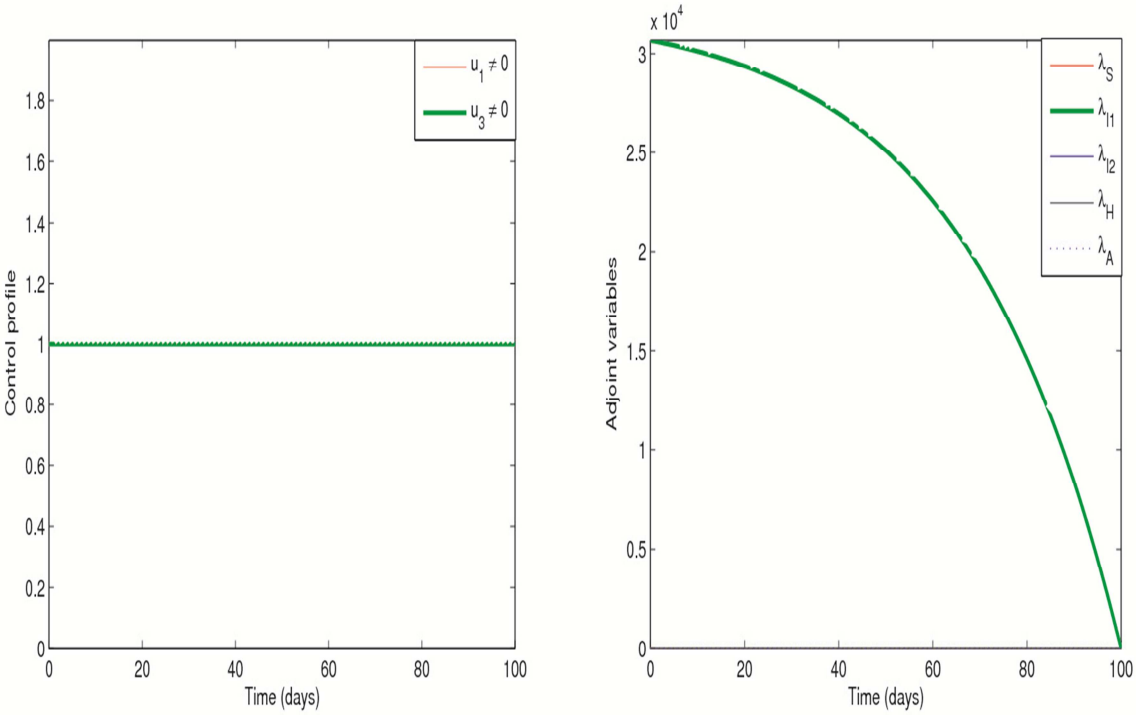



Fig 5.7 (c): Simulations showing control profiles and the effect of condom use and treatment on adjoints

In Fig 5.7, we observe that this control strategy results in a significant increase in the number of HIV positive individuals on treatment ($H$) which stabilizes at 45 and a significant reduction in the number of AIDS cases ($A$). The control $u_1$ is at the upper bound till the final time and the control $u_3$ is also maintained at the upper bound till the final time.

### 5.6.4 Condom Use, Screening and Treatment

With this strategy, the condom use control $u_1$, control on screening $u_2$ and the treatment control $u_3$ are all used to optimize the objective function $J$. In Fig 5.8, we observe that this control strategy results in a significant increase in the number of HIV positive individuals on treatment ($H$) which stabilizes at 140 and a significant reduction in the number of AIDS cases ($A$). Control profiles show that $u_1$ and $u_3$ are at the upper bound till the final time and $u_2$ drops gradually from the upper bound to the lower bound after 18 days.

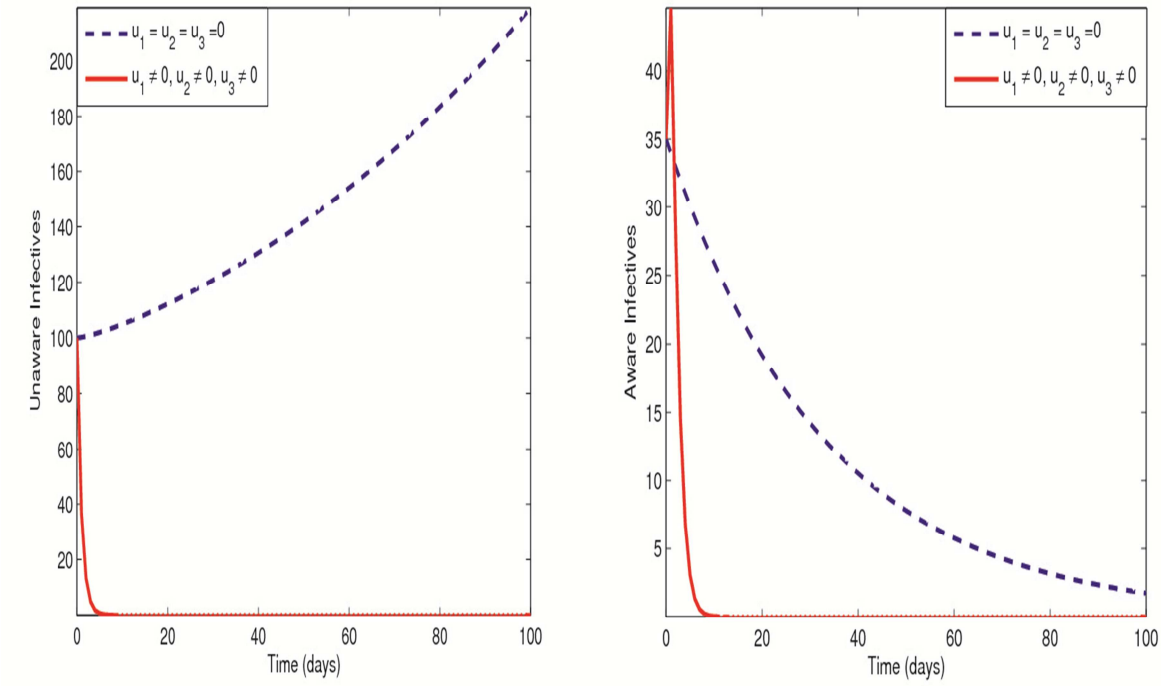



Fig 5.8 (a): Simulations showing the effect of all controls on infectives

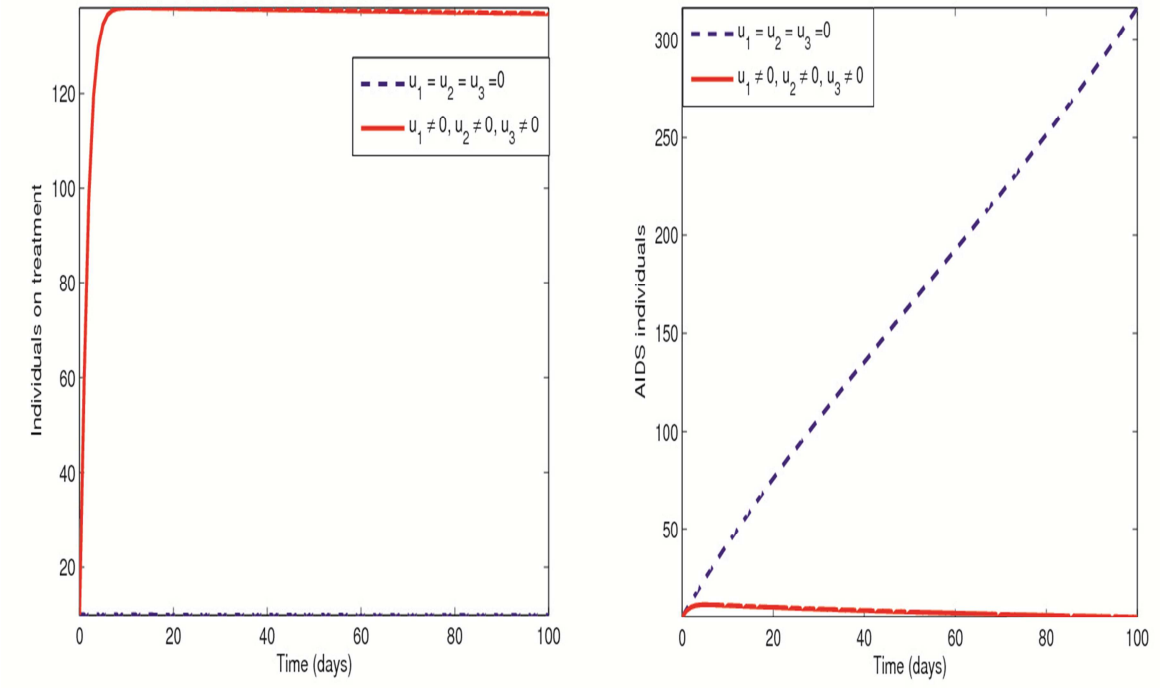



Fig 5.8 (b): Simulations showing the effect of all controls on the treated and AIDS individuals

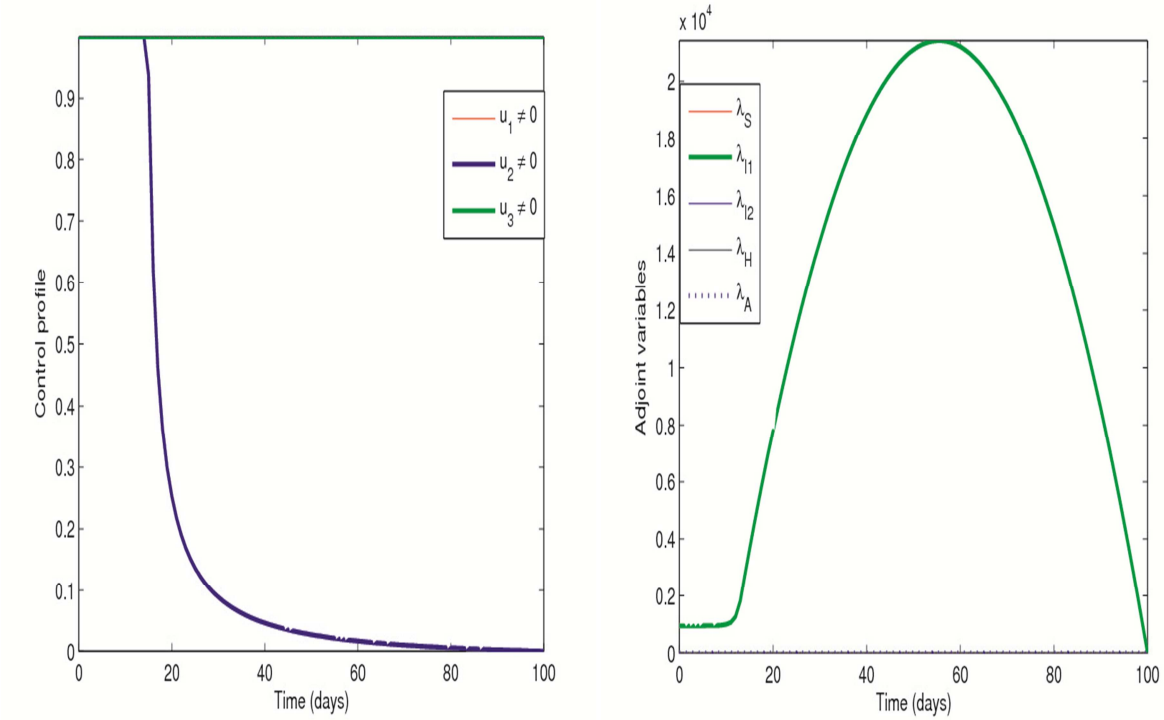



Fig 5.8 (c): Simulations showing control profiles and the effects of all controls on adjoints

Simulations of the effect of the control strategies on adjoint variables indicate that, in all the intervention strategies, the shadow price of the unaware infectives has the highest impact on the economy.

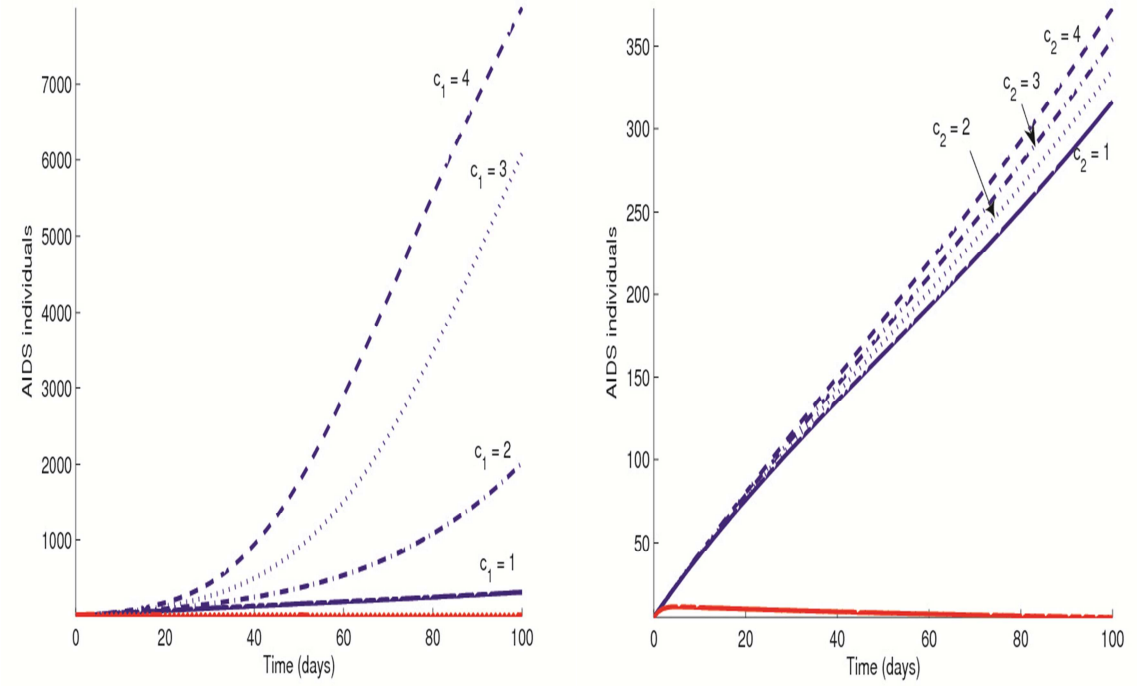



Fig 5.9: Simulations showing the effect of the number of sexual partners ($c_1$) and ($c_2$) on AIDS spread.

Fig 5.9 shows that the number of sexual partners of susceptibles with unaware infectives has a greater impact on the AIDS individuals in the absence of all controls. However, when all controls are used the number of sexual partners does not have a significant effect on the total number of AIDS individuals.

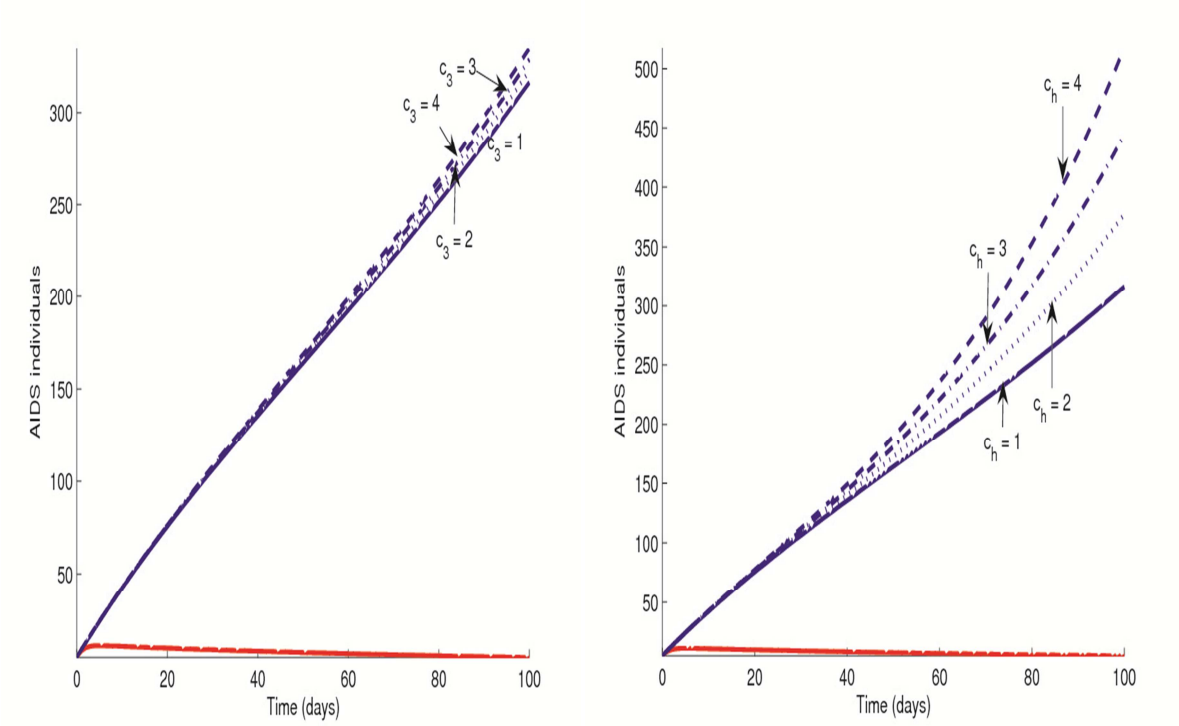



Fig 5.10: Simulations showing the effect of the number of sexual partners ($c_3$) and ($c_h$) on AIDS spread.

The red lines in Figs 5.9 and 5.10 indicate the effect on the spread of AIDS when there is optimal control of use of condom, screening of unaware infectives and treatment.

### 5.7 Cost Effective Analysis

To determine the most cost effective strategy to use to control the disease (combination of screening and condom use only, treatment and condom use only, combination of screening and treatment only, and combination of screening, treatment and condom use), we use cost effectiveness analysis. To achieve this purpose we need to compare the differences between the costs and health outcomes of these interventions. This is done by calculating the Incremental Cost-Effectiveness Ratio (ICER) which is generally described as the additional cost per additional health outcome. When comparing two or more competing intervention strategies incrementally, one intervention should be compared with the next-less-effective alternative. The ICER numerator includes the differences in intervention costs, averted disease costs, costs of prevented cases and averted productivity losses if applicable. The ICER denominator is the differences in health outcomes (e.g. total number of infections averted, number of susceptibility cases prevented).

We rank the strategies in increasing order of effectiveness, namely combination of screening and condom use only (strategy A), treatment and condom use only (strategy B), combination of screening and treatment only (strategy C) and combination of screening, treatment and condom use (strategy D) based on the model simulation results. The difference between the total infectious individuals without control and the total infectious individuals with control was used to determine the "total number of infections averted" used in the table of cost-effectiveness analysis.

| Strategy | Total Infections Averted | Total Costs ($) |
|---|---|---|
| A | 622 230 | 149 310 |
| B | 626 760 | 87 691 000 |

$$ICER(A) = \frac{149\ 310}{622\ 230} = 0.24$$

$$ICER(B) = \frac{87\ 691\ 000 - 149\ 310}{626\ 760 - 622\ 230} = 19\ 324.88$$

The comparison between ICER(A) and ICER(B) shows an additional cost $19 324.88 per infection averted for strategy B over strategy A. The ICER for strategy A indicates that strategy B is "strongly dominated". That is, strategy B is more costly and less effective than strategy A. Therefore, strategy B, the strongly dominated is excluded from the set of alternatives so it does not consume limited resources.

We exclude strategy B and compare strategy A with C. From the numerical results we have

| Strategy | Total Infections Averted | Total Costs ($) |
|---|---|---|
| A | 622 230 | 149 310 |
| C | 627 800 | 507 980 |

This leads to the following ICERs:

$$ICER(A) = \frac{149\ 310}{622\ 230} = 0.24$$

$$ICER(C) = \frac{507\ 980 - 149\ 310}{627\ 800 - 622\ 230} = 64.39$$

The comparison between ICER(A) and ICER(C) shows that it costs an additional $64.39 to avert one infection when switching fr0m strategy A to strategy C. Similarly, the ICER for

strategy A indicates that strategy C is “strongly dominated”. That is, strategy C is more costly and less effective than strategy A. Therefore, strategy C, the strongly dominated is excluded and then we compare strategies A and D. From the numerical results we have

| Strategy | Total Infections Averted | Total Costs ($) |
|---|---|---|
| A | 622 230 | 149 310 |
| D | 628 190 | 148 680 |

This leads to the following:

$$ICER(A) = \frac{149\ 310}{622\ 230} = 0.24$$

$$ICER(D) = \frac{148\ 680 - 149\ 310}{628\ 190 - 622\ 230} = -0.106$$

The comparison between ICER(A) and ICER(D) shows a cost saving of $0.106 for strategy D over strategy A. The negative ICER for strategy D indicates that strategy A is “strongly dominated”. That is, strategy A is more costly and less effective than strategy D. Therefore, strategy A, the strongly dominated is excluded.

With this result, we therefore conclude that strategy D (a combination of screening $u_2$ with treatment $u_3$ and condom use $u_1$) is the most cost-effective of all the strategies for HIV/AIDS disease control considered.

### 5.8 Conclusion

In this chapter, we performed optimal control analysis for a HIV/AIDS model. We derived and analyzed the conditions for optimal control of the disease with effective use of condoms, treatment regime and screening of infectives. We conclude that the successful screening of unaware infectives has a significant impact in reducing the endemicity of HIV/AIDS. This may be as a result of awareness by infectives who also took necessary precautionary measures not to spread the disease. Control programs that follow these strategies can effectively reduce the spread of HIV/AIDS in a population. Also, from the numerical results it is very clear that the impact and cost of unaware infectives in the community is very high.

# CHAPTER SIX

## CONCLUDING REMARKS

In this thesis, we considered the theoretical analysis of compartmental HIV/AIDS models. The work was motivated by the possibility that mathematical modelling could improve our understanding of the HIV/AIDS dynamics, particularly the impact of infection on an employee's productivity at the workplace. We developed relatively simple but reliable models which confirmed our expectations: that a combination of intervention strategies including enlightenment, prevention, screening and ART treatment has the potential to control HIV transmission at a community level, indirectly also improving the productivity of a labour force. We extended this analysis to recruitment and employment policies regarding wellness of staff. This was done by adapting principles from fields such as dynamical systems, control theory and economics utilising data available in literature. The end result is, in our opinion, a good framework for integrating available data with a toolkit of mathematical methods which can be continuously improved in accordance with the ever-changing picture of the HIV/AIDS epidemic.

Initially, motivated by the work of Tripathi et al, [113], we undertook investigations on the impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives by incorporating condom use, screening of unaware infectives and treatment of the infected. We observed that unawareness by infectives has a great cost impact on the community. We further investigated the impact of combinations of the strategies in the control of HIV/AIDS. Conducting cost-effectiveness analysis, we found that the most cost-effective strategy is the combination of all the control strategies. We then formulated realistic models that recognize five possible states for employees at the workplace: non-productive susceptible, productive susceptible, non-productive infected, productive infected and the AIDS class. The sensitivity of the models was tested with respect to changes in critical parameters: modification parameter on the productive susceptible, rate of progression to AIDS, mortality rate, proportion of recruited in non-productive susceptible class. Further, we showed that interventions result in more people being in the productive classes and less people in the non-productive and AIDS classes. Furthermore, the study showed that optimal control theory, numerical simulations and cost effectiveness analysis can be used to make meaningful decisions on choosing appropriate combinations of interventions to manage epidemics.

We know that the transition from one disease state to another is not instantaneous, it is worth considering time delay in the models formulated during this study as part of future work. The

importance of taking epidemiological modelling from the realm of the purely theoretical and applying it to real world situations cannot be overstated. Thus the future work will, therefore, extend to other problems related to HIV/AIDS dynamics, for instance substance abuse and TB, common problems faced by communities. Although this may limit the range of suitable mathematical tools, it is envisaged that even fairly simple models based on limited available data could lead to valuable insights. We would then have to cherry-pick the most useful mathematical tools and apply them to the most complete data in HIV. This may entail having to conduct surveys wherein it may become necessary to incorporate parameter estimation techniques.

## BIBLIOGRAPHY


[1] Adams, B. M., Banks, H. T., Kwon, H. D. and Tran, H. T. 2004. Dynamic Multidrug Therapies for HIV: Optimal and STI Control Approaches. Mathematical Biosciences and Engineering 1 (2): 223 - 241

[2] Anderson, R. M. and May, R. M. 1979. Population biology of infectious diseases: Part I. *Nature* 280 (5721): 361 – 367

[3] Anderson, R. M. and May R. M. 1991. *Infectious Diseases of Humans: Dynamics and Control.* Oxford University Press, Oxford

[4] Anderson, R. M., Medly, G. F., May, R. M. and Johnson, A. M. 1986. A Preliminary Study of the Transmission Dynamics of the Human Immunodeficiency Virus (HIV), the Causative Agent of AIDS, IMA J. Math. Appl. Med. Biol. 3: 229 – 263

[5] Asano, E., Gross, L. J., Lenhart, S. and Real, L. A. 2008. Optimal Control of vaccine distribution in Rabies metapopulation model. Mathematical Biosciences and Engineering Vol. 5 No. 2: pp. 219 – 238

[6] AVERTing HIV and AIDS. HIV and AIDS in South Africa (www.avert.org/aidssouthafrica.htm) Accessed 18/01/2011

[7] AVERTing HIV and AIDS. AIDS (www.avert.org/aids.htm) Accessed 18/01/2011

[8] Bakti Husada. 2008. Mathematical Model of HIV Epidemic in Indonesia 2008 - 2014

[9] Barnett, T. and Whiteside, A. 2006. *AIDS in the Twenty-First Century, Disease and Globalization*, Second Edition

[10] BBC Health News, 26 November 2010

[11] Bendavid, E., Young, S. D., Katzenstein, D. A., Bayoumi, A. M., Sanders, G. D. and Owens, D. K. 2008. Cost-effectiveness of HIV monitoring strategies in resource-limited settings: a southern African analysis. Arch Intern Med 168 (17): 1910 - 1918

[12] Bloom, D. et al. 2006. Business and HIV/AIDS: A Healthier Partnership? World Economic Forum, UNAIDS and the American Foundation for AIDS Research http://www.weforum.org/pdf/Initiatives/gbs2006_report.pdf

[13] Bowong, S. 2010. Optimal Control of the Transmission Dynamics of Tuberculosis. Nonlinear Dyn 61: 729 – 748

[14] Brannstrom, J., Akerlund, B., Arneborn, M., Blaxhult, A. and Giesecke, J. 2005. Unaware infection in HIV cases. International Journal of STD and AIDS Vol 16 (10): 702 – 706

[15] Brauer F., van den Driessche, P. and Jianhorg, W. U. n d. *Mathematical Epidemiology*. Mathematical Biosciences subseries. PK Maimi Oxford

[16] Buchbinder, S. P., Katz, M. H., Hessol, N. A., O'Malley, P. M. and Holmberg S. D. 1994. Long-term HIV-1 Infection without Immunologic Progression. AIDS 8 (8): 1123-8

[17] Burton, G. F., Keele, B. F., Estes, J. D., Thacker, T. C. and Gartner, S. 2002. Follicular dendritic cell contributions to HIV pathogenesis. Semin Immunol. 14 (4): 275 – 284

[18] Business & HIV/AIDS: A Healthier Partnership, 2005-2006

[19] Casale, M. and Whiteside, A. 2006. *The Impact of HIV/AIDS on Poverty, Inequality and Economic Growth*, IDRC Working Papers on Globalization, Growth and Poverty, Working Paper Number ; March 2006

[20] Center for Disease Control and Prevention. 2010. Prevalence and awareness of HIV infection among men who have sex with men - 21 cities , United States 2008, Morbidity and Mortality Weekly Report Vol. 59, No. 37

[21] Chatterji, P., Alegria, M., Lu, M. and Takeuchi, D. 2007. Psychiatric Disorders and Labour Market Outcomes: Evidence from the National Latino and Asian American Study. Health Economics 16: 1069 - 1090.

[22] Chitnis, N., Hyman, J. M. and Cushing, J. M. 2008. Determining Important Parameters in the Spread of Malaria through the Sensitivity Analysis of a Mathematical Model. Bulletin of Mathematical Biology 70: 1272 - 1296

[23] Christopher, M. K. and Jorge, X. V. 2000. A Simple Vaccination Model with Multiple Endemic States. Mathematical Biosciences 164: 183 - 201

[24] Coulibaly, I. 2005. The Impact of HIV/AIDS on Labour Force in sub-Saharan Africa: A Preliminary Assessment. ILO Programme on HIV/AIDS and the World of Work

[25] Culshaw, R. V. 2006. Mathematical Modelling of AIDS Progression: Limitations, Expectations, and Future Directions. Journal of American Physicians and Surgeons Vol. 11 No. 4

[26] Daar, E. S., Little, S. and Pitt, J. 2001. Diagnosis of Primary HIV-1 infection. Los Angeles County Primary HIV Infection Recruitment Network. Ann. Intern. Med. 134 (1): 25 - 29

[27] Daly, K. *2006.* The Business Response to HIV/AIDS: Impact and Responses. UNAIDS, The Prince of Wales Business Leaders Forum (PWBLF) and the Global Business Council on HIV&AIDS. 2000.

[28] Denis, K., Lenhart, S. and Steve, S. 1997. Optimal control of the chemotherapy of HIV. Journal Math. Biology 35: 775 – 792

[29] Deuchert, E. and Brody, S. 2007. Plausible and Implausible Parameters for Mathematical Modelling of Nominal Heterosexual HIV Transmission. Ann Epidemiol 17: 237 – 244

[30] Dhar, P. and Dhar, R. 2007. A Mathematical and Statistical Study on HIV: A Control Theoretic Approach. Journal of Physical Sciences Vol. 11: 10 - 16

[31] Diekmann, O and Heesterbeek, J. A. P. 2000. *Mathematical Epidemiology of Infectious Diseases: Model Building, Analyis and Interpretation*. John Wiley & Sons, New York

[32] Diekmann, O., Heesterbeek, J. A. P. and Metz, J. A. J. 1990. On the definition and the computation of the basic reproduction ratio R0 in models for infectious diseases in heterogeneous populations, J. Math. Biol. 28

[33] Diekmann, O., Heesterbeek, J. A. P. and Roberts, O. G. 2010. The Construction of Next Generation Matrices for Compartmental Epidemic Models. Journal of the Royal Society Interface 7 (47): 873 - 885

[34] Douek, D. C., Roederer, M. and Koup, R. A. 2009. Emerging Concepts in the Immunopathogenesis of AIDS. Annu. Rev. Med. 60: 471 - 484

[35] Ettner, S. L., Frank, R. G. and Kessler, R. C. 1997. The Impact of Psychiatric Disorders on Labour Market Outcomes. Industrial and Labour Relations Review 51 (1): 64-81.

[36] Elaiw, A. M. 2010. Global Properties of a Class of HIV Models. Nonlinear Analysis Real World Applications 11: 2253 - 2263

[37] Felippe de Souza, J.A.M., Caetano, M. A. L. and Yoneyama, T. 2000. Optimal Control Theory Applied to the Anti-Viral Treatment of AIDS. Proceedings of the IEEE Conference on Decision and Control Vol. 5

[38] Fister, K. R., Lenhart, S. and McNally, S. J. 1998. Optimizing Chemotherapy in an HIV Model. Electronic Journal of Differential Equations Vol. 1998 No. 32: 1 – 12

[39] Fleming, W. H. and Rishel, R. W. 1975. *Deterministic and Stochastic Optimal Control.* Springer Verlag, New York

[40] Gajic, V. R. 2009. Optimal Control of HIV Virus Dynamics. Annals of Biomedical Engineering Vol. 37 No. 6: 1251 – 1261

[41] Garnett, G. P. 2002. An Introduction to Mathematical Models in Sexually Transmitted Disease Epidemiology. Sex Transm Inf 78: 7 – 12

[42] Global HIV Prevention Working Group. 2007. *Bringing HIV Prevention to Scale: An Urgent Global Priority*; June 2007

[43] Gold, M. R., Siegel, J. E. and Russell, L. B. 1996. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press

[44] Greener, R. 2005. AIDS and Macroeconomic Impact. In S, Forsyth (ed.). State of The Art: AIDS and Economics. IAEN.: 49 - 55

[45] Greenhalgh, D. 1988. Some Results on Optimal Control Applied to Epidemics. Mathematical Biosciences 88: 125 - 158

[46] Guinness, L., Walker, D., Ndubani, P., Jama, J. and Kelly, P. 2007. Surviving the Impact of HIV-Related Illness in the Zambian Business Sector. AIDS Patient Care and STDs 17 (7): 353 - 363.

[47] Gumel, A. 2007. Modelling Transmission Dynamics of HIV/AIDS: Some Results, Issues and Challenges in DIMACS / SACEMA / AIMS / University of the Witwatersrand Workshop Report: Facing the Challenge of Infectious Diseases in Africa - The Role of Mathematical Modelling

[48] Hattaf, K., Rachik, M., Saadi, S. and Yousfi, N. 2009. Optimal Control of Treatment in a Basic Virus Infection Model. Applied Mathematical Sciences, Vol. 3 No. 20: 949 – 958

[49] Harvard Business Review, February 2003

[50] Hethcote, H.W. 2000. The Mathematics of Infectious Diseases. SIAM Review 42 (4): 599 - 653

[51] Ibrahima, C. 2003. *The impact of the HIV/AIDS on the labour force in Sub-Saharan Africa: a preliminary assessment*. International Labour Organization website www.ilo.org/aids

[52] ILO. 2006. *HIV/AIDS and Work: Global Estimates, Impact on Children and Youth, and Response*

[53] Joint United Nations Programme on HIV/AIDS. 2005. AIDS Epidemic Update, 2005. http://www.unaids.org/epi/2005/doc/EPIupdate2005_pdf_en/epi-update2005_en.pdf

[54] Joint United Nations Programme on HIV/AIDS. 2006. Overview of the Global AIDS Epidemic. 2006 Report on the Global AIDS Epidemic. ISBN 9291734799. http://data.unaids.org/pub/GlobalReport/2006/2006_GR_CH02_en.pdf

[55] Joly, M. and Pinto, J. M. 2005. The Role of Mathematical Modelling on the Optimal Control of HIV-1 Pathogenesis.

[56] Joshi, H. R. 2002. Optimal Control of an HIV Immunology Model, Optim. Control Appl. Math, 23: 199 – 213

[57] Joshi, H. R., Lenhart, S., Li, M. Y. and Wang, L. 2006. Optimal control methods applied to disease models. Comtemporary Mathematics vol 410

[58] Jung, O., Iwami, S., Takeuchi, Y. and Jo, T. C. 2009. Optimal Control Strategy for Prevention of Avian Influenza Pandemic. Journal of Theoretical Biology 260: 220 - 229

[59] Jun-jie, W., Reilly, K. H., Jing, L., Chun-peng, Z. and Ning, W. 2010. Dynamic Mathematical Models of HIV/AIDS Transmission in China. Chin Med J;123(15): 2120 – 2127

[60] Kahn, J. O. and Walker, B. D. 1998. Acute Human Immunodeficiency Virus type 1 Infection. N. Engl. J. Med. 331 (1): 33 – 39

[61] Kamien, M. I. and Schwartz, N. L. 1991. *Dynamic Optimization. Advanced Textbooks in Economics Vol. 3.* North-Holland Publishing Co.

[62] Kaiser, H. J. Family Foundation. 2007. The Multisectoral Impact of the HIV/AIDS Epidemic – A Primer

[63] Karrakchou, J., Rachik, M. and Gourari, S. 2006. Optimal Control and Infectiology: Application to an HIV/AIDS Model. Applied Mathematics and Computation 177: 807 – 818

[64] Kermack, W. O. and McKendrick, A. G. 1927. A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society of London Series A* 115 (772): 700 – 721

[65] Khan, S. A. 2006. Socio-Economic and Psychological Impact of HIV/AIDS on Society. PhD Thesis, University of Agriculture, Faisalabad

[66] Kibona, I. 2010. Modelling the Spread of AIDS with Vertical Transmission in the Presence of Infected Immigrants. MSc Dissertation. University of Dar es Salaam

[67] Kirschner, D., Lenhart, S. and Serbin, S. 1997. Optimal Control of the Chemotherapy of HIV, J. Math. Biol. 35: 775 – 792

[68] Kitahata, M. M., Gange, S. J., Abraham, A. G. 2009. Effect of early versus deferred antiretroviral therapy for HIV on survival. N. Engl. J. Med. 360 (18): 1815 - 1826

[69] Koenig, S. P., Leandre, F. and Farmer, P. E. 2004. Scaling-up HIV Treatment Programmes in a Resource-Limited Settings:The Rural Haiti Experience. *AIDS 13* (3): S21-S25.

[70] Kohn, R. V. 2009. A Brief Introduction to Optimal Control. NYU

[71] Landi, A., Mazzoldi, A., Andreoni, C., Matteo Bianchi, M., Cavallini, A., Laurino, M., Ricotti, L., Iuliano, R., Matteoli, B. and Ceccherini-Nelli, L. 2008. Modelling and Control of HIV Dynamics. Computer Methods and Programs in Biomedicine 89: 162 - 168

[72] Lenhart, S. and Workman, J. T. 2007. *Optimal Control Applied to Biological Models*, Chapman and Hall

[73] Lenhart, S.M. and Yong, J. 1995. Optimal control for degenerate parabolic equations with logistic growth. Nonlinear Anal. 25: 681 – 698

[74] Lenhart, S. M. and Yong, J. 1997. *Optimal Control for Degenerate Parabolic Equations with Logistic Growth.* Preprint Institute for Mathematics and Application

[75] Levy, J. A. 1993. HIV pathogenesis and long-term survival. AIDS 7 (11):1401-1410

[76] Lewis, A. D. 2006. The Maximum Principle of Pontryagin in Control and in Optimal Control

[77] Li, G. and Jin, Z. 2005. Global Stability of a SEIR Epidemic Model with Infectious Force in Latent, Infected and Immune Period. Chaos, Solutions and Fractals 25: 1177 – 1184

[78] Long, E. F. and Brandeau, M. L. 2009. OR's Next Top Model: Decision Models for Infectious Disease Control. Tutorials in Operations Research. INFORMS

[79] Lopez-Cruz, R. 2006. Structured SI Epidemic Models with Applications to HIV Epidemic. DPhil Dissertation. Arizona State University

[80] Lori, B., John, S. and Eleni, S. 1999. *The Economic Impact of AIDS in Ethiopia*

[81] Makinde, O.D and Okosun, K.O. 2011. Impact of chemo-therapy on optimal control of malaria disease with infected immigrants. BioSystems, 104 (1): 32 - 41 doi:10.1016/j.biosystems.2010.12.010.

[82] Mathieu, E., Foucher, Y., Dellamonica, P. and Daures, J. P. 2007. Parametric and Non Homogeneous Semi-Markov Process for HIV Control. Methodol Comput Appl Probab 9: 389 – 397

[83] Matthews, A., Gow, J. and George, G. 2011. HIV Prevalence and Incidence: Evidence from Four Industries of the KwaZulu-Natal Economy. Southern African Journal of Demography Vol 12 (1): 63 - 108

[84] May, R. M. and Anderson, R. M. 1979. Population biology of infectious diseases: Part II. *Nature* 280 (5722): 455 – 461

[85] McIntosh, P. T. G. n d. Effects of HIV in the Workplace and Consequences for African Economic Growth Potentials

[86] McNally, J. 1997. Combination Therapy of HIV Infection: An Analysis in Optimal Control. Senior Thesis. University of Tennessee, Knoxville

[87] Miller Neilan, R. L., Schaefer, E., Gaff, H., Fister, K. R. and Lenhart, S. 2010. Modelling Optimal Intervention Strategies for Cholera. Bulletin of Mathematical Biology

[88] Morgan, D., Mahe, C., Mayanja, B., Okongo, J. M., Lubega, R. and Whitworth, J. A. 2002. HIV-1 Infection in Rural Africa: Is there a Difference in Median Time to AIDS and Survival Compared with that in Industrialized Countries?. AIDS 16 (4): 597-632.

[89] Mukandavire, Z., Gumel, A. B., Garira, W. and Tchuenche, J. M. 2009. Mathematical Analysis of a Model for HIV-Malaria Co-infection. Mathematical Biosciences and Engineering 6: 333 – 362

[90] Murray, J. D. 2002. *Mathematical Biology - An Introduction*. Third Edition, Springer

[91] Mwange, N. N. N., 2010, Essays on HIV/AIDS, Exports and Poverty in Kenyan Manufacturing

[92] Myer, L. 2008. HIV in South Africa - The Numbers. Quest Science Magazine 4 (4). Academy of Science of South Africa

[93] Nikolaos, I. S., Dietz, K. and Schenzle, D. 1997. Analysis of a Model for the Pathogenesis of AIDS. Mathematical Biosciences 145: 27 - 46

[94] Okosun, K. O. 2010. Mathematical Epidemiology of Malaria Disease Dynamics and Its Optimal Control Analyses. Doctor Scientiae. University of the Western Cape

[95] Okosun, K.O., Ouifki, R., Marcus, N. 2011. Optimal control analysis of a malaria disease transmission model that includes treatment and vaccination with waning immunity. BioSystems 106: 136 – 145 doi:10.1016/j.biosystems.2011.07.006

[96] Palella, F. J. Jr, Delaney, K. M., Moorman, A. C., Loveless, M. O., Fuhrer, J., Satten, G. A., Aschman D. J. and Holmberg, S. D. 1998. Declining Morbidity and Mortality among Patients with Advanced Human Immunodeficiency Virus Infection. HIV Outpatient Study Investigators. N. Engl. J. Med 338 (13): 853 – 860

[97] Pantaleo, G., Graziosi, C., Fauci, A.S. 1993. New concepts in the immunopathogenesis of human immunodeficiency virus infection. N. Engl. J. Med. 328: 327 – 335

[98] Perko, L. 2000. *Differential equations and dynamical systems*, Text in Applied Mathematics, 7, Springer, Berlin

[99] Phaswana-Mafuya, N. and Peltzer, K. 2005. Perceived HIV/AIDS Impact among Stafff in Tertiary Institutions in Eastern Cape, South Africa. *Journal des Aspects Sociaux du VIH/SIDA 2* (2): 277 - 285.

[100] Piatak, M. Jr, Saag, M. S., Yang, L. C., Clark, S. J., Kappes, J. C., Luk, K. C., Hahn, B. H., Shaw, G. M. and Lifson, J.D. 1993. High levels of HIV-1 in plasma during all stages of infection determined by competitive PCR. Science 259 (5102): 1749 – 1754

[101] Piekarski, J. M. 2009. Construction of a Dual Infection Mechanism for HIV. M. S. Dissertation. University of Maryland, Baltimore County

[102] Policy Project for Bureau of Africa, 2001

[103] Pontryagin, L. S., Boltyanskii, V. G., Gamkrelidze, R. V. and Mishchenko, E. F. 1962. *The Mathematical Theory of Optimal Processes.* Wiley, New York

[104] Press, W. H., Flannery, B. P., Teukolsky, S. A. and Vetterling, W. T. 1992. "Runge-Kutta Method" and "Adaptive Step Size Control for Runge-Kutta." §16.1 and 16.2 in *Numerical Recipes in FORTRAN: The Art of Scientific Computing, 2nd ed.* Cambridge, England: Cambridge University Press

[105] Rehle, T. M. and Shisana, O. 2003. Epidemiological and Demographic HIV/AIDS Projections: South Africa. African Journal of AIDS Research 2(1): 1 – 8

[106] Reichman, N. E., Corman, H., Noonan, K. and Dave, D. 2009. Infant Health Production Functions: What a Difference the Data Make. Health Economics 18: 761-82.

[107] Roberts, M. G. and Heesterbeek, J. A. P. 2003. Mathematical Models in Epidemiology. Mathematical Models Vol 3. EOLSS

[108] Rosen, S., Simon, J., Thea, D. & Vincent, J. 2000. Care and treatment to extend the working lives of HIV-positive employees: calculating the benefits to business. South African Journal of Science 96: 300– 304.

[109] Rosen, S. et al. 2003. AIDS is Your Business. Harvard Business Review, Vol. 81, No. 1, February 2003. http://hbswk.hbs.edu/archive/3338.html

[110] Schneider, M. F., Gange, S. J., Williams, C. M., Anastos, K., Greenblatt, R. M., Kingsley, L., Detels, R. and Munoz, A. 2005. Patterns of the Hazard of Death after AIDS through the Evolution of Antiretroviral Therapy: 1984-2004. AIDS 19 (17): 2009 – 18

[111] Simon, C. P. and Jacquez, J. A. 1992. Reproduction numbers and the stability of equilibria of SI models for heterogeneous populations. SIAM J. Appl. Math. 52: 541 – 576

[112] The POLICY Project for Bureau for Africa. 2001. HIV/AIDS in Southern Africa: Background, Projections, Impacts and Interventions.

[113] Tripathi, A., Naresh, R. and Sharma, D. 2007. Modelling the Effect of Screening of Unaware Infectives on the Spread of HIV Infection, Applied Mathematics and Computation 184: 1053 – 1068

[114] Trottier, H. and Philippe, P. 2001. Deterministic Modelling of Infectious Diseases: Theory and Methods. The Internet Journal of Infectious Diseases. Volume 1 Number 2. DOI: 10.5580/261d

[115] UN. 2004. *The Impact of AIDS*

[116] UNAIDS. 2005. AIDS Epidemic Update

[117] UNAIDS. 2007. AIDS Epidemic Update

[118] UNAIDS. 2010. UNAIDS Report on the Global AIDS Pandemic

[119] UNAIDS. 2011. World AIDS Day Report

[120] van den Driessche, P. and Watmough, J. 2002. Reproduction Numbers and sub-Threshold Endemic Equilibria for Compartmental Models of Disease Transmission. Mathematical Biosciences 180: 29 – 48

[121] Vass, J. 2005. *A review of labour markets in South Africa: The impact of HIV/AIDS on the labour market* Employment and Economic Policy Research Programme Human Sciences Research Council.

[122] Waxman, M. J., Kimaiyo, S., Ongaro, N., Wools-Kaloustian, K. K., Flanigan, T. P. and Carter, E. J. 2007. Initial Outcomes of an Emergency Department Rapid HIV Testing Program in Western Kenya. AIDS Patient Care and STDs 21 (12): 981 - 986

[123] Weehuizen, R. M. 2008. Mental Capital: The Economic Significance of Mental Health. *Economics and Business Administration.* Maastricht: Universiteit Maastricht, 2008, 297.

[124] Weiss, R. A. 1993. How does HIV cause AIDS? Science 260 (5112): 1273-9.

[125] Wickwire, K. 1977. Mathematical Models for the Control of Pests and Infectious Diseases - A Survey. Theoretical Population Biology 11: 182 – 238

[126] World Economic Forum Report on HIV/AIDS 2004-2005

[127] Yau, M. A. 2009. A Mathematical Model of HIV Transmission Dynamics in a Closed Population. Research Journal of Applied Science 5 (4): 283 – 284

[128] Yazdanpanah, Y., Sloan, C. E., Charlois-ou, C., Le Vu, S., Semaille, C., Costagliola, D., Pillonel, J., Poullie, A., Scemama, O., Deuffic-Burban, S., Losina, E., Walensky, R. P., Freedberg, K. A. and Paltiel, A.D. 2010. Routine HIV Screening in France: Clinical Impact and Cost-Effectiveness. Jounal PLoS ONE—www.plosone.org, Vol. 5 (10), e13132