Mathematical Modelling and Analysis of HIV Transmission Dynamics

A thesis submitted for the degree of

Doctor of Philosophy

by

Nafiu Hussaini

Supervisor

Dr. Matthias Winter

Department of Mathematical Sciences
School of Information Systems, Computing and Mathematics
Brunel University, West London

September 2010

Abstract

This thesis firstly presents a nonlinear extended deterministic Susceptible-Infected (SI) model for assessing the impact of public health education campaign on curtailing the spread of the HIV pandemic in a population. Rigorous qualitative analysis of the model reveals that, in contrast to the model without education, the full model with education exhibits the phenomenon of backward bifurcation (BB), where a stable disease-free equilibrium coexists with a stable endemic equilibrium when a certain threshold quantity, known as the *effective reproduction number* ($\mathcal{R}_{eff}$), is less than unity. Furthermore, an explicit threshold value is derived above which such an education campaign could lead to detrimental outcome (increase disease burden), and below which it would have positive population-level impact (reduce disease burden in the community). It is shown that the BB phenomenon is caused by imperfect efficacy of the public health education program. The model is used to assess the potential impact of some targeted public health education campaigns using data from numerous countries.

The second problem considered is a Susceptible-Infected-Removed (SIR) model with two types of nonlinear treatment rates: (i) piecewise linear treatment rate with saturation effect, (ii) piecewise constant treatment rate with a jump (Heaviside function). For Case (i), we construct travelling front solutions whose profiles are heteroclinic orbits which connect either the disease-free state to an infected state or two endemic states with each other. For Case (ii), it is shown that the profile has the following properties: the number of susceptible individuals is monotone increasing and the number of infectives approaches zero, while their product converges to a constant. Numerical sim-

ulations are shown which confirm these analytical results. Abnormal behavior like travelling waves with non-monotone profile or oscillations are observed.

Certificate of Originality

I hereby certify that the work presented in this thesis is my original research and has not been presented for a higher degree at any other university or institute.

Signed:_____ Dated: _____

Nafiu Hussaini

Dedication

To everyone who supports me

Acknowledgements

This thesis owes a great deal to the support and encouragement of many people:

My supervisor, Dr Matthias Winter, who has been a constant source of inspiration, ideas and advice, and has always been incredibly generous with his time. Thus, I am deeply indebted to him for his unwavering support and guidance. I am thankful to Prof. A. B. Gumel for introducing me to the world of mathematical biology and for useful suggestions and comments with regard to chapters 3 and 4. I would like to acknowledge, with thanks, Kano State Government of Nigeria for funding this research. Special thanks go to Abdallah K. Ally, Adnan Masood and Hakim Mizali for their kind hospitality, help and support which kept me sane outside of mathematical biology. Finally, huge thanks go to my family. I am indebted to them for their love and support throughout the period of my study.

Author's Publication

Journal Papers

1. **N. Hussaini**, M. Winter and A. B. Gumel, Qualitative assessment of the role of public health education program on HIV transmission dynamics, *Mathematical Medicine and Biology: A Journal of the IMA* , (2010) 10.1093/*imammb*/*dqq*009.

2. **N. Hussaini** and M. Winter, Travelling waves for an epidemic model with nonsmooth treatment rates, *Journal of Statistical Mechanics: Theory and Experiment*, To Appear.

Conference Papers (selected)

1. **N. Hussaini**, "The Impact of Education on HIV Transmission Dynamics", *The AIMS' Seventh International Conference on Dynamical Systems, Differential Equations and Applications*, 18-21 May 2008, University of Texas at Arlington, Texas, USA.

2. **N. Hussaini**, "Effects of Public Health Education Campaign on HIV Transmission Dynamics", *European Consortium for Mathematics in Industry Conference*, 30 June - 4 July 2008, University Collage London, UK, "Best Student Poster Award".

3. **N. Hussaini**, "The role of public health education program on HIV transmission dynamics", *Young Researchers in Mathematics 2010*, 25-27 March 2010, University of Cambridge, UK.

Contents

List of Figures

List of Tables

Chapter 1

Introduction

"Policy is of course based on theory, though not always on the best theory."

Hobsbawm (1969)

1.1 Global HIV/AIDS epidemic

Since its emergence in the 1980s, the human immunodeficiency virus (HIV), and the associated syndrome of opportunistic infections which lead to the late stage HIV disease, known as the acquired immunodeficiency syndrome (AIDS), continue to be one of the most serious global public health menace. Global and regional estimates of HIV have been provided by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) since the late 1980s and country specific estimates since 1996 (UNAIDS, 2009; Garcia-Calleja et al., 2006). Unlike the early years of

AIDS epidemic where the majority of infected individuals were homosexuals, hemophiliacs, and intravenous drug users, today there is no geographical area, class, and cultural group of the world untouched by this pandemic (Koob and Harvan, 2003). Over 33 million people are currently living with HIV (see, Table 1.1). Based on the current trends, over 7300 persons become infected with HIV, and 5400 die from AIDS-related causes including more than 760 children, every day (UNAIDS, 2009). In other words, almost five people become infected with HIV and four people (i.e., three adults and one child) die from AIDS per minute. AIDS is the leading cause of death in sub-Saharan Africa, especially in the southern part of the continent where nine countries with the highest HIV prevalence worldwide are all located in this subregion, with each of these countries experiencing adult HIV prevalence greater than 10%. With an estimated adult HIV prevalence of 26% in 2007, Swaziland has the most severe level of infection in the world (UNAIDS, 2008). The recent statistics have shown that an estimate of 22.4 million [20.8 million - 24.1 million] people (women account for approximately 60%) living with HIV in sub-Saharan Africa at the end of 2008 (UNAIDS, 2009; Garcia-Calleja et al., 2006). Moreover, 72% of world's AIDS-related deaths, 68% of new HIV infections among adults and 91% of new HIV infections among children occurred in sub-Saharan Africa (UNAIDS, 2009, 2007). In addition, the epidemic has left behind more than 14 million AIDS orphans in the region in 2008.

Table 1.1: The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information (UNAIDS, 2009).

Global summary of the AIDS epidemic	(December 2008)
Number of people living with HIV	Total 33.4 million [31.1 million - 35.8 million] Adults 31.3 million [29.2 million - 33.7 million] Women 15.7 million [14.2 million - 17.2 million] Children under 15 years 2.1 million [1.2 million - 2.9 million]
People newly infected with HIV	Total 2.7 million [2.4 million - 3.0 million] Adults 2.3 million [2.0 million - 2.5 million] Children under 15 years 430 000 [240 000 - 610 000]
AIDS-related deaths	Total 2.0 million [1.7 million - 2.4 million] Adults 1.7 million [1.4 million - 2.1 million] Children under 15 years 280 000 [150 000 - 410 000]

1.2 The Immunology of HIV

Once HIV has entered the body, its major target is a class of lymphocytes, or white blood cells, known as $CD4^+$ T cells. Thus, the immune system initiates anti-HIV antibody and cytotoxic T cell production. However, it can take two to ten weeks for an individual exposed to HIV to produce measurable quantities of antibody. When the $CD4^+$ T cell count, which is normally around $1000mm^{-3}$ reaches $200mm^{-3}$ or below in an HIV-infected patient; then that person is classified as having AIDS. Because of the central role of $CD4^+$ T cells in immune regulation, their depletion has widespread deleterious effects on the functioning of the immune system as a whole and leads to the immunodeficiency that characterizes AIDS. Therefore, HIV levels in the bloodstream are typically highest when a person is first infected and again in the late stages of the illness as depicted in Figure 1.1. The progression of HIV infection to AIDS probably depends on how well the body can replace cells destroyed by virus (Perelson and Nelson, 1999).

1.3 Modes of HIV transmission

Epidemiological evidence shows that HIV is transmitted only through the intimate exchange of body fluids, such as blood, semen, vaginal secretion, and mother's milk (Dane and Miller, 1990). Thus, HIV could be passed from an infected mother to her child (i.e., vertical infection) during pregnancy, birth or through infected breast milk. High-risk behaviors include unprotected sexual intercourse and intravenous drug use through sharing needles or syringes.

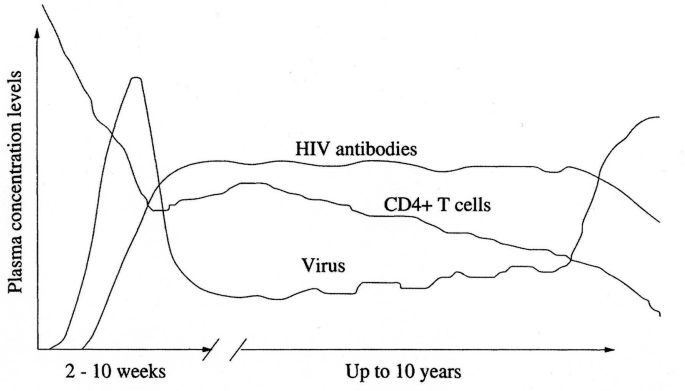


Figure 1.1: Time course of HIV infection in a typical infected adult. The viral load and level of antibodies against HIV are depicted. The early peak in viral load corresponds to primary infection. Primary infection is followed by a long asymptomatic period during which the viral load changes little. Ultimately, the viral load increases and the symptoms of full-blown AIDS appear. On average, the time from infection to AIDS is 10 years, but still some patients progress to AIDS much more rapidly, while others progress more slowly. The graphs here are only meant to be schematic and are not data from any particular patient.

Many people in the past have been infected with HIV through transfusions of infected blood or blood-clotting factors, before blood screening began in 1986. Therefore, this is no longer a significant risk in most parts of the world today, as blood donations are routinely tested for HIV.

1.4 Spatial spread of HIV

HIV is classified as an infectious disease which rapidly spreads amongst communities and changes its distributions in space, time and "social space" (Wallace, 1991). Many factors, including increased mobility, are associated with an increased risk of HIV infection (Welz et al., 2007). The transmission of HIV is also strongly associated with the spatial distribution of high risk groups. The

distribution of AIDS cases not only varies by cities and states, but also by geographical regions (Lange et al., 1988). The spread of HIV has been attributed to migration from rural to urban areas and its concomitant return migration. Furthermore, the trends in geographic diffusion could be explained by the mobility and travel patterns of high risk populations and their activities while travelling (McCoy et al., 1996). Fullilove et al. (1992) stated that our ability to predict the future of the HIV epidemic will depend on our understanding of the movement of HIV from established epicenters to areas where the prevalence of risk behaviors may be high but the prevalence of HIV infection is currently low. Standard mathematical models of the spread of infectious diseases are well known and have been widely applied for many diseases including HIV in different regions in the world (Anderson and May, 1991).

1.5 Public health education campaigns

There is still no cure or vaccine for HIV, and anti-retroviral drugs (ARVs) are still not widely accessible, particularly in the resource-poor nations (which suffer the vast majority of the HIV burden globally). Yet, HIV remains preventable through the avoidance of high-risk behaviour, such as unprotected sexual intercourse and sharing of drug injection needles. Thus, in the absence of pharmaceutical interventions (such as a vaccine or ARVs) in areas where the HIV pandemic is more rampant (notably developing nations), the effective control of HIV would depend, primarily, on reducing behavioural risks. This could be achieved through effective public heath education campaign.

Unfortunately, surveys around the world show alarming low level of awareness and understanding about HIV and its preventive measures (Keitshokil et al., 2007; Pérez et al., 2008). Recent studies indicate that the most effective available means to control the prevalence of HIV is to provide HIV-related education, which could lead to safe lifestyles among sexually-active members of the public (Bortolotti et al., 1992; Morton et al., 1996). Moreover, education, as a sole anti-HIV intervention strategy, may not be sufficient to motivate behaviour change (Berker and Joseph, 1988). Studies show that public health education increases self-efficacy, which is a determinant for controlling risky behaviour (Lindan et al., 1991). Furthermore, as noted by Cassell et al. (2006), the benefits of new methods of HIV prevention could be jeopardized if they are not accompanied by positive efforts to change risky behaviour. This is in line with the well-known fact that sexual education and awareness of the risk and life-threatening consequences of AIDS can lower the incidence rate in HIV infection (Valesco-Hernandez and Hsieh, 1994).

Public health education campaigns have been successfully implemented in numerous countries and communities, such as: Uganda, Thailand, Zambia and the US gay community (Daniel and Rand, 2003; De Walque, 2007). Between 1991-1998, HIV prevalence dramatically declined in Uganda from 21% to 9.8% (with a corresponding reduction in non-regular sexual partners by 65% coupled with greater levels of awareness about HIV/AIDS; Daniel and Rand (2003)). The Ugandan programme fostered community mobilization towards change in risky behaviour, without increasing stigma (Green et al., 2006; Wilson, 2004). In Zambia and Zimbabwe, the decline in HIV incidence since

early and late 1990s, respectively, is attributed to behavioural changes. Drops in national HIV incidence were also reported in Tanzania between 2004 and 2008 (Fylkesnes et al., 2001; UNAIDS, 2009). There are a number of ways (or strategies) public health education campaigns can be implemented (or targeted) effectively to combat the burden of HIV disease (measured in terms of new cases, mortality etc) in a community. This thesis amongst other things examines the following targeted strategies and their impact:

- targeting adult ("established") sexually-active susceptible individuals only;
- targeting newly-recruited sexually-active susceptible individuals only;
- targeting HIV-infected individuals without clinical AIDS symptoms only; or
- targeting HIV-infected individuals with AIDS symptoms only.

One of the primary goals of this study is to theoretically determine which of the aforementioned targeted strategies (or combination of strategies) is (are) the most effective in curtailing HIV spread in a community.

1.6 Treatment

Antiretroviral treatment is the best option for long lasting viral suppression and, subsequently, for reduction of mortality. Currently available drugs do not completely eradicate HIV infection, therefore, lifelong treatment might

be needed. The goal of antiretroviral treatment is to decrease the morbidity and mortality that is generally associated with HIV infection. A combination of three or more active drugs is needed to achieve this aim in most patients (Simon et al., 2006).

The extremely high prevalence of HIV suggests an urgent need to allocate adequate resources for HIV prevention and treatment (Welz et al., 2007). Still the treatment access gaps remain, as more than half of all people in need of treatment are still not receiving such services. For example, Kenya was offering antiretroviral therapy to roughly 190 000 adults in nearly 500 treatment sites in mid-2008, only 12% of the estimated 1.4 million HIV-infected adults who required daily co-trimoxazole were receiving it in 2007 (UNAIDS, 2009). While treatment of HIV-infected people with antiretroviral drugs and drugs for prevention and treatment of opportunistic infections benefits individuals and communities, in lowering AIDS-related death rates in multiple countries and regions, it is also contributing in increasing HIV prevalence (UNAIDS, 2009; Weidle et al., 2002). Furthermore, treatment may include quarantine of all seropositive persons as successfully practiced by Cuba between 1986 and 1994. However, by 2003, half of all HIV-positive Cubans still lived in the sanatoriums (Hansen and Groce, 2003; Perez-Stable, 1991).

Over the last two decades, some mathematical models assessing the impact of treatment on HIV have been designed and analyzed by many authors (see, for instance, Wang and Ruan, 2004; Wang, 2006; Arino et al., 2008; Brauer, 2008; Gul et al., 2009; Kgosimore and Lungu, 2006, and references therein).

1.7 Reproduction number

In Epidemiology, it is essential to quantify the severity of actual (or potential) outbreaks of infectious diseases. The standard procedure is to calculate a parameter called the *basic reproduction number* ($\mathcal{R}_0$) that characterizes the potential of an outbreak to cause an epidemic. Anderson and May (1991), defined $\mathcal{R}_0$ as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible. Further, if $\mathcal{R}_0$ is greater than one then the outbreak will lead to an epidemic (i.e., a stable endemic equilibrium point (EEP) exists), and if $\mathcal{R}_0$ is less than one then the outbreak will become extinct and the disease dies out in time (in this case the corresponding disease-free equilibrium (DFE) is locally asymptotically stable (LAS)). The DFE and an EEP exchange their stability at $\mathcal{R}_0 = 1$ which is known as forward bifurcation (or transcritical bifurcation). This phenomenon was first noted by Kermack and McKendrick (1927), and has been observed in many disease transmission models ever since (see for instance, Castillo-Chavez et al., 1989b; Castillo-Chavez and Song, 2004; Hethcote, 2000, and references therein). In general, for models that exhibit forward bifurcation, the requirement $\mathcal{R}_0 < 1$ is necessary and sufficient for disease elimination (i.e., the number of infectives at steady state depends continuously on $\mathcal{R}_0$). In the presence of control measure, such as the use of public health education enlightenment campaign in a community, the dynamics of the model is governed by another threshold quantity, known as the *effective reproduction number*, denoted by $\mathcal{R}_{eff}$. The threshold, $\mathcal{R}_{eff}$, represents the average number of secondary cases a typical infected individual will generate

in a population where a fraction of the susceptible individuals are educated. A number of studies have shown that whilst $\mathcal{R}_{eff} < 1$ is necessary for disease elimination, this requirement may not be sufficient. This is owing to the phenomenon of backward bifurcation, where a stable endemic equilibrium coexists with a stable disease-free equilibrium for $\mathcal{R}_{eff} < 1$. This phenomenon has been observed in numerous disease transmission models such as those for behavioral responses to a perceived risks (Hadeler and Castillo-Chavez, 1995), multiple groups (Castillo-Chavez et al., 1989a), vaccination (Arino et al., 2008; Elbasha and Gumel, 2006; Kribs-Zaleta and Halesco-Hernandez, 2000; Sharomi et al., 2007), transmission of mycobacterium tuberculosis with exogenous reinfection (Castillo-Chavez and Song, 2004), and transmission of dengue (Garba and Gumel, 2010). In a backward bifurcation, disease control is only feasible if $\mathcal{R}_{eff}$ is reduced further to values below another sub-threshold less than unity. The phenomenon of backward bifurcation has important public health implication, since it renders the classical requirement of reproduction number being less than unity to be insufficient (in general) for disease elimination.

1.8 Organisation of the Thesis

After this introductory chapter, the thesis is structured as follows.

Chapter 2: The purpose of this chapter is to introduce several mathematical concepts and tools that will be used throughout the thesis to qualitatively analyze the models presented in the subsequent chapters. Mathematical tools like equilibria and stability theory, their general categories and

applications are briefly introduced. The chapter also briefly discussed some of the principles and methods associated with dynamical system. Other core concepts that are of particular interest to infectious disease modelling developers and researchers were also highlighted.

Chapter 3: A basic HIV model with public health education campaign as a sole intervention strategy is formulated and analysed in this chapter. Threshold analysis of the effective reproduction number is conducted and the model is used to assess the potential impact of some targeted public health education campaigns using data from numerous countries.

Chapter 4: The existence of backward bifurcation (BB) is established in this chapter. The process of removing such phenomenon by perfecting efficacy of the public health education program is also presented and discussed.

Chapter 5: A Susceptible-Infected-Removed (SIR) model with two types of nonlinear treatment rates model is introduced, first in its spatially independent then in its spatially dependent form. Results on its disease-free and endemic equilibria are stated. The existence of travelling wave front solutions are established in Section 5.4. Finally, we concluded by briefly discussing our results in Section 5.5. It is noteworthy that this chapter is independent of chapters 3 and 4, and the model considered can be applied to some infectious diseases in addition to HIV.

Chapter 6: The last chapter discusses the main contributions of this thesis and highlights some possible refinement of the current research and

potential directions for future work.

Chapter 2

Mathematical Preliminaries I

2.1 Introduction

In this chapter, some mathematical concepts, definitions and theories needed for model analysis especially in chapters 3 and 4 will be presented. First of all, in this chapter autonomous system of ordinary differential equations

$$\dot{x} = \mathbf{f}(x), \qquad x \in \mathbb{R}^n. \tag{2.1}$$

are considered as opposed to non-autonomous system

$$\dot{x} = \mathbf{f}(x, t), \qquad x \in \mathbb{R}^n. \tag{2.2}$$

where the function $\mathbf{f}$ can depend on the independent variable t. Here, the dot represents differentiation with respect to t.

2.2 Equilibria and Linearization

The following are standard definitions and theorems required to analyze the stability of an equilibrium point of an autonomous system (see, Perko, 2001; Hale and Koçak, 1991).

Definition 1. *A point $\bar{x} \in \mathbb{R}^n$ is called an equilibrium point (also critical point, steady state solution, etc.) of (2.1), if $\mathbf{f}(\bar{x}) = 0$. Further, an equilibrium point $\bar{x}$ is called a hyperbolic equilibrium point of (2.1) if none of the eigenvalues of the matrix $D\,\mathbf{f}(\bar{x})$ have zero real part.*

Consider the linear system

$$\dot{x} = A\,x, \tag{2.3}$$

with the matrix $A = D\,\mathbf{f}(\bar{x})$. The linear function $A\,x = D\,\mathbf{f}(\bar{x})x$ is the linear part of $\mathbf{f}$ at $\bar{x}$.

Definition 2. *The linear system (2.3) with the matrix $A\,x = D\,\mathbf{f}(\bar{x})x$ is called the linearization of (2.1) at $\bar{x}$.*

Definition 3. *An equilibrium point of (2.3) is called a sink if all of the eigenvalues of the matrix $D\,\mathbf{f}(\bar{x})$ have negative real part; it is called a source if all the eigenvalues of $D\,\mathbf{f}(\bar{x})$ have positive real part; and it is called a saddle if it is a hyperbolic equilibrium point and $D\,\mathbf{f}(\bar{x})$ has at least one eigenvalue with a positive real part and at least one with negative real part.*

Theorem 1. *(Grobman-Hartman).*
If $\bar{x}$ is a hyperbolic equilibrium point of (2.1), then there is a neighbourhood of

$\bar{x}$ in which $\mathbf{f}$ *is topologically equivalent to the linear system (2.3).*

2.3 Stability of Equilibria

The notion of stability of an equilibrium point is of considerable theoretical and practical importance, and it has been widely discussed in the literature, for example, books on the dynamical systems: theory (Guckenheimer and Holmes, 2002; Lakshmikantham et al., 1989; LaSalle, 1976; Perko, 2001; Hale and Koçak, 1991; Ruelle, 1989) and application (Murray, 2002, 2003; Brauer and Castillo-Chavez, 2001; Anderson and May, 1991).

An equilibrium point $\bar{x}$ is said to be stable if all solutions sufficiently close to $\bar{x}$ stay nearby for all $t \geq 0$. It is asymptotically stable if nearby solutions actually converge to $\bar{x}$ as $t \to \infty$. Thus the formal definitions are:

Definition 4. *(Liapunov Stability).*
An equilibrium point $\bar{x}$ of (2.1) is said to be stable if given $\epsilon > 0$, there exists a $\delta(\epsilon) > 0$, such that, for any x_0 for which $|\bar{x} - x_0| < \delta(\epsilon)$, the solution $y(t, x_0)$ of (2.1) through x_0 at 0 satisfies $|y(t, x_0) - \bar{x}| < \epsilon$ for all $t \geq 0$.

Definition 5. *An equilibrium point $\bar{x}$ is said to be unstable if it is not stable.*

Definition 6. *(Asymptotic Stability).*
An equilibrium point $\bar{x}$ of (2.1) is said to be asymptotically stable if it is stable and, in addition, there exists a constant $c > 0$ such that if $|\bar{x} - x_0| < c$ then $|y(t, x_0) - \bar{x}| \to 0$ as $t \to \infty$.

Definition 7. *An equilibrium point $\bar{x}$ is said to be globally asymptotically stable if it is asymptotically stable and the domain of asymptotic stability $D_{\bar{x}} = \{x_0 \in$*

$\mathbb{R}^n : \lim_{t\to\infty} |y(t,x_0)-\bar{x}| = 0\} = \mathbb{R}^n$ *(i.e., every solution* $y(t,x_0)$ *of (2.1) possesses the property* $|y(t,x_0) - \bar{x}| \to 0$ *as* $t \to \infty$*).*

Theorem 2. *Suppose all the eigenvalues of* $D\,\mathbf{f}(\bar{x})$ *have negative real parts. Then the equilibrium point* $\bar{x}$ *of the system (2.1) is locally asymptotically stable, and unstable if at least one of the eigenvalues has positive real part.*

Theorem 3. *If* $\mathbf{f} : \mathbf{E} \to \mathbb{R}^{\mathbf{n}}$ *and an open set* $E \subset \mathbb{R}^n$*. Then* $\mathbf{f} \in C^1(E)$ *if and only if the partial derivatives* $\frac{\partial f_i}{\partial x_j}$*,* $i, j = 1, ..., n$*, exist and continuous on* E*.*

Theorem 4. *(The Stable Manifold Theorem).*
Let E *be an open subset of* $\mathbb{R}^n$ *containing the origin, let* $\mathbf{f} \in C^1(E)$*, and let* ϕ_t *be the flow of non-linear system (2.1). Suppose that* $\mathbf{f}(\mathbf{0}) = \mathbf{0}$ *and that* $D\,\mathbf{f}(\mathbf{0})$ *has* k *eigenvalues with negative real part and* $(n-k)$ *eigenvalues with positive real part. Then there exists a* k*-dimensional differentiable manifold* S *tangent to the stable subspace* E^s *of the linear system (2.3) at* $\mathbf{0}$ *such that for all* $t \geq 0$*,* $\phi_t(S) \subset S$ *and for all* $\bar{x} \in S$*.*

$$\lim_{t\to\infty} \phi_t(\bar{x}) = \mathbf{0};$$

and there exists an $(n-k)$ *dimensional differentiable manifold* U *tangent to the unstable subspace* E^u *of (2.3) at* $\mathbf{0}$ *such that for all* $t \leq 0$*,* $\phi_t(U) \subset U$ *and for all* $\bar{x} \in U$

$$\lim_{t\to-\infty} \phi_t(\bar{x}) = \mathbf{0}.$$

The above Theorem is a very important result describing some local qualitative behaviour of ordinary differential equations. The theorem refers S

and U as *local* stable and unstable manifolds of the origin respectively. The *global* stable and unstable manifolds of (2.1) at the origin are defined below:

Definition 8. *Let ϕ_t be the flow of the nonlinear system (2.1). The global stable and unstable manifolds of (2.1) at $\mathbf{0}$ are defined by*

$$W^s(\mathbf{0}) = \bigcup_{t \leq 0} \phi_t(S)$$

and

$$W^u(\mathbf{0}) = \bigcup_{t \geq 0} \phi_t(U)$$

respectively; $W^s(\mathbf{0})$ and $W^u(\mathbf{0})$ are also referred to as the global stable and unstable manifolds of the origin respectively. It can be shown that the global stable and unstable manifolds $W^s(\mathbf{0})$ and $W^u(\mathbf{0})$ are unique and that they are invariant with respect to the flow ϕ_t; furthermore, for all $x \in W^s(\mathbf{0})$, $\lim_{t \to \infty} \phi_t(x) = \mathbf{0}$ and for all $x \in W^u(\mathbf{0})$, $\lim_{t \to -\infty} \phi_t(x) = \mathbf{0}$.

The next Theorem (see, for example, (Perko, 2001)) shows the existence of an invariant centre manifold $W^c(\mathbf{0})$ tangent to E^c at $\mathbf{0}$.

Theorem 5. *(The Centre Manifold Theorem)*
Let E be an open subset of $\mathbb{R}^n$ containing the origin, let $\mathbf{f} \in C^r(E)$, and $r \geq 1$. Suppose that $\mathbf{f}(\mathbf{0}) = \mathbf{0}$ and that $D\,\mathbf{f}(\mathbf{0})$ has k eigenvalues with negative real part, j eigenvalues with positive real part, and $m = n - k - j$ eigenvalues with zero real part. Then there exists a m-dimensional centre manifold $W^c(\mathbf{0})$ of class C^r tangent to the centre subspace E^c of the linear system (2.3) at $\mathbf{0}$, there exists a k-dimensional stable manifold $W^s(\mathbf{0})$ of class C^r tangent to the stable

subspace E^s of the linear system (2.3) at $\mathbf{0}$ and there exists a j-dimensional unstable manifold $W^u(\mathbf{0})$ tangent to the unstable subspace E^u of (2.3) at $\mathbf{0}$; furthermore, $W^c(\mathbf{0})$, $W^s(\mathbf{0})$ and $W^u(\mathbf{0})$ are invariant under the flow ϕ_t of (2.1).

2.4 Liapunov Function

Liapunov function can be thought of as modified energy function. There is no general method to construct or find a Liapunov function which proves the stability of an equilibrium.

Definition 9. *Let $\mathcal{U}$ be a neighbourhood of $\bar{x}$. A function $V : \mathcal{U} \to \mathbb{R}$ is said to be a positive definite function if*

(i) $V(x) > 0$ for all $x \neq 0$,

(ii) $V(x) = 0$ if and only if $x = 0$,

(iii) $V(x) \to \infty$ as $x \to \infty$.

Theorem 6. *If there exists a positive definite function V such that $\dot{V} < 0$ outside M and $\dot{V} \leq 0$ on M, where M is a set which contains no entire trajectories apart from the point $\mathbf{0}$, then the equilibrium point $\mathbf{0}$ is asymptotically stable.*

Theorem 7. *Let $\bar{x}$ be an equilibrium point of (2.1) and let $V : \mathcal{U} \to \mathbb{R}$ be a C^1 function defined on some neighbourhood $\mathcal{U}$ of $\bar{x}$ such that*

(i) $V(\bar{x}) = 0$ and $V(x) > 0$ if $x \neq \bar{x}$.

(ii) $\dot{V}(x) \leq 0$ in $\mathcal{U} - \{\bar{x}\}$.

Then $\bar{x}$ is stable. Moreover, if

(iii) $\dot{V}(x) < 0$ *in* $\mathcal{U} - \{\bar{x}\}$

then $\bar{x}$ *is asymptotically stable.*

Furthermore, if $\mathcal{U}$ can be chosen to be all of $\mathbb{R}^n$, then $\bar{x}$ is said to be *globally asymptotically stable* (GAS), if (i) and (iii) hold. The idea is that if V is a Liapunov function then V decreases along trajectories, and hence (since V is strictly positive except at zero) trajectories tend to zero, which is a minimum value of V. Thus, any function V that satisfies the conditions in Theorem 7 is called a Liapunov function (Wiggins, 2003; Glendinning, 1994; Barbashin, 1970).

2.5 Invariance Principle

Since general epidemiology models monitor human populations, it is necessary to consider that associated population sizes can never be negative. Thus, epidemiological models should be considered in (feasible) regions where such property (non-negative) is preserved. Wiggins (2003), for example, gives the following definitions.

Definition 10. *A point* $x_0 \in \mathbb{R}^n$ *is called an* ω*-limit point of* $x \in \mathbb{R}^n$*, denoted by* $\omega(x)$*, if there exists a sequence* $\{t_i\}$*,* $t_i \to \infty$*, such that*

$$\phi(t_i, x) \to x_0.$$

Definition 11. *A point* $x_0 \in \mathbb{R}^n$ *is called an* α*-limit point of* $x \in \mathbb{R}^n$*, denoted by* $\alpha(x)$*, if there exists a sequence* $\{t_i\}$*,* $t_i \to -\infty$*, such that*

$$\phi(t_i, x) \to x_0.$$

Definition 12. *The set of all ω-limit points of a flow is called the ω-limit set. Similarly, the set of all α-limit points of a flow is called the α-limit set.*

Definition 13. *A set M is invariant if and only if for all $x \in M$, $\phi(x,t) \in M$ for all t. A set is positively (negatively) invariant if for all $x \in M$, $\phi(x,t) \in M$ for all $t > 0$ ($t < 0$) (Barbashin, 1970).*

Theorem 8. *(LaSalle Invariance Principle(LaSalle, 1968)).*
Suppose that the equilibrium point of system (2.1) $\bar{x} = 0$ and V is a Liapunov function on some neighbourhood $\mathcal{U}$ of $\bar{x} = 0$. If $x_0 \in \mathcal{U}$ has its forward trajectory bounded with limit points in $\mathcal{U}$ and M is the largest invariant set of

$$E = \{\bar{x} \in \mathcal{U} : \dot{V}(\bar{x}) = 0\},$$

then $\phi(x_0, t) \to M \quad \text{as} \quad t \to \infty$.

2.6 Non-existence of Periodic Orbit

Here, we give some criteria implying that there cannot be a periodic orbit in a given region. Such results are of interest in situations where there is an asymptotically stable equilibrium and wish to conclude that all orbits tend to it.

Theorem 9. *(Bendixson's Criterion).*
Suppose that $F_x(x,y) + G_y(x,y)$ is either strictly positive or strictly negative

in a simple connected region D. Then there is no period orbit of $\dot{x} = F(x, y)$, $\dot{y} = G(x, y)$ in D.

A more general result of this type is given the following theorem:

Theorem 10. *(Dulac's Criterion).*
Let $\beta(x, y)$ be continuously differentiable and suppose that

$$\frac{\partial(\beta(x,y)F(x,y))}{\partial x} + \frac{\partial(\beta(x,y)G(x,y))}{\partial y}$$

is either strictly positive or strictly negative in a simple connected region D. Then there is no period orbit of $\dot{x} = F(x, y)$, $\dot{y} = G(x, y)$ in D.

Theorem 11. *(Poincaré-Bendixson).*
Let M be a positively invariant region for the vector field containing a finite number of fixed points. Let $p \in M$, and consider $\omega(p)$. Then one of the following possibilities holds.
i) $\omega(p)$ is a fixed point;
ii) $\omega(p)$ is a closed orbit;
iii) $\omega(p)$ consists of a finite number of fixed points $p_1, ..., p_n$ and orbits γ with $\alpha(\gamma) = p_i$ and $\omega(\gamma) = p_j$.

2.7 Analytical Derivation of $\mathcal{R}_0$

Heffernan et al. (2005) recently reviewed *the basic reproduction number* $\mathcal{R}_0$ in a broader context, which includes various methods currently in use for the derivation of $\mathcal{R}_0$ and an overview of the recent use of $\mathcal{R}_0$ in assessing emerg-

ing and re-emerging infectious diseases. In compartmental models of disease transmission, there are two methods mainly used for the analytical derivation of $\mathcal{R}_0$: namely, survival function (Heesterbeek and Dietz, 1996) and next generation method (see, Diekmann et al., 1990; Diekmann and Heesterbeek, 2000; van den Driessche and Watmough, 2002). The latter method is used in this thesis and a brief description of it is given below.

Let us assume that there are n compartments of which m are infected. We define the vector $x = x_i,\ i = 1, ..., n$, where x_i denotes the number or proportion of individuals in the ith compartment. Let $\mathcal{F}_i(x)$ be the rate of appearance of new infections in compartment i and let $\mathcal{V}_i(x) = \mathcal{V}_i^-(x) - \mathcal{V}_i^+(x)$, where $\mathcal{V}_i^+$ is the rate of transfer of individuals into compartment i by all other means and $\mathcal{V}_i^-$ is the rate of transfer of individuals out of the ith compartment.

$$\dot{x}_i = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x). \tag{2.4}$$

Note that $\mathcal{F}_i(x)$ should include only infections that are newly arising, but does not include terms which describe the transfer of infectious individuals from one infected compartment to another. Assuming that $\mathcal{F}_i$ and $\mathcal{V}_i$ satisfy the following axioms outlined by Diekmann et al. (1990) and van den Driessche and Watmough (2002). Let $X_s = \{x \geq 0 | \, x_i = 0, \quad i = 1, ..., m\}$ be the disease-free states (non-infected state variables) of the model, where $x = (x_1, ..., x_m)$, $x \geq 0$.

(A1) if $x \geq 0$, then $\mathcal{F}_i,\ \mathcal{V}_i^+,\ \mathcal{V}_i^- \geq 0$ for $i = 1, ..., m$.

(A2) if $x = 0$, then $\mathcal{V}_i^- = 0$. In particular, if $x \in X_s$ then $\mathcal{V}_i^-$ for $i = 1, ..., m$.

(A3) $\mathcal{F}_i = 0$ if $i > m$

(A4) if $x \in X_s$, then $\mathcal{F}_i(x) = 0$ and $\mathcal{V}_i^+ = 0$ for $i = 1, ..., m$.

(A5) if $\mathcal{F}(x)$ is set to zero, then all eigenvalues of $D\,f(x_0)$ have negative real parts, where $D\,f(x_0)$ is the Jacobian matrix evaluated at the DFE x_0.

Definition 14. *(M-Matrix) An $n \times n$ matrix A is an M-matrix if and only if every off-diagonal entry of A is non-positive and the diagonal entries are all positive.*

Lemma 1. *If x_0 is a DFE of (2.4) and $f_i(x)$ satisfies $(A1)$-$(A5)$, then the derivatives $D\,\mathcal{F}(x_0)$ and $D\,\mathcal{V}(x_0)$ are partitioned as*

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

where F and V are the $m \times m$ matrices defined by

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0)\right], \quad V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0)\right], \quad \textit{with} \quad 1 \leq i, j \leq m.$$

Further, F is non-negative, V is a non-singular M-matrix and all eigenvalues of J_4 have positive real part.

Following Diekmann et al. (1990), $F\,V^{-1}$ is called the next generation matrix for the model (2.4) and set

$$\mathcal{R}_0 = \rho(F\,V^{-1}), \tag{2.5}$$

where ρ is the spectral radius (dominant eigenvalue) of the matrix $F\,V^{-1}$.

Theorem 12. *Consider the disease transmission model given by (2.4) with $f(x)$ satisfying conditions $(A1)$-$(A5)$. If x_0 is a DFE of the model, then x_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$, but unstable if $\mathcal{R}_0 > 1$, where $\mathcal{R}_0$ is defined by (2.5).*

2.8 Bifurcation Theory

A study of changes in the qualitative structure of the flow of a differential equation as parameters are varied is called bifurcation theory. The parameter where bifurcation occurs are called bifurcation values. There are various types of bifurcations, including saddle-node, transcritical, pitchfork, Hopf, backward, etc. Guckenheimer and Holmes (2002); Wiggins (2003); Ruelle (1989) dealt with bifurcation theory in great detail. However, only two types of these bifurcations are related to this thesis; namely, forward and backward bifurcations. Castillo-Chavez and Song (2004), based on the general centre manifold theory, proved an important result which we need in Chapter 4 of this thesis. Thus, the result is mentioned below without proof.

Consider a general system of ODEs with a parameter ϕ:

$$\dot{x} = f(x, \phi), \quad f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n \text{ and } f \in C^2(\mathbb{R}^n \times \mathbb{R}). \tag{2.6}$$

Without loss of generality, it is assumed that 0 is an equilibrium for system (2.6) for all values of the parameter ϕ, that is

$$f(0, \phi) \equiv 0 \quad \text{for all } \phi.$$

Theorem 13. *Assume*

B1: $A = D_x f(0,0) = \frac{\partial f_i}{\partial x_j}(0,0)$ *is the linearization matrix of system (2.6) around the equilibrium* 0 *with* ϕ *evaluated at* 0. *Zero is a simple eigenvalues of* A *and all other eigenvalues of* A *have negative real part;*

B2: *Matrix* A *has a nonnegative right eigenvector* w *and a left eigenvector* v *corresponding to the zero eigenvalue.*

Let f_k *be the* k*th component of* f *and*

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0), \tag{2.7a}$$

$$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0). \tag{2.7b}$$

The local dynamics of system (2.7) around 0 *are totally determined by* a *and* b.

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

(ii) $a < 0$, $b < 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is unstable; when* $0 < \phi \ll 1$, 0 *is locally asymptotically stable, and there exists a positive unstable equilibrium;*

(iii) $a > 0$, $b < 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is unstable, and there exists a*

locally asymptotically stable negative equilibrium; when $0 < \phi \ll 1$, 0 *is stable, and a positive unstable equilibrium appears;*

(iv) $a < 0$, $b > 0$. *When* ϕ *changes from negative to positive,* 0 *changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.*

The results of Theorem 13 are summarized in the Table 2.1.

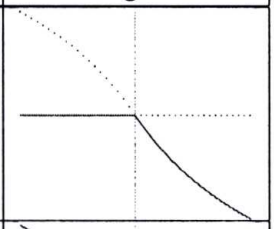
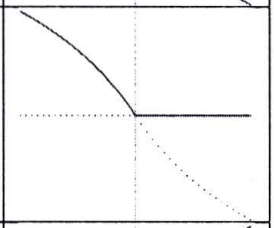
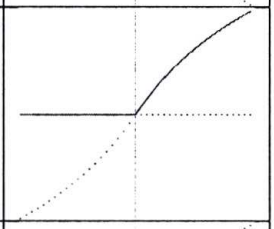
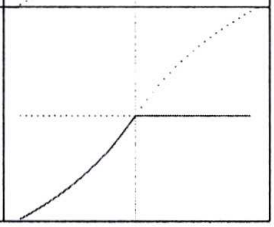
a and b	stability of 0	stability and sign of x^*	diagram
$a > 0, b > 0$	$\phi < 0$, S $\phi > 0$, U	$\phi < 0, x^* > 0$, U $\phi > 0, x^* < 0$, S	
$a < 0, b < 0$	$\phi < 0$, U $\phi > 0$, S	$\phi < 0, x^* > 0$, S $\phi > 0, x^* < 0$, U	
$a < 0, b > 0$	$\phi < 0$, S $\phi > 0$, U	$\phi < 0, x^* < 0$, U $\phi > 0, x^* > 0$, S	
$a > 0, b < 0$	$\phi < 0$, U $\phi > 0$, S	$\phi < 0, x^* < 0$, S $\phi > 0, x^* > 0$, U	

Figure 2.1: In the bifurcation diagrams, the vertical axis represents equilibrium points x^*, and the horizontal axis is the parameter ϕ. Solid lines and dashed lines symbolize stable (S) and unstable (U), respectively.

Corollary 1.

When $a > 0$ and $b > 0$, the bifurcation at $\phi = 0$ is subcritical (backward).

2.9 System of Reaction–Diffusion Equations

Consider the following system

$$\begin{aligned} u_t &= d_1 \Delta u + u\, M(u,v), \\ v_t &= d_2 \Delta v + v\, N(u,v), \quad (t,x) \in \mathbb{R}_+ \times \Omega, \end{aligned} \tag{2.8}$$

which satisfy the initial condition $(u(0,x), v(0,x)) = (u_0(x), v_0(x))$, $x \in \Omega$, together with the boundary condition

$$\partial u/\partial n \equiv \hat{n}.\nabla u = 0, \quad \partial v/\partial n = 0, \quad (t,x) \in \mathbb{R}_+ \times \partial\Omega. \tag{2.9}$$

where Ω is a bounded domain in $\mathbb{R}^n$ and $\hat{n}$ denote an outward pointing normal. We have the following result about the stability of the system (2.8).

Theorem 14. *(Conway and Smoller, 1977)*

Suppose that $M_v(u,v) < 0$, $N_u(u,v) > 0$ and $(\bar{u}, \bar{v}) \neq (0,0)$ be a nondegenerate rest point of the vector field $F(u,v) = (u\, M(u,v), v\, N(u,v))$ which lies on the u or v axis. Then the eigenvalues of the linearization at $(\bar{u}, \bar{v})$ are both real, and if they are both negative, $u \equiv \bar{u}$ and $v \equiv \bar{v}$ is a stable solution of the system (2.8), in the sense that there is a rectangle R in $u \geq 0$, $v \geq 0$ containing $U = (u,v)$ such that if the initial data $(u_0(x), v_0(x)) \in R$ for all $x \in \Omega$, then the corresponding solution of (2.8) decays exponentially to $(\bar{u}, \bar{v})$, uniformly in

$x \in \Omega$, as $t \to \infty$. Conversely, if $(\bar{u}, \bar{v})$ is a stable solution of (2.8), then the eigenvalues of the linearization at $(\bar{u}, \bar{v})$ are both negative.

2.9.1 Contracting Rectangles

Following the papers of Rauch and Smoller (1978) and Mimura (1979), we require the following definitions and lemmas:

Definition 15. *A bounded convex set $R \subset \mathbb{R}^n$ is contracting for the vector field $G(J)$ if for every point $J \in \partial R$ and every outward unit normal $\mathbf{n}$ at J, $G(J).\mathbf{n} < 0$.*

Definition 16. *A bounded rectangle Q is called semi-contracting for a given vector field $F(U)$, if there exists some positive constant η such that*

$$F(U).n_1 < -\eta \text{ for } U \in \partial Q_1$$

and

$$F(U).n_2 = 0 \text{ for } U \in \partial Q_2,$$

where ∂Q_1 is the sub-boundary of ∂Q which consists of the upper, left and right hand sides, ∂Q_2 of the lower and n_i are unit outer normal vectors to ∂Q_i for $i = 1, 2$.

Chapter 3

Role of public health education program on HIV transmission dynamics

3.1 Introduction

A number of mathematical models have been designed and used to study the impact of preventive control strategies on the spread of HIV/AIDS in given populations. Some of these studies have shown that a change in risky behaviour is necessary to prevent raging HIV/AIDS prevalence, even in the presence of a vaccine and/or treatment (see, for instance, Anderson (1988); Blower and Dowlatabadi (1994); Del Valle et al. (2004); Kribs-Zaleta and Halesco-Hernandez (2000)). Anderson (1988) predicts rapid transmission of HIV when the infected individuals engage in risky behaviours. Smith and Blower (2004) reported that disease-modifying vaccines will reduce HIV transmission if they

cause a reduction of 1.5 log_{10} copies/mL or more in viral load and if risky behaviours do not increase. The studies mentioned above tend to emphasize the use of pharmaceutical interventions (such as vaccine and ARVs), which are not readily and widely available (especially in resource-poor nations, which constitute the vast majority of the global HIV prevalence). Thus, it is instructive to study models that focus on non-pharmaceutical interventions, such as the use of public health education campaign. A few modelling studies, such as those by Mukandavire et al. (2009); Mukandavire and Garira (2007); Del Valle et al. (2004), have investigated the impact of public health educational campaigns on the transmission dynamics of HIV/AIDS in some populations. The purpose of the current study is to extend some of the aforementioned studies, by designing and analyzing a new comprehensive model, for HIV transmission in a population, that incorporates the role of public health education campaign (and using the model to evaluate the impact of some targeted public health education strategies).

3.2 Model Formulation

The total population at time t, denoted by $N(t)$, is sub-divided into the following mutually exclusive sub-populations: uneducated susceptible individuals ($S_u(t)$), educated susceptible individuals ($S_e(t)$), uneducated infected individuals with no AIDS symptoms ($I_u(t)$), educated infected individuals with no AIDS symptoms ($I_e(t)$), uneducated infected individuals with AIDS symptoms ($A_u(t)$) and educated infected individuals with AIDS ($A_e(t)$). Here,

(un)educated means individuals who (do not) receive proper public health education or counseling against risky practices that may result in HIV infection. The model takes the form of the following deterministic system of nonlinear differential equations:

$$\begin{aligned}
\frac{dS_u}{dt} &= \Pi(1-p) - \xi S_u - [\lambda_u + (1-\kappa)\lambda_e]S_u - \mu S_u, \\
\frac{dS_e}{dt} &= \Pi p + \xi S_u - (1-\epsilon)[\lambda_u + (1-\kappa)\lambda_e]S_e - \mu S_e, \\
\frac{dI_u}{dt} &= [\lambda_u + (1-\kappa)\lambda_e]S_u - \sigma_u I_u - \mu I_u - \psi_1 I_u, \\
\frac{dA_u}{dt} &= \sigma_u I_u - \psi_2 A_u - \mu A_u - \delta_u A_u, \\
\frac{dI_e}{dt} &= (1-\epsilon)[\lambda_u + (1-\kappa)\lambda_e]S_e + \psi_1 I_u - \sigma_e I_e - \mu I_e, \\
\frac{dA_e}{dt} &= \sigma_e I_e + \psi_2 A_u - \mu A_e - \delta_e A_e,
\end{aligned} \tag{3.1}$$

where,

$$\lambda_u = \frac{\beta(I_u + \eta_u A_u)}{N} \quad \text{and} \quad \lambda_e = \frac{\beta(I_e + \eta_e A_e)}{N}.$$

The rates λ_u and λ_e above are the *forces of infection* associated with HIV transmission by uneducated (at the rate λ_u) and educated (at the rate λ_e) infected individuals, respectively. The parameter β is the effective contact

rate (that is, contact that may result in HIV infection), while the parameters $\eta_u > \eta_e > 1$ account for the relative infectiousness of individuals with AIDS symptoms in comparison to the corresponding infected individuals with no AIDS symptoms. Unlike in the other related modelling studies, such as those by Mukandavire et al. (2009); Mukandavire and Garira (2007); Del Valle et al. (2004), this study allows for the transmission of HIV by individuals with AIDS symptoms (in line with Elbasha and Gumel (2006) and also Garba and Gumel (2010)).

Recruitment into the sexually-active population occurs at a rate Π (all newly-recruited individuals are assumed to be susceptible to HIV infection), and a fraction, p, of these newly-recruited sexually-active individuals are assumed to be educated about the risks and consequences of the HIV disease. Uneducated susceptible individuals (excluding the newly-recruited individuals) receive education about safer sex practices at a rate ξ. Susceptible people acquire infection following effective contact with infected individuals (at the rates λ_u and λ_e). It is assumed that educated infected individuals (in I_u or A_u class) modify their behaviour positively, thereby reducing their risk of HIV transmission by a factor κ, with $0 < \kappa < 1$. In other words, it is assumed that HIV-infected individuals that received public health education transmit the disease at a lower rate in comparison to uneducated HIV infected individuals. Educated susceptible individuals acquire infection at a reduced rate $(1-\epsilon)[\lambda_u+(1-\kappa)\lambda_e]$, where $0 < \epsilon < 1$ is the efficacy of public health education in preventing new infection of educated susceptible individuals.

Uneducated infected individuals progress to AIDS at a rate σ_u, while

educated infected individuals progress at a reduced rate $\sigma_e < \sigma_u$ (in other words, infected individuals who received public health education progress to AIDS at a slower rate in comparison to those who do not). Uneducated infected individuals without AIDS symptoms (I_u) are educated at a rate ψ_1, and move to the corresponding educated infected class (I_u). Individuals in all classes suffer natural death at a rate μ. Additionally, individuals with AIDS die at a rate δ_u (for the uneducated class) or δ_e (for the educated class) such that $\delta_e < \delta_u$. Thus, it is assumed that AIDS patients who received public health education die due to AIDS at a slower rate than the AIDS patients who do not. Uneducated individuals with symptoms of AIDS (A_u) are educated at a rate ψ_2, and move to the corresponding educated class (A_e). A schematic diagram of the model is depicted in Figure 3.1, and the associated variables and parameters are described in Table 3.1.

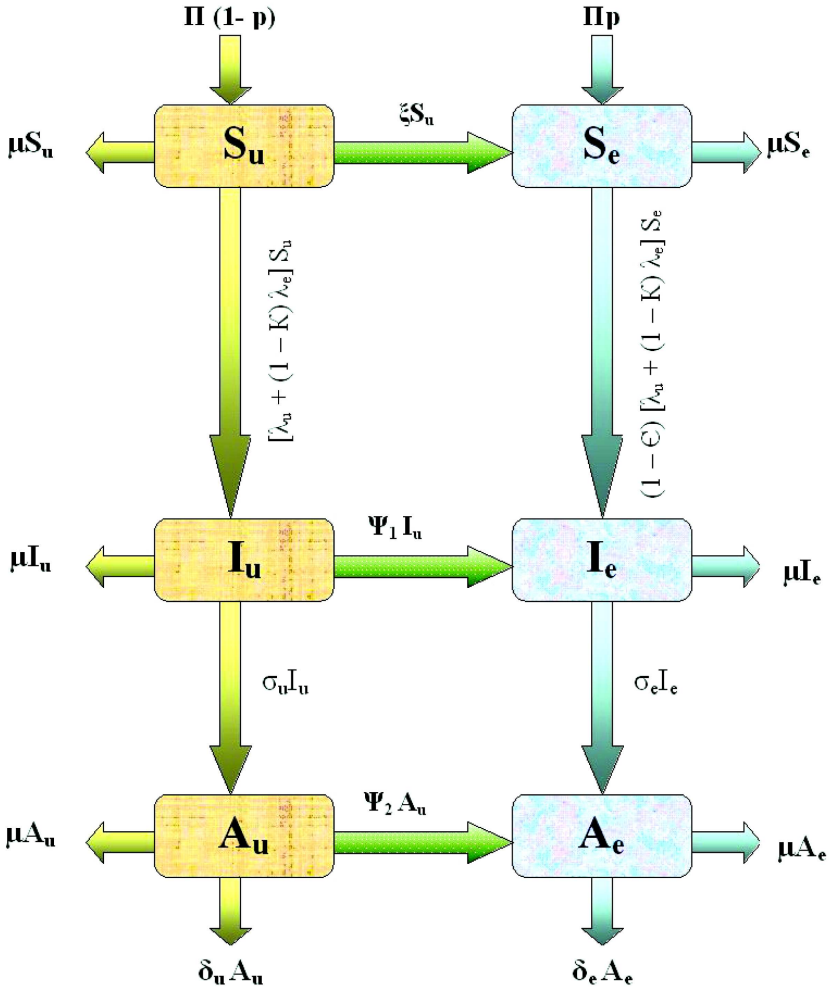


Figure 3.1: Schematic Diagram of the Model (3.1)

The model (3.1) is an extension of the models by Mukandavire et al. (2009); Mukandavire and Garira (2007); Del Valle et al. (2004), by

(i) allowing for HIV transmission by the individuals with AIDS symptoms;

(ii) offering public health education to all infected individuals (except for the education of high-risk people with AIDS in Mukandavire and Garira

(2007); public health education is only restricted to susceptible individuals in Mukandavire et al. (2009); Del Valle et al. (2004));

(iii) stratifying the infected population in terms of whether or not they received public health education (and those who received public health education are assumed to transmit HIV at a lower rate, as well as progress to AIDS and die at a slower rate, in comparison to those who do not receive public health education).

(iv) The model extends the model by Garba and Gumel (2010) by including a class of susceptible individuals who receive public health education, educating a fraction of newly-recruited sexually-active individuals and allowing infection of educated susceptible individuals. Furthermore, in this study, the infected individuals who received public health education progress to AIDS at a slower rate in comparison to those who do not.

In addition to the aforemention extensions, this study will contribute to the literature by giving detailed qualitative analysis of the model (3.1).

Variables	Description
N	Adult population
S_u	Uneducated susceptible individuals
S_e	Educated susceptible individuals
I_u	Uneducated infecteds with no AIDS symptoms
I_e	Educated infecteds with no AIDS symptoms
A_u	Uneducated infecteds with AIDS symptoms
A_e	Educated infecteds with AIDS symptoms
λ_u	Force of infection of uneducated individuals
λ_e	Force of infection of educated individuals

Parameters	Description
Π	Recruitment rate of susceptibles
μ	Natural mortality rate
δ_u, δ_e	Disease-induced mortality rates
p	Fraction of educated newly-recruited individuals
ξ	Rate of educating susceptibles
ψ_1, ψ_2	Education rates of individuals in I_u and A_u classes
β	Effective contact rate
η_u, η_e	Modification parameters
ϵ	Efficacy of education in preventing infection
$1-\kappa$	Reduction in transmissibility of educated individuals
σ_u, σ_e	Progression rates to AIDS classes

Table 3.1: Description of Variables and Parameters of the Model (3.1).

Parameters	Nominal value	References
δ_u, δ_e	$0.47, 0.04$	Gumel et al. (2006)
p, ξ	$0.5,\ 0.5$	Assume
ψ_1, ψ_2	$0.5,\ 0.5$	Assume
β	0.4	Elbasha and Gumel (2006)
η_u, η_e	$1.5, 1.2$	Sharomi and Gumel (2008)
ϵ	0.8	Karen and Susan (1999)
$1-\kappa$	0.3	Assumed
σ_u, σ_e	$2.6,\ 1/15$	Gumel et al. (2006); Hyman et al. (1999);

Table 3.2: Epidemiological Data for Model (3.1).

3.2.1 Model Fitting

To test the suitability of the model (3.1) to effectively enable the assessment of targeted public health education strategies against HIV spread in a population, the model is fitted using data from Uganda as follows. The average lifespan of a Ugandan $(1/\mu)$ is assumed to be 50 years (Uganda Bureau of Statistics Census, 1991) and the recruitment rate (Π) is estimated at 3.2% of the total population (Uganda Bureau of Statistics Census, 1991). The total population of Uganda, as of 1990, given by N=16.7 millions (Uganda Bureau of Statistics Census, 1991) is used. The initial conditions used are as follows: $S_u(0) = 14$ million, $S_e(0) = 0.4121$ million, $I_u(0) = 2$ million, $A_u(0) = 0.2$ million, $I_e(0) = 0.087$ million, and $A_e(0) = 0.0009$ million. Thus, the total

initial HIV-infected population (i.e., $I_u(0) + A_u(0) + I_e(0) + A_e(0)$) is 2.2879 million (UNAIDS, 2008), corresponding to 13.7% of the total population. The associated epidemiological data is presented in Table 3.2.

Using the aforementioned data, the model (3.1) gives a very good fit of the Ugandan HIV/AIDS data for the period 1990-2007 (UNAIDS/WHO/Unicef, 2008), as depicted in Figure 3.2. Furthermore, to qualitatively assess the closeness of the model against the real data, Ordinary Least Squares (OLS) approach is employed (Kendall and Stuart, 1979). This entails regressing the actual observed data on predicted cases from the model as follows.

Let y_{obs} denotes the observed data. Then, the model prediction ($\hat{y}_{pred}$) is evaluated using the OLS regression equation:

$$y_{obs} = \alpha_0 + \alpha_1 \hat{y}_{pred} + \varepsilon, \tag{3.2}$$

where α_0 and α_1 represent the intercept and slope of the regression line, respectively; and ε account for the random error. The model is said to be "perfect" if the coefficients $\alpha_0 = 0$ and $\alpha_1 = 1$ and the coefficient of determination $R^2 = 1$ (which measures the proportion of variation in the y_{obs}). Using MATLAB's Statistical Toolbox, we obtained $\alpha_0 = 0.0636$ and $\alpha_1 = 0.9603$ (with their corresponding 95% confidence intervals [0.0261 0.1012] and [0.9380 0.9826], respectively) and $R^2 = 0.9981$ for the above initial data and parameter values in Table 3.2 and 3.3. Thus, the OLS regression analysis confirms the closeness of the fit. Hence, the model (3.1) can be used to gain realistic insight into HIV transmission dynamics in the presence of public health education campaign.

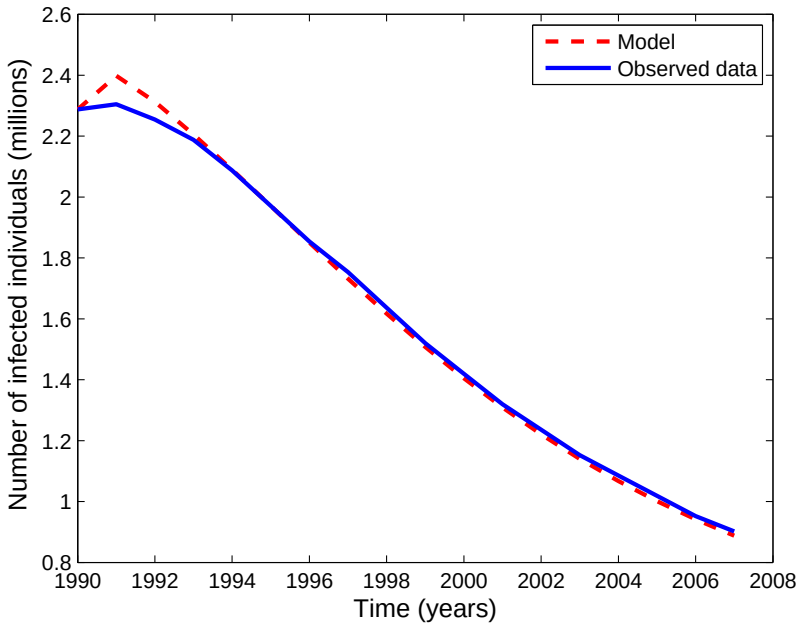


Figure 3.2: Comparison of observed HIV/AIDS data from Uganda (solid lines) and model prediction (dashed line). Parameter values used are as in Table 3.2 with ξ=0.01, $\psi_1 = \psi_2$=0.001, p=0.3, and β=0.325.

3.3 Basic properties

Since the model (3.1) monitors human population, all its associated parameters and state variables are assumed to be non-negative for all $t \geq 0$. Before analysing the model, it is instructive to show that the state variables of the model remain non-negative for all non-negative initial conditions. Thus, we claim the following result.

Table 3.3: 2002 Demographic of Data Used as Initial Conditions.

Demographic Parameters	India (millions)	Nigeria (millions)	China (millions)	Ethiopia (millions)	Russia (millions)	References
$N(0)$	1025.1	116.9	1285	64.5	144.7	United Nations (2004)
$1/\mu$	64 (years)	52 (years)	71 (years)	53 (years)	66 (years)	United Nations (2004)
Π	1.51%	2.54%	0.87%	2.64%	0.33%	CIA (2002)
$S_u(0)$	1010	110	800	60	100	Assumed
$S_e(0)$	10	3.3	483.75	1.5	43.84	Assumed
Infecteds	5.1	3.6	1.25	3	0.86	CIA (2008)
$I_u(0)$	3	2	1	2	0.7	Assumed
$I_e(0)$	1	1	0.1	0.4	0.1	Assumed
$A_u(0)$	1	0.5	0.1	0.4	0.05	Assumed
$A_e(0)$	0.1	0.1	0.05	0.2	0.01	Assumed

Lemma 2. *The closed set*

$$\mathcal{D} = \left\{ (S_u, S_e, I_u, A_u, I_e, A_e) \in \mathbb{R}^6_+ : N \leq \frac{\Pi}{\mu} \right\}$$

is positively-invariant and attracting with respect to the model (3.1).

Proof. Adding all the equations in the model (3.1) gives:

$$\frac{dN}{dt} = \Pi - \mu N - \delta_e A_e - \delta_u A_u, \quad \text{where} \quad N = S_u + I_u + A_u + S_e + I_e + A_e.$$

Since $\frac{dN(t)}{dt} \leq \Pi - \mu N$, it follows that $\frac{dN(t)}{dt} < 0$ if $N(t) > \frac{\Pi}{\mu}$. Thus, from standard comparison theorem (Hsieh and Sibuya, 1999; Lakshmikantham et al., 1989), $N(t) \leq N(0)e^{-\mu t} + \Pi/\mu(1 - e^{-\mu t})$. In particular, $N(t) \leq \Pi/\mu$ if $N(0) \leq \Pi/\mu$. Thus, $\mathcal{D}$ is positively-invariant. Further, if $N(t) > \frac{\Pi}{\mu}$, then either the solution enters $\mathcal{D}$ in finite time, or $N(t)$ approaches Π/μ. Hence, $\mathcal{D}$ is attracting (i.e., all solutions in $\mathbb{R}^6_+$ eventually approach, enter or stay in $\mathcal{D}$). □

Therefore, the model is mathematically well-posed and epidemiologically reasonable, since all the variables remain nonnegative for all $t \geq 0$. Hence, it is sufficient to consider the dynamics of the model (3.1) in $\mathcal{D}$ (Hethcote, 2000).

3.4 Analysis of sub-model

In this section, all education-related parameters and variables are set to zero in order to understand the dynamical behaviour of education-free sub-model

(i.e., model (3.1) without education). By setting $I_e = A_e = p = \xi = \epsilon = \kappa = \sigma_e = \psi_1 = \psi_2 = 0$ in (3.1), education-free model is obtained as follows:

$$\begin{aligned} \frac{dS_u}{dt} &= \Pi - (\lambda_u + \mu)S_u \\ \frac{dI_u}{dt} &= \lambda_u S_u - (\sigma_u + \mu)I_u \\ \frac{dA_u}{dt} &= \sigma_u I_u - (\mu + \delta_u)A_u \end{aligned} \tag{3.3}$$

where, $\lambda_u = \dfrac{\beta(I_u + \eta_u A_u)}{N_u}$ with $N_u = S_u + I_u + A_u$. For this model, it can be shown, by using similar argument as above, that the region

$$D_u = \{(S_u, I_u, A_u,) \in \mathbb{R}^3_+ : N_u \leq \frac{\Pi}{\mu}\}$$

is attracting and positively-invariant. Thus, the dynamics of the model will be considered in D_u.

3.4.1 Local stability of Disease-free equilibrium (DFE)

The disease-free equilibrium of (3.3) is

$$Y_0 = (S_u^*, I_u^*, A_u^*) = (\frac{\Pi}{\mu}, 0, 0).$$

It can be seen that Y_0 attracts the region (stable manifold of Y_0)

$$D_u = \{(S_u, I_u, A_u,) \in \mathbb{R}^3_+ : N_u \leq \frac{\Pi}{\mu}\}.$$

By using the next generation method (see, Section 2.7), the matrices F and V for the new infection terms and the remaining transfer terms respectively, are given by

$$F = \begin{pmatrix} \beta \frac{S_u^*}{N_u^*} & \beta \eta_u \frac{S_u^*}{N_u^*} \\ 0 & 0 \end{pmatrix},$$

and

$$V = \begin{pmatrix} \sigma_u + \mu & 0 \\ -\sigma_u & \mu + \delta_u \end{pmatrix}.$$

It follows that the reproduction number, denoted by R_0, is given by

$$\mathcal{R}_0 = \rho(FV^{-1}) = \frac{\beta[\mu + \delta_u + \eta_u \sigma_u]}{(\sigma_u + \mu)(\mu + \delta_u)}$$

Lemma 3. *The DFE, Y_0, of the education-free model is locally asymptotically stable (LAS) if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.*

The quantity $\mathcal{R}_0$ is the reproduction number which measures the average number of new cases of HIV infection generated by a single HIV infected individual in a totally uneducated population.

3.4.2 Global stability of DFE

Theorem 15. *The DFE, Y_0, of the education-free model is globally asymptotically stable (GAS) whenever $\mathcal{R}_0 < 1$.*

Proof.

Consider the following Liapunov function:

$$\mathcal{F} = \beta I_u(\mu + \delta_u + \sigma_u\eta_u) + \beta\eta_u A_u(\mu + \sigma_u),$$

with Liapunov derivative given by (where a dot represents differentiation with respect to t)

$$\begin{aligned}
\dot{\mathcal{F}} &= \beta\dot{I}_u(\mu + \delta_u + \sigma_u\eta_u) + \beta\eta_u\dot{A}_u(\mu + \sigma_u) \\
&= \beta[\lambda_u S_u - (\sigma_u + \mu)I_u](\mu + \delta_u + \sigma_u\eta_u) + \beta\eta_u[\sigma_u I_u - (\mu + \delta_u)A_u](\mu + \sigma_u) \\
&= \beta\lambda_u S_u(\mu + \delta_u + \sigma_u\eta_u) - \beta(\mu + \delta_u)(\mu + \sigma_u)[I_u + \eta_u A_u] \\
&= \beta\lambda_u S_u(\mu + \delta_u + \sigma_u\eta_u) - (\mu + \delta_u)(\mu + \sigma_u)\lambda_u N_u \\
&= \lambda_u N_u(\mu + \delta_u)(\mu + \sigma_u)\left(\frac{\beta S_u(\mu + \delta_u + \sigma_u\eta_u)}{(\mu + \delta_u)(\mu + \sigma_u)N_u} - 1\right) \\
&\leq \lambda_u N_u(\mu + \delta_u)(\mu + \sigma_u)\left(\frac{\beta(\mu + \delta_u + \sigma_u\eta_u)}{(\mu + \delta_u)(\mu + \sigma_u)} - 1\right); \quad \text{since} \quad S_u \leq N_u \\
&= \beta(I_u + \eta_u A_u)(\mu + \delta_u)(\mu + \sigma_u)(\mathcal{R}_0 - 1) \leq 0 \quad \text{for} \quad \mathcal{R}_0 < 1.
\end{aligned}$$

Since all the model parameters are assumed to be non-negative, it follows that

$\dot{\mathcal{F}} \leq 0$ if $\mathcal{R}_0 < 1$ with $\dot{\mathcal{F}} = 0$ if and only if $I_u = A_u = 0$. Hence, $\dot{\mathcal{F}}$ is a Liapunov function on D_u. At DFE $S_u \to \Pi/\mu$ as $t \to \infty$. Since D_u is invariant and attracting, it follows that the largest compact invariant set in $\{(S_u, I_u, A_u,) \in D_u : \dot{\mathcal{F}} = 0\}$ is the singleton $\{Y_0\}$. Therefore, by the LaSalle Invariance Principle (LaSalle, 1968), every solution to the equations in the education-free model (3.3), with initial conditions in D_u, approaches D_u as $t \to \infty$. □

This result shows that HIV will be eliminated from the community within a certain period of time if the threshold $\mathcal{R}_0 < 1$.

3.4.3 Existence of endemic equilibrium

The education-free model has a unique positive endemic equilibrium point (EEP), where at least one of the infected components (I_u *or* A_u) is non-zero, given by $Y^{**} = (S_u^{**}, I_u^{**}, A_u^{**})$. To establish this, the equations in model (3.3) are solved in terms of the force of infection at steady-state (λ_u^{**}), given by

$$\lambda_u^{**} = \frac{\beta(I_u^{**} + \eta_u A_u^{**})}{N_u^{**}}. \tag{3.4}$$

Setting the right hand sides of the model to zero gives

$$S_u^{**} = \frac{\Pi}{\lambda_u^{**} + \mu}, \; I_u^{**} = \frac{\Pi\lambda_u^{**}}{(\lambda_u^{**} + \mu)(\sigma_u + \mu)}, \; A_u^{**} = \frac{\sigma_u \Pi\lambda_u^{**}}{(\delta + \mu)(\lambda_u^{**} + \mu)(\sigma_u + \mu)} \tag{3.5}$$

substituting the expressions in equation (3.5) into equation (3.4), and simplify, gives

$$a_{11}\lambda_u^{**} - a_{12} = 0, \tag{3.6}$$

where,

$$a_{11} = \mu + \delta_u + \sigma_u, \quad a_{12} = (\mathcal{R}_0 - 1)(\sigma_u + \mu)(\delta + \mu).$$

Since all the parameters are nonnegative the $a_{11} > 0$, and $a_{12} > 0$ for $\mathcal{R}_0 > 1$. Thus, the linear system (3.6) has a unique positive solution, given by $\lambda_u^{**} = \frac{a_{12}}{a_{11}}$, whenever $\mathcal{R}_0 > 1$. Further, $a_{12} < 0$ whenever $\mathcal{R}_0 < 1$, thus, if $\mathcal{R}_0 < 1$ then the force of infection at steady-state (λ_u^{**}) is negative. Hence, the model has no positive equilibria in this case. These results are summarized as follows:

Lemma 4. *The education-free model (3.3) has a unique positive endemic equilibrium wherever* $\mathcal{R}_0 > 1$, *and no positive endemic equilibrium whenever* $\mathcal{R}_0 < 1$.

Global stability of the endemic equilibrium

The lemma 4 shows the existence of a unique endemic equilibrium if $\mathcal{R}_0 > 1$. Now study the global stability of the unique positive endemic equilibrium

$$Y^{**} = (S_u^{**}, I_u^{**}, A_u^{**})$$

when the disease-induced mortality rate is negligible. We claim the following:

Theorem 16. *The endemic equilibrium of education-free model (3.3) with* $\delta_u = 0$ *is globally asymptotically stable (GAS) in* $D_u \setminus Y_0$ *whenever* $\mathcal{R}_0 > 1$.

Proof. Since $S_u = N_u - I_u - A_u$ and $N_u \to \Pi/\mu$ as $t \to \infty$, substituting these in last two equations of model (3.3) with $\delta_u = 0$ gives

$$\begin{aligned} \frac{dI_u}{dt} &= \lambda_u[\Pi/\mu - I_u - A_u] - (\sigma_u + \mu)I_u \\ \frac{dA_u}{dt} &= \sigma_u I_u - \mu A_u \end{aligned} \tag{3.7}$$

which forms a system in $D_1 = \{I_u > 0,\ A_u > 0,\ I_u + A_u \leq \Pi/\mu\}$. Using the Dulac's multiplier $1/I_u A_u$, it follows that

$$\begin{aligned} \frac{\partial}{\partial I_u}\left(\frac{\dot{I}_u}{I_u A_u}\right) + \frac{\partial}{\partial A_u}\left(\frac{\dot{A}_u}{I_u A_u}\right) &= \frac{\partial}{\partial I_u}\left[\frac{1}{I_u A_u}\left(\lambda_u(\Pi/\mu - I_u - A_u) - (\sigma_u + \mu)I_u\right)\right] \\ &\quad + \frac{\partial}{\partial A_u}\left(\frac{1}{I_u A_u}(\sigma_u I_u - \mu A_u)\right) \\ &= -\frac{\beta\eta_u}{I_u^2} - \frac{\beta\mu}{\Pi A_u} + \frac{\beta\eta_u A_u}{I_u^2 \Pi/\mu} - \frac{\sigma_u}{A_u^2} \\ &= -\left(\frac{\beta\mu}{\Pi A_u} + \frac{\beta\eta_u}{I_u^2}(1 - \frac{A_u}{\Pi/\mu}) + \frac{\sigma_u}{A_u^2}\right) < 0, \end{aligned}$$

since $A_u \leq \Pi/\mu$ in D_1. It follows from the Bendixson-Dulac criterion (Hale and Koçak, 1991) that there can be no periodic orbit. Since system (3.7) is two-dimensional, the Poincaré-Bendixson theorem (Hale and Koçak, 1991) shows that the equilibrium (I_u^{**}, A_u^{**}) is globally asymptotically stable in D_1. Thus, $I_u \to I_u^{**}$ and $A_u \to A_u^{**}$ as $t \to \infty$. Since $N \to \Pi/\mu$ as $t \to \infty$ then

$S_u \to \Pi/\mu - I_u^{**} - A_u^{**}$ as $t \to \infty$. Hence, Y^{**} is globally asymptotically stable in $D_u \setminus Y_0$. □

In conclusion, for $\mathcal{R}_0 > 1$, the disease remains endemic in education-free model (3.3) with negligible mortality rate induced by the disease.

3.5 Analysis of the Full Model

In this section, system (3.1) (i.e., the full model) is analyzed and some results of public health importance are obtained.

3.5.1 Local stability of Disease-free equilibrium (DFE)

The model (3.1) has a unique disease-free equilibrium, obtained by setting the right-hand sides of the equations in the model (3.1) to zero, given by

$$\mathcal{X} = (S_u^*, S_e^*, I_u^*, A_u^*, I_e^*, A_e^*) = \left(\frac{\Pi(1-p)}{\xi+\mu}, \frac{\Pi(p\mu+\xi)}{\mu(\xi+\mu)}, 0, 0, 0, 0\right). \tag{3.8}$$

It can be shown that $\mathcal{X}$ attracts the region (the stable manifold of $\mathcal{X}$)

$$\mathcal{D}_{\mathcal{X}} = \{(S_u, S_e, I_u, A_u, I_e, A_e) \in \mathcal{D} : I_u = A_u = I_e = A_e = 0\}.$$

Using the next generation operator method (see, Section 2.7), the associated matrices F_e, for the new infection terms, and V_e, for the remaining transition terms, are, respectively, given by (noting that $N^* = \dfrac{\Pi}{\mu}$ at $\mathcal{X}$)

$$F_e = \begin{pmatrix} \beta\frac{S_u^*}{N^*} & \eta_u\beta\frac{S_u^*}{N^*} & \beta(1-\kappa)\frac{S_u^*}{N^*} & \beta(1-\kappa)\eta_e\frac{S_u^*}{N^*} \\ 0 & 0 & 0 & 0 \\ \beta(1-\epsilon)\frac{S_e^*}{N^*} & \beta(1-\epsilon)\frac{S_e^*}{N^*}\eta_u & \beta(1-\kappa)(1-\epsilon)\frac{S_e^*}{N^*} & \beta(1-\kappa)(1-\epsilon)\eta_e\frac{S_e^*}{N^*} \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and,

$$V_e = \begin{pmatrix} K_1 & 0 & 0 & 0 \\ -\sigma_u & K_2 & 0 & 0 \\ -\psi_1 & 0 & K_3 & 0 \\ 0 & -\psi_2 & -\sigma_e & K_4 \end{pmatrix},$$

where,

$$K_1 = \mu + \sigma_u + \psi_1, \quad K_2 = \mu + \delta_u + \psi_2, \quad K_3 = \mu + \sigma_e \quad \text{and} \quad K_4 = \mu + \delta_e.$$

It follows that the *effective reproductive number*, denoted by $\mathcal{R}_{eff}$, is given by

$$\mathcal{R}_{eff} = \rho(F_e V_e^{-1}) = \frac{\beta(A+B+C)}{K_1K_2K_3K_4(\xi+\mu)}, \tag{3.9}$$

where ρ is the spectral radius, and

$$\begin{aligned} A &= K_1K_2(1-\epsilon)(1-\kappa)(p\mu+\xi)(K_4+\eta_e\sigma_e), \\ B &= \mu K_4K_3(1-p)(K_2+\sigma_u\eta_u), \\ C &= \mu(1-p)(1-\kappa)(\psi_1K_2K_4+\psi_2\sigma_uK_3\eta_e+\sigma_e\eta_e\psi_1K_2). \end{aligned}$$

Biologically-speaking, the effective reproduction number measures the average number of new infections generated by a single HIV infected person in a community where a public health enlightenment campaign is used as a control strategy (Anderson and May, 1991; Hethcote, 2000; van den Driessche and Watmough, 2002). Moreover, in the absence of public health education ($I_e = A_e = p = \kappa = \delta_e = \xi = \epsilon = \sigma_e = \psi_1 = \psi_2 = 0$), the quantity $\mathcal{R}_{eff} = \dfrac{\beta(\mu+\delta_u+\eta_u\sigma_u)}{(\sigma_u+\mu)(\mu+\delta_u)} = \mathcal{R}_0$, where $\mathcal{R}_0$ is the *basic reproduction number* (i.e., $\mathcal{R}_0$ represents the average number of new cases generated by a single infected individual in a completely susceptible population).

Using Theorem 12 of Chapter 2 (i.e., Theorem 2 of van den Driessche and Watmough (2002)), the following result is established.

Theorem 17. *The DFE, $\mathcal{X}$, of the system (3.1), given by (6), is locally asymptotically stable (LAS) if $\mathcal{R}_{eff} < 1$, and unstable if $\mathcal{R}_{eff} > 1$.*

Theorem 17 implies that HIV can be eliminated from the community when $\mathcal{R}_{eff} < 1$, provided the initial sizes of the sub-populations of the model (3.1) are within the domain of attraction of $\mathcal{X}$. To ensure that HIV elimination is independent of the initial sizes of the sub-populations, we need to show that the DFE is globally asymptotically stable (GAS). This is established in the

next Chapter, for the special case where the efficacy of public health education is assumed to be 100% (i.e., $\epsilon = 1$).

3.5.2 Assessment of Impact of Public Health Education

Before using the model (3.1) to assess the impact of public health education in combatting HIV spread in a population, it is instructive to assess the behaviour of the model under the worst case scenario (i.e., the case where no public health education is provided in the community). By setting all education-related parameters to zero (i.e., $p = \kappa = \delta_e = \xi = \epsilon = \sigma_e = \psi_1 = \psi_2 = 0$) and using the data in Tables 3.2 and 3.3, simulations of the model (3.1) show that India, Nigeria, China, Ethiopia, and Russia will record around 23.5 million, 12.5 million, 10.1 million, 8.8 million and 6 million total HIV/AIDS cases in eight years, respectively (Figures 3.3A and 3.3B). These projections of the model (3.1) are consistent with the estimates given by the US-based National Intelligence Council (2002), which predicts that, by the year 2010, India, Nigeria, China, Ethiopia, and Russia could have about 20 to 25 million, 10 to 15 million, 10 to 15 million, 7 to 10 million, and 5 to 8 million HIV/AIDS cases if the governments of the respective countries do not take serious action against the spread of HIV/AIDS.

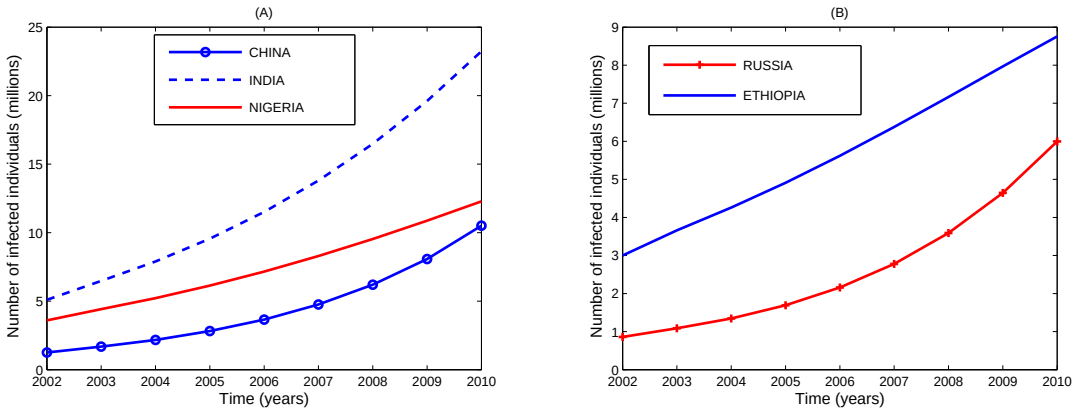


Figure 3.3: Worst-case scenarios for: (A) China, India and Nigeria; and (B) Russia and Ethiopia. Parameter values used are as in Table 3.2 with all education-related parameters set to zero.

Threshold analysis

In this section, the impact of public health education campaign will be assessed by carrying out threshold analysis on the effective reproduction number, $\mathcal{R}_{eff}$, as follows.

Let $\omega = \dfrac{S_e^*}{N^*}$ be the fraction of susceptible individuals educated at the DFE $\mathcal{X}$. Hence, $\mathcal{R}_{eff}$ can now be rewritten as a function of ω.

$$\mathcal{R}_{eff} = \mathcal{R}_{eff}(\omega) = \frac{\beta(Z_1 + Z_2)}{K_1 K_2 K_3 K_4}, \tag{3.10}$$

where,

$$Z_1 = \omega K_1 K_2 (1-\epsilon)(1-\kappa)(K_4 + \eta_e \sigma_e),$$

$$Z_2 = (1-\omega)[(1-\kappa)(\psi_1 K_2 K_4 + \psi_2 K_3 \sigma_e \eta_e + \psi_2 K_2 \sigma_u \eta_e) + K_3 K_4 (K_2 + \eta_u \sigma_u)].$$

Differentiating $\mathcal{R}_{eff}$, given in (3.10), partially with respect to ω gives

$$\frac{\partial \mathcal{R}_{eff}(\omega)}{\partial \omega} = -Z_3(1-\nabla),$$

where,

$$Z_3 = \frac{\beta[(1-\kappa)(\psi_1 K_2 K_4 + \psi_2 K_2 \sigma_e \eta_e + \psi_2 K_3 \sigma_u \eta_e) + K_3 K_4 (K_2 + \eta_u \sigma_u)]}{K_1 K_2 K_3 K_4} > 0,$$

$$\nabla = \frac{K_1 K_2 (1-\epsilon)(1-\kappa)(K_4 + \eta_e \sigma_e)}{(1-\kappa)(\psi_1 K_2 K_4 + \psi_2 K_3 \sigma_e \eta_e + \psi_2 K_2 \sigma_u \eta_e) + K_3 K_4 (K_2 + \eta_u \sigma_u)} > 0. \tag{3.11}$$

Since Z_3 and ∇ are both non-negative (noting that $0 < \kappa < 1$ and $0 < \epsilon < 1$), then $\frac{\partial \mathcal{R}_{eff}(\omega)}{\partial \omega} < 0$ whenever $\nabla < 1$. Further, $\frac{\partial \mathcal{R}_{eff}(\omega)}{\partial \omega} > 0$ if $\nabla > 1$. This result is summarized below.

Lemma 5. *The use of public health education campaign would have*

(i) a positive population-level impact (reduce disease burden) if $\nabla < 1$*;*

(ii) no population-level impact if $\nabla = 1$*;*

(iii) a detrimental population-level impact (increase disease burden) if $\nabla > 1$*.*

Biologically-speaking, ∇ could be interpreted as the measure of increase or decrease in risky behaviour (or negative attitude) of the individuals in the community who received public health education. That is, $\nabla < 1$, $\nabla = 1$ and $\nabla > 1$ mean that public health education campaign is able to reduce, cause no change of, and induce an increase in risky behaviour amongst the individuals who received such education, respectively. It is worth noting that if the efficacy of public health education is 100% (i.e., $\epsilon = 1$), then $\nabla = 0$, so that public health education campaign will always have positive population-level impact. Thus, the detrimental effect of public health education is only feasible if the efficacy is not perfect ($0 < \epsilon < 1$).

Alternatively, the impact of public health education campaign can be assessed by re-writing $\mathcal{R}_{eff}$ as

$$\mathcal{R}_{eff} = \mathcal{R}_0 \left[1 - \Omega \left(1 - \frac{\mathcal{R}_{0e}}{\mathcal{R}_0}\right)\right], \tag{3.12}$$

where,

$$\mathcal{R}_0 = \frac{\beta(\mu + \delta_u + \eta_u \sigma_u)}{(\sigma_u + \mu)(\mu + \delta_u)}, \tag{3.13}$$

and,

$$\mathcal{R}_{0e} = \frac{\beta(1-\epsilon)(1-\kappa)(K_4+\sigma_e\eta_e)}{K_3K_4}. \tag{3.14}$$

The quantity $\mathcal{R}_0$ is the basic reproduction number (defined earlier) and $\mathcal{R}_{0e}$ is the reproduction number for the case when every individual in the community received public health education against risky practices that could lead to HIV infection. Furthermore,

$$\Omega = \frac{(\sigma_u+\mu)(\mu+\delta_u)(\gamma_1+\gamma_2)}{\gamma_3 K_1K_2(\xi+\mu)[K_1K_2K_3K_4(\xi+\mu)\mathcal{R}_0+\beta(A+B+C)]},$$

where,

$$\begin{aligned}
\gamma_1 &= \mathcal{R}_0{}^2K_1{}^2K_2{}^2K_3{}^2K_4{}^2(\xi+\mu)^2+\beta^2(A+B+C)^2,\\
\gamma_2 &= \beta K_3K_4(\mu+\delta_u+\sigma_u\eta_u)+(1-\epsilon)(1-\kappa)(K_2+\sigma_e\eta_e)(\sigma_u+\mu)(\delta_u+\mu),\\
\gamma_3 &= \beta K_3{}^2K_4{}^2(\mu+\delta_u+\sigma_u\eta_u)^2+(1-\epsilon)^2(1-\kappa)^2(K_2+\sigma_e\eta_e)^2(\sigma_u+\mu)^2(\delta_u+\mu)^2.
\end{aligned} \tag{3.15}$$

It follows from (3.12) that the *education impact factor* (denoted by Υ) is given by

$$\Upsilon = \Omega\left(1-\frac{\mathcal{R}_{0e}}{\mathcal{R}_0}\right).$$

Thus, we have established the following result.

Theorem 18. *The use of public health education campaign in the community*

will have

(i) positive population-level impact if $\Upsilon > 0$ $(\mathcal{R}_{0e} < \mathcal{R}_0)$*;*

(ii) negative population-level impact in the community if $\Upsilon < 0$ $(\mathcal{R}_{0e} > \mathcal{R}_0)$*; and*

(iii) no population-level impact in the community if $\Upsilon = 0$ *(*$\mathcal{R}_{0e} = \mathcal{R}_0$*).*

Numerical simulations of the model, using appropriate demographic and epidemiological data for Ethiopia, given in Tables 3.2 and 3.3, show the following interesting cases:

$\nabla < 1$: Using the aforementioned realistic set of parameter values (Tables 3.2 and 3.3), it follows that $\nabla = 0.0517 < 1$, $\mathcal{R}_{eff} = 0.6898$ and $\mathcal{R}_{0e} = 0.6619 < \mathcal{R}_0 = 1.3712$, so that the use of public health education campaign will have positive population-level impact (Figure 3.4A). In other words, the public health education campaign results in positive behaviour change (in reducing risky practices) in the individuals who received such education (in this case).

$\nabla > 1$: Consider the case with $\xi = 0.01$, $p = \psi_1 = \psi_2 = 0.001$ and $\epsilon = 0.4$ (that is, the efficacy of public health education is low) and all other parameters as above. Here, $\nabla = 1.4211 > 1$, $\mathcal{R}_{eff} = 1.5866$ and $\mathcal{R}_{0e} = 1.9857 > \mathcal{R}_0 = 1.3712$. The simulation results obtained, depicted in Figure 3.4B, shows that in this setting, the use of public health education increases the number of HIV cases in comparison to the worst-case scenario. This result could be interpreted as follows: the use of "ineffective" public health education campaign (characterize by low efficacy)

induces an increase in risky behaviour amongst people after receiving it. For example, an individual who believes that consistent and correct use of condoms provides absolute protection against HIV may indulge in risky behaviour that could be avoided. In this way, the rate of HIV/AIDS transmission will actually increase over time. Furthermore, Richens et al. (2000) reported that a condom-based approach, which creates a false sense of security on the part of users, has exacerbated the problem of HIV.

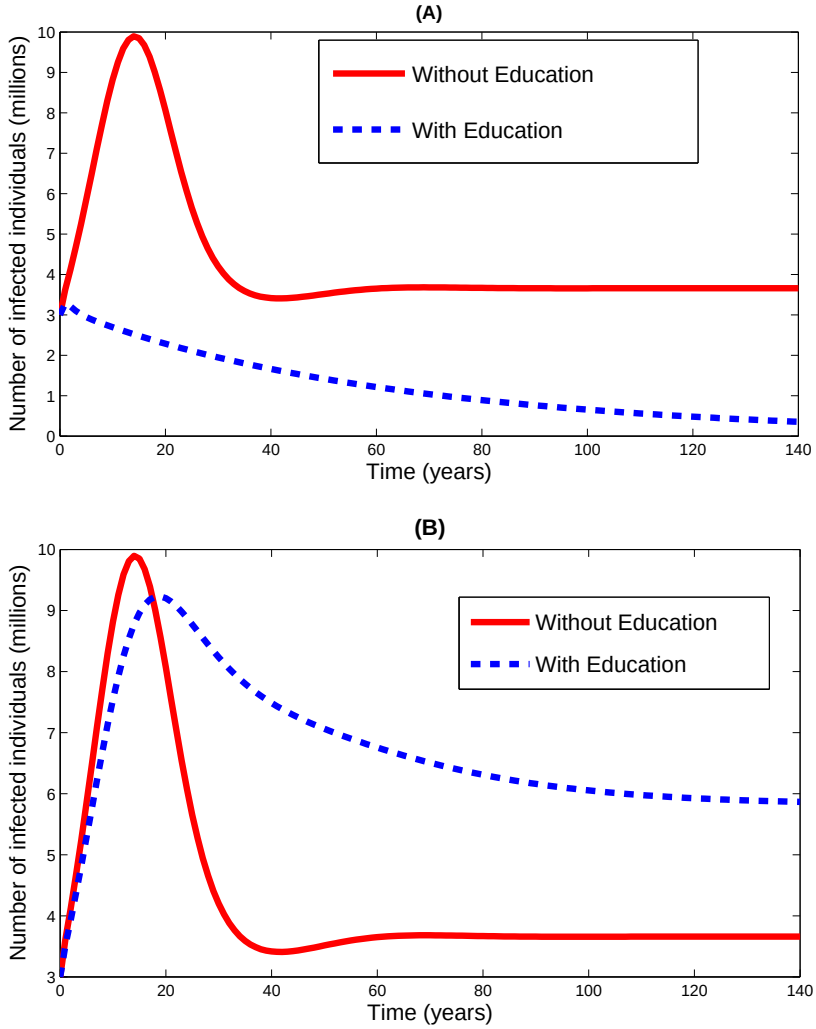


Figure 3.4: Simulation of the model (3.1) showing the total infected population as a function of time, using appropriate demographic and epidemiological data for Ethiopia, given in Tables 3.2 and 3.3. Dashed line represents the model with public health education campaign and solid line represents the model without education public health education campaign (i.e., all education parameters are zero). For: (A) $\nabla = 0.0517 < 1$, $\mathcal{R}_{eff} = 0.6898$ and $\mathcal{R}_{0e} = 0.6619 < \mathcal{R}_0 = 1.3712$; and (B) $\nabla = 1.4211 > 1$, $\mathcal{R}_{eff} = 1.5866$ and $\mathcal{R}_{0e} = 1.9857 > \mathcal{R}_0 = 1.3712$, with $\xi = 0.01$, $p = \psi_1 = \psi_2 = 0.001$ and $\epsilon = 0.4$.

Contour plots of $\mathcal{R}_{eff}$ as a function of efficacy of public health education

and the fraction of individuals who received public health education (i.e., public health education coverage level) at steady-state are depicted in Figure 3.5. As expected, an increase in efficacy and coverage level leads to a decrease in $\mathcal{R}_{eff}$. This is an important result because the main objective of public health education is to reduce $\mathcal{R}_{eff}$ as much as possible (since reduction in $\mathcal{R}_{eff}$ is positively correlated with a reduction in disease burden), which could lead to effective disease control or elimination.

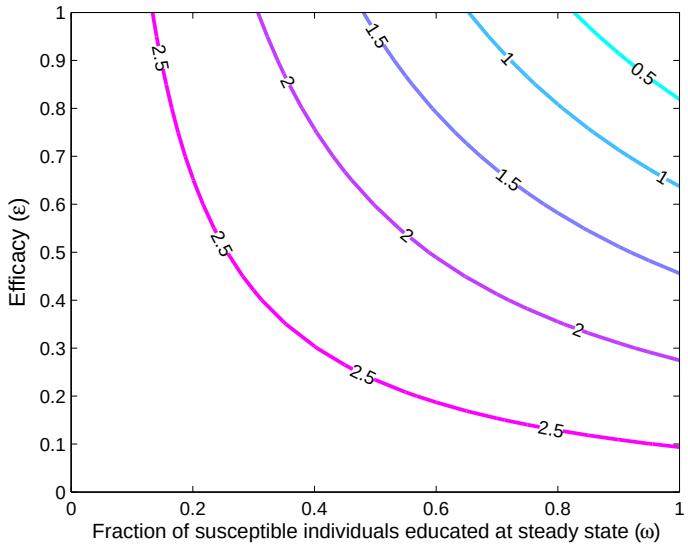


Figure 3.5: Contour plot of $\mathcal{R}_{eff}$ as a function of the fraction individuals educated at steady state (ω) and education efficacy (ϵ). Parameter values used are as in Table 3.1 with $\psi_1 = \psi_2 = 1$.

It is evident from Figure 3.5 that the prospect of effective control of HIV increases with increasing efficacy and coverage rate of the public health education campaign. For instance, a public health education program with efficacy and coverage level of 60% (each) will fail to control the disease (since

$\mathcal{R}_{eff} > 1$ in this case). On the other hand, the use of public health education campaign with efficacy and coverage level of 90% (each) could eliminate HIV from the population (see also Figure 3.6 below).

3.5.3 Evaluation of Targeted Education Strategies

The model is used to evaluate the impact of the following targeted public health education strategies:

- Strategy I: educating adult ("established") sexually-active susceptible individuals only (at the rate ξ),
- Strategy II: educating a fraction p of newly-recruited sexually-active susceptible individuals only,
- Strategy III: educating HIV-infected individuals without clinical AIDS symptoms only (at the rate ψ_1), or
- Strategy IV: educating HIV-infected individuals with clinical AIDS symptoms only (at the rate ψ_2).

Using demographic data from India, Nigeria, China, Ethiopia, and Russia, tabulated in Table 3.3 together with the associated epidemiological data given in Table 3.2, simulations of model (3.1) show that Strategy I can prevent more than 0.8642 million, 0.5474 million, 0.3321 million, 0.4064 million, and 0.2116 million new cases in India, Nigeria, China, Ethiopia, and Russia respectively within a year (see Table 3.4A). Furthermore, Strategy I seems to be the most effective amongst all targeted single group strategies. It is also

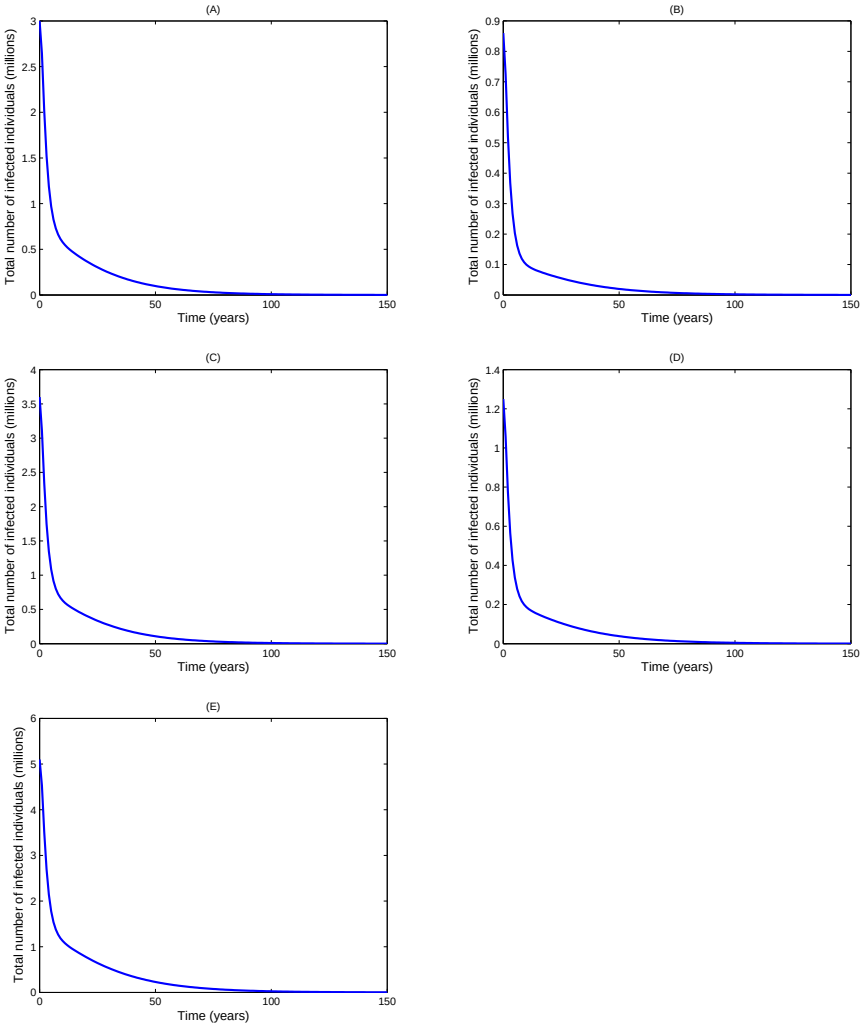


Figure 3.6: Simulations of the model (1) showing the time needed to eliminate HIV in (A) Ethiopia (B) Russia (C) Nigeria (D) China and (E) India. Parameter values used are as in Tables 3.2 and 3.3 with $\xi = p = \epsilon = 0.9$, $\psi_1 = \psi_2 = 0$, $\kappa = 0.8$ and $\beta = 0.2$ (so that, $\nabla = 0.1609 < 1$, $\mathcal{R}_{eff} = 0.1115$ and $\mathcal{R}_{0e} = 0.1103 < \mathcal{R}_0 = 0.6856$).

shown that combining Strategies I and IV gives the most effective strategy for reducing new HIV cases in comparison to all other possible 2-group combined strategies. Moreover, Table 3.4C shows that the combination of Strategy I, Strategy III and Strategy IV is the best in reducing the total number of new cases than any of the others except the universal strategy (i.e., educating every class of uneducated individuals at a certain rate). The Universal Strategy can prevent more than 1.1590 million, 0.7580 million, 0.3858 million, 0.5731 million, and 0.253 million new cases of HIV in India, Nigeria, China, Ethiopia, and Russia respectively within a year (see Table 3.4D).

Table 3.4 further shows that the use of single-group strategy can be more effective than some 3-group or 2-group strategies. For instance, Strategy I is more effective in reducing the number of new infections than the combination of Strategies II, III and IV. Additionally, a 2-group combined strategy can be better in curtailing the number of new cases than a 3-group strategy (this table shows that combining Strategies I and IV gives fewer new cases than some 3-group strategies, which include the combination of Strategies I, II and III and also the combination of Strategies II, III and IV).

3.6 Conclusions

A realistic deterministic model, which incorporates public health education campaign as a sole intervention strategy for HIV/AIDS prevention, is designed and rigorously analyzed to get insight into its dynamical features and to obtain associated epidemiological thresholds. Some of the main theoretical findings

Education strategy	India (millions)	Nigeria (millions)	China (millions)	Ethiopia (millions)	Russia (millions)
(A)					
Strategy I	0.8642	0.5474	0.3321	0.4064	0.2116
Strategy II	0.3633	0.2108	0.2584	0.1390	0.1510
Strategy III	0.5266	0.3095	0.2912	0.2321	0.1770
Strategy IV	0.5862	0.3718	0.2938	0.2510	0.1805
(B)					
Strategies I and II	0.8717	0.5564	0.3331	0.4140	0.2119
Strategies I and III	0.9918	0.6290	0.3588	0.4831	0.2320
Strategies I and IV	1.0359	0.6760	0.3604	0.4966	0.2344
Strategies II and III	0.5353	0.3200	0.2924	0.2408	0.1773
Strategies II and IV	0.5946	0.3818	0.2950	0.2595	0.1808
Strategies III and IV	0.7440	0.4723	0.3250	0.3449	0.2046
(C)					
Strategies I, II and III	0.9986	0.6373	0.3597	0.4899	0.2322
Strategies I, II and IV	1.0425	0.6839	0.3613	0.5033	0.2347
Strategies I, III and IV	1.1530	0.7508	0.3850	0.5670	0.2531
Strategies II, III and IV	0.7516	0.4814	0.3260	0.3526	0.2049
(D)					
Universal Strategy	1.1590	0.7580	0.3858	0.5731	0.2534

Table 3.4: Total new cases averted within a year using (A) Single targeted public health campaign strategy (B) Pair combination of targeted public health campaign strategies (C) Combination of three strategies (D) Universal strategy. Parameters as in Tables 3.2 and 3.3.

of the study are:

- The case when the public health education program is 100% effective, the disease-free equilibrium of the model (3.3) is globally-asymptotically stable whenever the *basic reproduction number* is less than or equal to a quantity less than unity.

- Threshold analysis of the effective reproduction number shows that the use of public health education campaign could have positive, no, or detrimental impact depending on whether or not an impact factor, defined as Υ, is less than, equal to, or greater than unity (this result is also expressed in terms of a measure of risky behaviour, denoted by ∇, given by (3.11)).

The impact of public health education strategies are assessed numerically by simulating the model with a reasonable set of parameter values (mostly chosen from the literature) and initial (demographic) data from five different countries (India, Nigeria, China, Ethiopia, and Russia) where the number of HIV-infected people is expected to grow. Numerical simulations of the model show the following:

- The universal use of public heath education campaign in India, Nigeria, China, Ethiopia, and Russia could avert more than 1.1590 million, 0.7580 million, 0.3858 million, 0.5731 million, and 0.253 million new HIV cases within a year, respectively.

- The universal strategy is more effective than any other strategy in reducing new HIV cases.
- Combining Strategies I, III and IV is the next most effective in reducing the total number of new cases (after the universal strategy).
- Amongst the 2-group combined strategies, combining Strategies I and IV is most effective than some 3-group combined strategies.
- Strategy I averts more new cases in comparison to all other single-group strategies (and some 3-group combination of strategies).
- The prospect of effective control of HIV increases with increasing efficacy and coverage rate of the public health education campaign.

Chapter 4

Backward Bifurcation

4.1 Introduction

Backward, or subcritical, bifurcation in epidemiological models is typically associated with the co-existence of disease-free equilibrium and endemic equilibria when the *basic reproduction number* ($\mathcal{R}_0$) is less than unity. This phenomenon has been found in many epidemiological settings (see, for instance, Elbasha and Gumel, 2006; Hadeler and van den Driessche, 1997; Kribs-Zaleta and Halesco-Hernandez, 2000, and references therein). Furthermore, such phenomenon has been established in a model for public health education campaign by Mukandavire et al. (2009). The epidemiological implication of such a phenomenon is that the classical requirement of having the associated reproduction number less than unity, while necessary is not sufficient condition for disease control. Following the result in Mukandavire et al. (2009), it is in-

structive to determine whether or not the model (3.1) also undergoes backward bifurcation. This is explored below.

4.2 Existence of Backward Bifurcation

In this Section, we consider model (3.1) and show the existence of backward bifurcation. Let

$$G^{**} = \beta \frac{[I_u^{**} + \eta_u A_u^{**} + (1-\kappa)(I_e^{**} + \eta_e A_e^{**})]}{N^{**}} \tag{4.1}$$

be the force of infection at an arbitrary equilibrium of (3.1), denoted by

$$\mathcal{E} = (S_u^{**}, S_e^{**}, I_u^{**}, A_u^{**}, I_e^{**}, A_e^{**}).$$

Thus, at steady-state, the equations of the model (3.1) can be re-written as:

$$\begin{aligned}
S_u^{**} &= \frac{\Pi(1-p)}{\mu+\xi+G^{**}}, \\
S_e^{**} &= \frac{\Pi(p\mu+\xi+pG^{**})}{(\mu+\xi+G^{**})[(1-\epsilon)G^{**}+\mu]}, \\
I_u^{**} &= \frac{\Pi(1-p)G^{**}}{K_1(\mu+\xi+G^{**})}, \\
A_u^{**} &= \frac{\sigma_u\Pi(1-p)G^{**}}{K_1K_2(\mu+\xi+G^{**})}, \\
I_e^{**} &= \frac{G^{**}\Pi(G^{**}C^*+D^*)}{K_1K_3(\mu+\xi+G^{**})[(1-\epsilon)G^{**}+\mu]}, \\
A_e^{**} &= \frac{G^{**}\Pi(G^{**}A^*+B^*)}{K_1K_2K_3K_4(\mu+\xi+G^{**})[(1-\epsilon)G^{**}+\mu]},
\end{aligned} \tag{4.2}$$

with,

$$\begin{aligned}
A^* &= (1-\epsilon)[(1-p)(\psi_2\sigma_uK_3+\psi_1\sigma_eK_2)+K_1K_2\sigma_ep], \\
B^* &= \sigma_eK_1K_2(1-\epsilon)(p\mu+\xi)+\mu(1-p)(\sigma_eK_2\psi_1+\sigma_uK_3\psi_2), \\
C^* &= [K_1p+\psi_1(1-p)](1-\epsilon), \\
D^* &= K_1(1-\epsilon)(\xi+p\mu)+\psi_1\mu(1-p).
\end{aligned}$$

Substituting (4.2) into (4.1), and simplifying, leads to $G^{**}=0$ (corresponding

to the DFE, $\mathcal{X}$) and the following quadratic equation (in terms of G^{**}):

$$a_{11}^*(G^{**})^2 + a_{12}^* G^{**} + a_{13}^* = 0, \tag{4.3}$$

where,

$$\begin{aligned}
a_{11}^* &= K_3K_4(1-\epsilon)(1-p)(K_2+\sigma_u) + C^* + A^*, \\
a_{12}^* &= K_1K_2K_3K_4[(1-p)(1-\epsilon)+p] + \mu K_3K_4(1-p)(K_2+\sigma_u) + K_2K_4D^* + B^* \\
&\quad -\beta[K_3K_4(1-p)(1-\epsilon)(K_2+\sigma_u\eta_u) + (1-\kappa)(K_2K_4C^* + \eta_e A^*)], \\
a_{13}^* &= K_1K_2K_3K_4(\mu+\xi)(1-\mathcal{R}_{eff}).
\end{aligned} \tag{4.4}$$

Thus, the following results from the quadratic equation (4.3).

Theorem 19. *(a) If $a_{12}^* > 0$ then model (3.1) has forward bifurcation at $\mathcal{R}_{eff} = 1$.*

(b) If $a_{12}^* < 0$, then the model (3.1) undergoes backward bifurcation at $\mathcal{R}_{eff} = 1$.

Theorem 20. *(a) If $a_{12}^* > 0$ and*

(i) $a_{13}^* \geq 0$, the model (3.1) has no positive equilibrium

(ii) $a_{13}^* < 0$, the model (3.1) has a unique positive equilibrium

(b) If $a_{12}^* < 0$ and $a_{13}^* > 0$ and

(i) $(a_{12}^*)^2 - 4a_{11}^*a_{13}^* > 0$, the model (3.1) has two positive equilibria,

(ii) $(a_{12}^*)^2 - 4a_{11}^*a_{13}^* = 0$, the model (3.1) has a unique positive equilibrium,

(iii) $(a_{12}^*)^2 - 4a_{11}^* a_{13}^* < 0$, *the model (3.1) has no positive equilibrium.*

(c) If $a_{12}^* < 0$ *and* $a_{13}^* \leq 0$, *the model (3.1) has a unique positive equilibrium.*

Since all the model parameters are non-negative (and $0 < \epsilon < 1$, $0 < \kappa < 1$), it is clear that $a_{11}^* > 0$. We consider the following cases:

Case I. Suppose $\mathcal{R}_{eff} > 1$. Then, clearly $a_{13}^* < 0$. Thus, the quadratic equation (4.1) is concave up and has two real roots of opposite signs. This implies that the model has a unique positive equilibrium whenever $\mathcal{R}_{eff} > 1$.

Case II. Suppose $\mathcal{R}_{eff} = 1$. Then $a_{13}^* = 0$ and the quadratic reduces to $G^{**}(a_{11}^* G^{**} + a_{12}^*) = 0$, with roots $G^{**} = 0$ (corresponding to the disease-free equilibrium, $\mathcal{X}$) and $G^{**} = \frac{-a_{12}^*}{a_{11}^*}$. Thus, for $\mathcal{R}_{eff} = 1$, the model has a unique positive endemic equilibrium when $a_{12}^* < 0$.

Case III. Suppose $\mathcal{R}_{eff} < 1$. Then $a_{13}^* > 0$ and equation (4.3) has either zero, one or two positive real roots. In order to obtain two positive real roots we need $(a_{12}^*)^2 - 4a_{11}^* a_{13}^* > 0$ and $a_{12}^* < 0$. If $a_{12}^* < 0$ and $(a_{12}^*)^2 - 4a_{11}^* a_{13}^* = 0$, then there is one positive real root. Otherwise, there is no positive solution. This case indicates the possibility of a backward bifurcation in the model (3.1) when $\mathcal{R}_{eff} < 1$ (since it suggests the possibility of multiple endemic equilibria when $\mathcal{R}_{eff} < 1$).

It should be noted that Theorem 19 does not give a local description of the bifurcating curve including its stability. Thus, it is instructive to determine

the local behaviour of the bifurcating branch. Therefore, we alternatively use centre manifold theorem (Carr, 1981), in line with Theorem 13 of Chapter 2, to prove the existence of backward bifurcation.

Theorem 21.

If (4.10) holds, then the model (3.1) has a backward bifurcation at $\mathcal{R}_{eff} = 1$ *and the bifurcating branch is unstable near* $\mathcal{R}_{eff} = 1$.

Proof. The centre manifold theorem is used (see, Theorem 13 of Chapter 2) to show the existence backward bifurcation in the model (3.1) when $\mathcal{R}_{eff} = 1$. For convenience, let $S_u = x_1,\ S_e = x_2,\ I_u = x_3,\ A_u = x_4,\ I_e = x_5,\ A_e = x_6$, so that $N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6$. The model (3.1) can be written as follows:

$$\begin{aligned}
\frac{dx_1}{dt} &= \phi_1 = \Pi(1-p) - (\xi+\mu)x_1 - \frac{\beta x_1[(x_3+\eta_u x_4) + (1-\kappa)(x_5+\eta_e x_6)]}{x_1+x_2+x_3+x_4+x_5+x_6},\\
\frac{dx_2}{dt} &= \phi_2 = \Pi p + \xi x_1 - \frac{\beta(1-\epsilon)x_2[(x_3+\eta_u x_4) + (1-\kappa)(x_5+\eta_e x_6)]}{x_1+x_2+x_3+x_4+x_5+x_6} - \mu x_2,\\
\frac{dx_3}{dt} &= \phi_3 = \frac{\beta x_1[(x_3+\eta_u x_4) + (1-\kappa)(x_5+\eta_e x_6)]}{x_1+x_2+x_3+x_4+x_5+x_6} - K_1 x_3,\\
\frac{dx_4}{dt} &= \phi_4 = \sigma_u x_3 - K_2 x_4,\\
\frac{dx_5}{dt} &= \phi_5 = \frac{\beta(1-\epsilon)x_2[(x_3+\eta_u x_4) + (1-\kappa)(x_5+\eta_e x_6)]}{x_1+x_2+x_3+x_4+x_5+x_6} + \psi_1 x_3 - K_3 x_5,\\
\frac{dx_6}{dt} &= \phi_6 = \sigma_e x_5 + \psi_2 x_4 - K_4 x_6.
\end{aligned} \tag{4.5}$$

The Jacobian of $\Phi = (\phi_1, \phi_2, \phi_3, \phi_4, \phi_5, \phi_6)^T$, around the DFE $\mathcal{X}$, denoted by J_β, is given by

$$J_\beta = \begin{pmatrix} -\xi-\mu & 0 & -\beta H_1 & -\beta\eta_u H_1 & -\beta(1-\kappa)H_1 & -\beta\eta_e(1-\kappa)H_1 \\ \xi & -\mu & -\beta H_2 & -\beta\eta_u H_2 & -\beta(1-\kappa)H_2 & -\beta\eta_e(1-\kappa)H_2 \\ 0 & 0 & \beta H_1 - K_1 & \beta\eta_u H_1 & \beta(1-\kappa)H_1 & \beta\eta_e(1-\kappa)H_1 \\ 0 & 0 & \sigma_u & -K_2 & 0 & 0 \\ 0 & 0 & \beta H_2 + \psi_1 & \beta\eta_u H_2 & \beta(1-\kappa)H_2 - K_3 & \beta\eta_e(1-\kappa)H_2 \\ 0 & 0 & 0 & \psi_2 & \sigma_e & -K_4 \end{pmatrix},$$

where, $H_1 = \dfrac{\mu(1-p)}{\xi+\mu}$ and $H_2 = \dfrac{(1-\epsilon)(p\mu+\xi)}{\xi+\mu}$. It can also be shown from J_β, as in (3.9), that

$$R_{eff} = \frac{\beta(A+B+C)}{K_1K_2K_3K_4(\xi+\mu)}. \tag{4.6}$$

Consider the case when $\mathcal{R}_{eff} = 1$ and β is chosen as a bifurcation parameter. Solving (4.6) for $\mathcal{R}_{eff} = 1$ gives

$$\beta = \beta^{**} = \frac{K_1K_2K_3K_4(\xi+\mu)}{A+B+C}.$$

Note that the above linearized system, of the transformed system (4.5) with $\beta = \beta^{**}$, has the eigenvalues $-(\xi + \mu) < 0$, $-\mu < 0$ and the eigenvalues of the sub-matrix

$$J_1 = \begin{pmatrix} \beta^{**}H_1 - K_1 & \beta^{**}\eta_u H_1 & \beta^{**}(1-\kappa)H_1 & \beta^{**}\eta_e(1-\kappa)H_1 \\ \sigma_u & -K_2 & 0 & 0 \\ \beta^{**}H_2 + \psi_1 & \beta^{**}\eta_u H_2 & \beta^{**}(1-\kappa)H_2 - K_3 & \beta^{**}\eta_e(1-\kappa)H_2 \\ 0 & \psi_2 & \sigma_e & -K_4 \end{pmatrix}. \quad (4.7)$$

It is clear that 0 is one of the eigenvalues of J_1, and the other three are the roots of

$$\lambda^3 + c_1\lambda^2 + c_2\lambda + c_3 = 0,$$

where, $c_1 = \dfrac{m_1 + m_2}{m_3}$, $c_2 = \dfrac{m_4 + m_5 + m_6 + m_7}{m_3}$ and $c_3 = \dfrac{m_8 + m_9 + m_{10} + m_{11}}{m_3}$,

with,

$$
\begin{aligned}
m_1 &= (K_1+K_2+K_3+K_4)[(1-\epsilon)(1-\kappa)(p\mu+\xi)K_1K_2\sigma_e\eta_e + B + C],\\
m_2 &= (K_1+K_2+K_4)(1-\epsilon)(1-\kappa)(p\mu+\xi)K_1K_2K_4,\\
m_3 &= A+B+C,\\
m_4 &= (1-\epsilon)(1-\kappa)(p\mu+\xi)K_1K_2[(K_1K_2+K_1K_4+K_2K_4)(K_2+\sigma_e\eta)\\
&\quad +(K_1K_3+K_2K_3)\sigma_e\eta_e],\\
m_5 &= (1-p)(1-\kappa)\mu[(K_1K_2+K_1K_4+K_2K_3+K_2K_4+K_3K_4)(\psi_1K_2K_4\\
&\quad +\psi_2K_3\sigma_u\eta_e+\psi_1K_2\sigma_e\eta_e)],\\
m_6 &= (1-p)(1-\kappa)\mu K_1K_3(\psi_2K_3\sigma_u\eta_e+\psi_1K_2\sigma_e\eta_e),\\
m_7 &= (1-p)\mu K_3K_4[(K_2K_3+K_2K_4+K_3K_4)(K_2+\sigma_u\eta_u)+\sigma_u\eta_uK_1(K_3+K_4)],\\
m_8 &= {K_1}^2K_2K_4(1-\epsilon)(1-\kappa)(p\mu+\xi)(K_4+\sigma_e\eta_e),\\
m_9 &= (1-p)\mu(1-\kappa)\psi_1{K_2}^2\sigma_e\eta_e(K_1K_3+K_1K_4+K_3K_4),\\
m_{10} &= (1-p)(1-\kappa)\mu\{[K_1K_2+(K_1+K_2)K_4]{K_3}^2\psi_2\sigma_u\eta_e+(K_1+K_3){K_2}^2{K_4}^2\psi_1\},\\
m_{11} &= \mu K_2{K_3}^2{K_4}^2(1-p)(K_2+\sigma_u\eta_u)+K_1K_3K_4\sigma_u\eta_u.
\end{aligned}
$$

According to the Routh-Hurwitz criterion, the necessary and sufficient conditions for all the eigenvalues of J_1 to have negative real parts are (i) $c_1>0$ and $c_3>0$ and (ii) $c_1c_2-c_3>0$. Since all the parameters of the model are nonnegative and $0<p,\ \kappa,\ \epsilon<1$, then (i) holds. It can be shown that (ii) holds. Thus, all the eigenvalues of J_1 have negative real part. Hence, the center manifold theory (Carr, 1981) can be used to analyze the dynamics of (4.5) near $\beta=\beta^{**}$.

Eigenvectors of $J_\beta\mid_{\beta=\beta^{**}}$:

The right and left eigenvectors associated with the zero eigenvalue of the Jaco-

bian J_β evaluated at β^{**} are given, respectively, by $\mathbf{w} = [w_1, w_2, w_3, w_4, w_5, w_6]^T$ and $\mathbf{v} = [v_1, v_2, v_3, v_4, v_5, v_6]$, where

$$w_1 = -\frac{\beta^{**}H_1\{w_3 + \eta_u w_4 + (1-\kappa)w_5 + \eta_e(1-\kappa)w_6\}}{\xi + \mu} < 0,$$

$$w_2 = \frac{\xi w_1 - \beta^{**}H_2\{w_3 + \eta_u w_4 + (1-\kappa)w_5 + \eta_e(1-\kappa)w_6\}}{\mu} < 0,$$

$$w_3 = w_3 > 0, \qquad w_4 = \frac{\sigma_u}{K_2}w_3,$$

$$w_5 = w_5 > 0, \qquad w_6 = \frac{\psi_2 w_4 + \sigma_e w_5}{K_4},$$

$$v_1 = v_2 = 0, \quad v_3 = v_3 > 0, \quad v_4 = \frac{\beta^{**}\eta_u H_1 v_3 + \beta^{**}\eta_u H_2 v_5 + \psi_2 v_6}{K_2},$$

$$v_5 = v_5 > 0, \qquad v_6 = \frac{\beta^{**}\eta_e(1-\kappa)(H_1 v_3 + H_2 v_5)}{K_4}.$$

To determine the direction of bifurcation, following Castillo-Chavez and Song (2004), we find the signs of a and b, where

$$a = \sum_{k,i,j=1}^{6} v_k w_i w_j \frac{\partial^2 \phi_k}{\partial x_i \partial x_j}(0,0) \quad \text{and} \qquad b = \sum_{k,i=1}^{6} v_k w_i \frac{\partial^2 \phi_k}{\partial x_i \partial \beta^{**}}(0,0).$$

It can be shown, after using the associated nonzero partial derivatives of Φ at the DFE ($\mathcal{X}$), that

$$a = \frac{2\beta^{**}\mu P_{11}}{\Pi(\xi + \mu)}(P_{12} - P_{13}), \tag{4.8}$$

where,

$$P_{11} = w_3 + \eta_u w_4 + (1-\kappa)w_5 + (1-\kappa)\eta_e w_6 > 0,$$

$$P_{12} = -v_3\mu(1-p)(w_1+w_2) - v_5(1-\epsilon)\{(p\mu+\xi)w_1 + (1+p)\mu w_2\} > 0,$$

$$P_{13} = (v_3\mu(1-p) + (1-\epsilon)(p\mu+\xi)v_5)(w_3+w_4+w_6+w_5) > 0, \tag{4.9}$$

Hence, $a > 0$ iff

$$P_{12} > P_{13} \tag{4.10}$$

For the sign of b, we substitute vectors $\mathbf{v}$ and $\mathbf{w}$ and the respective associated nonzero partial derivatives of Φ at the DFE into

$$b = \sum_{k,i=1}^{6} v_k w_i \frac{\partial^2 \phi_k}{\partial x_i \partial \beta^{**}}(0,0),$$

which gives,

$$b = \frac{(1-\epsilon)(p\mu+\xi)v_5 + v_3\mu(1-p)}{\xi+\mu} P_{11} > 0.$$

□

To illustrate this phenomenon with respect to the above Theorem, the same parameter values for Figure 3.4B are used and the backward bifurcation diagrams are depicted in Figure 4.1. For this set of parameter values, the associated backward bifurcation coefficients (a and b) have the values: $a = 0.02069982715$ and $b = 1.930595939$. It is worth noting that when $\epsilon = 1$ (i.e., public health education campaign is 100% effective), the threshold quantity

$\mathcal{R}_{eff}$ reduces to

$$\tilde{\mathcal{R}}_{eff} = \mathcal{R}_{eff}\Big|_{\epsilon=1} = \frac{\beta(B+C)}{K_1K_2K_3K_4(\xi+\mu)}. \tag{4.11}$$

Similarly, the coefficients of the quadratic (4.3) reduce to

$$\begin{aligned}
a_{11}^* &= 0,\\
a_{12}^* &= K_1K_2K_3K_4p + \mu(1-p)[K_3K_4(K_2+\sigma_u) + K_2\psi_1(K_4+\sigma_e) + \sigma_uK_3\psi_2] > 0,\\
a_{13}^* &= K_1K_2K_3K_4(\mu+\xi)(1-\tilde{\mathcal{R}}_{eff}).
\end{aligned}$$

Thus, the quadratic equation (4.3) becomes linear in G^{**}, with $G^{**} = \frac{-a_{13}^*}{a_{12}^*}$. In this case, the model (3.1) has a unique endemic equilibrium if and only if $\tilde{\mathcal{R}}_{eff} > 1$ (i.e., $a_{13}^* < 0$) and no endemic equilibria when $\tilde{\mathcal{R}}_{eff} < 1$ (since, in this case, $G^{**} = \frac{-a_{13}^*}{a_{12}^*} < 0$). Hence, backward bifurcation is ruled out in this case (since no multiple endemic equilibria exist when $\tilde{\mathcal{R}}_{eff} < 1$). Alternatively, it can easily be seen that the inequality (4.10) fails whenever $\epsilon = 1$. This result is summarized below.

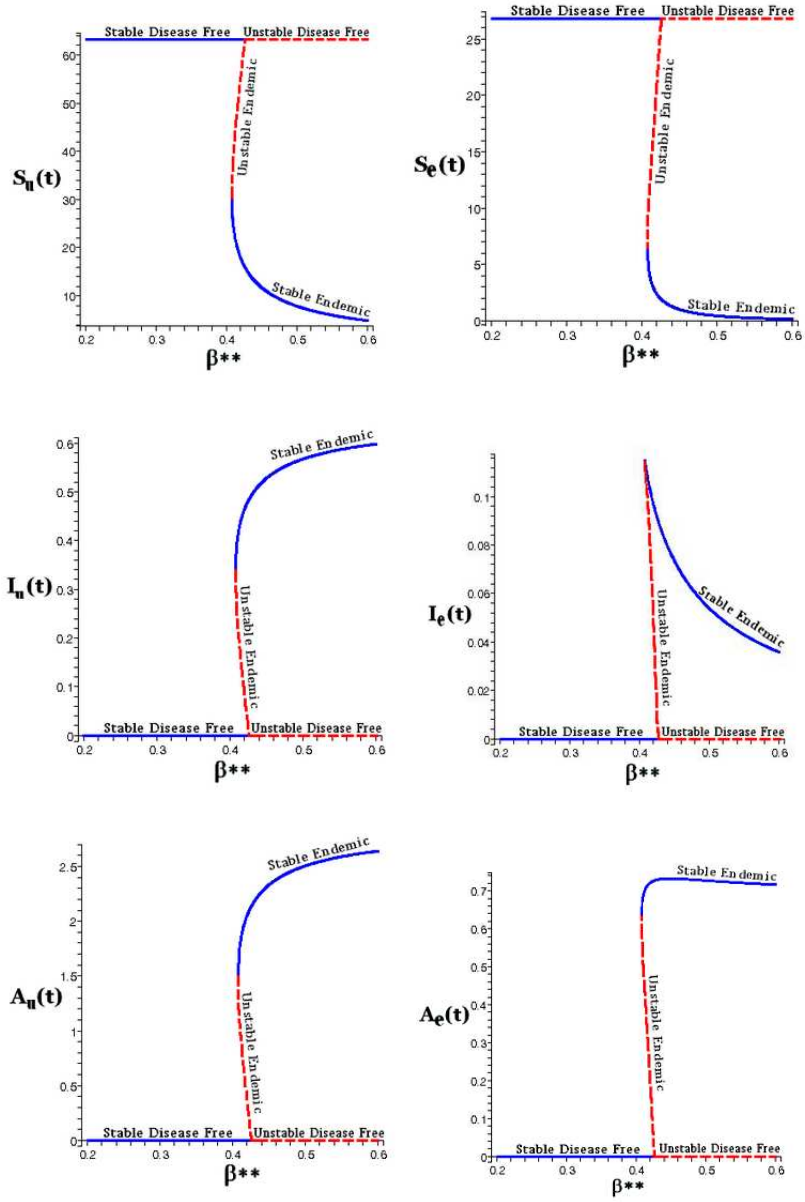


Figure 4.1: Backward bifurcation diagrams using demographic data from Ethiopia. Parameter values used are as in Table 3.2 and 3.3 with $\xi = 0.01$, $p = \psi_1 = \psi_2 = 0.001$ and $\epsilon = 0.4$ (so that, $a = 0.02069982715$ and $b = 1.930595939$).

Theorem 22.

The model (3.1) with $\epsilon = 1$ does not have a positive endemic equilibrium when $\tilde{\mathcal{R}}_{eff} < 1$.

Further, to show that HIV elimination is independent of the initial sizes of the sub-populations of the model when $\epsilon = 1$ (i.e., the efficacy of public health education is 100%), we claim the following result:

Theorem 23. *The DFE of the model (3.1) with $\epsilon = 1$ is GAS in $\mathcal{D}$ if $\tilde{\mathcal{R}}_{eff} \leq \frac{S_u^*}{N^*} \leq 1$.*

Proof. Consider the model (3.1) with $\epsilon = 1$. Further, consider the Lyapunov function

$$\mathcal{F} = f_1 I_u + f_2 A_u + f_3 I_e + f_4 A_e,$$

where,

$$\begin{aligned}
f_1 &= (1-\kappa)[\psi_1 K_2 K_4 + \eta_e \psi_2 \sigma_u K_3 + \eta_e \sigma_e \psi_1 K_2] + K_3 K_4 (K_2 + \eta_u \sigma_u), \\
f_2 &= K_1 K_3 [\eta_u K_4 + \eta_e \psi_2 (1-\kappa)], \\
f_3 &= K_1 K_2 (1-\kappa)[K_4 + \eta_e \sigma_e], \\
f_4 &= K_1 K_2 K_3 \eta_e (1-\kappa),
\end{aligned}$$

with Lyapunov derivative given by (where a dot represents differentiation with respect to t)

$$
\begin{aligned}
\dot{\mathcal{F}} &= f_1\dot{I}_u + f_2\dot{A}_u + f_3\dot{I}_e + f_4\dot{A}_e, \\
&= f_1\Big[\lambda_u S_u + (1-\kappa)\lambda_e S_u - K_1 I_u\Big] + f_2(\sigma_u I_u - K_2 A_u) \\
&+ f_3(\psi_1 I_u - K_3 I_e) + f_4(\sigma_e I_e + \psi_2 A_u - K_4 A_e), \\
&= K_1K_2K_3K_4\left(\frac{N^* S_u}{S_u^* N}\tilde{\mathcal{R}}_{eff} - 1\right) I_u + K_1K_2K_3K_4\eta_u\left(\frac{N^* S_u}{S_u^* N}\tilde{\mathcal{R}}_{eff} - 1\right) A_u \\
&+ K_1K_2K_3K_4\left(\frac{N^* S_u}{S_u^* N}\tilde{\mathcal{R}}_{eff} - 1\right) I_e + K_1K_2K_3K_4\eta_e(1-\kappa)\left(\frac{N^* S_u}{S_u^* N}\tilde{\mathcal{R}}_{eff} - 1\right) A_e \\
&- I_u[K_1(1-\kappa)(\psi_1 K_2K_4 + \eta_e\sigma_e\psi_1 K_2)] \\
&= K_1K_2K_3K_4(I_u + \eta_u A_u + I_e + \eta_e(1-\kappa)A_e)\left(\frac{N^* S_u}{S_u^* N}\tilde{\mathcal{R}}_{eff} - 1\right) \\
&- I_u[K_1(1-\kappa)(\psi_1 K_2K_4 + \eta_e\sigma_e\psi_1 K_2)] \\
&\leq K_1K_2K_3K_4(I_u + \eta_u A_u + I_e + \eta_e(1-\kappa)A_e)\left(\frac{N^*}{S_u^*}\tilde{\mathcal{R}}_{eff} - 1\right) \\
&- I_u[K_1(1-\kappa)(\psi_1 K_2K_4 + \eta_e\sigma_e\psi_1 K_2)] \quad \text{since} \quad S_u \leq N \ \text{ in } \mathcal{D} \\
&\leq 0 \quad \text{for} \quad \tilde{\mathcal{R}}_{eff} \leq \frac{S_u^*}{N^*} \leq 1.
\end{aligned}
$$

Thus, $\dot{\mathcal{F}} \leq 0$ if $\tilde{\mathcal{R}}_{eff} \leq \frac{S_u^*}{N^*}$ with $\dot{\mathcal{F}} = 0$ if and only if $I_u = A_u = I_e = A_e = 0$. Further, the largest compact invariant set in $\{\mathcal{X} : (S_u^*, S_e^*, I_u^*, A_u^*, I_e^*, A_e^*) \in \mathcal{D} : \dot{\mathcal{F}} = 0\}$ is the singleton $\mathcal{D}_{\mathcal{X}}$. It follows from the LaSalle Invariance Principle (LaSalle, 1968), that every solution to the equations in (3.1) with initial conditions in $\mathcal{D}$ converge to $\mathcal{D}_{\mathcal{X}}$ as $t \to \infty$. That is, the disease dies out. Further, substituting $I_u = A_u = I_e = A_e = 0$ in the model shows that $S_u \to S_u^*$ and $S_e \to S_e^*$ as $t \to \infty$. Thus, $(S_u, S_e, I_u, A_u, I_e, A_e) \to (S_u^*, S_e^*, 0, 0, 0, 0)$ as $t \to \infty$. Hence, since the region $\mathcal{D}$ is positively-invariant, it follows that the DFE of (3.1), with $\epsilon = 1$, is GAS in $\mathcal{D}$ for all non-negative initial conditions,

whenever $\tilde{\mathcal{R}}_{eff} \leq \frac{S_u^*}{N^*} \leq 1$. □

In summary, it is clear from Theorems 22 and 23 that the backward bifurcation phenomenon of the model is caused by the imperfect nature of the public health education campaign (i.e., $0 < \epsilon < 1$). In the case where the public health education is perfect, $\tilde{\mathcal{R}}_{eff} \leq \frac{S_u^*}{N^*} \leq 1$ is necessary and sufficient condition for the effective control of HIV in the community. In other words, the public health education with perfect efficacy could lead to effective control (or theoretical elimination) of HIV in the community provided the associated threshold quantity, $\tilde{\mathcal{R}}_{eff}$, is brought to (and maintained at) a value less than $\frac{S_u^*}{N^*}$. Thus, this study emphasizes the pressing need for the design of perfect public health education campaign to handle HIV.

Theorem 24. *The DFE of the model (3.1) with $\epsilon = 1$ does not undergo backward bifurcation at $\tilde{\mathcal{R}}_{eff} = 1$.*

Proof. The result follows from Theorem 22, where the model has no positive equilibrium when $\tilde{\mathcal{R}}_{eff} < 1$, and Theorem 23, where the DFE of the model (1) is GAS in $\mathcal{D}$ if $\tilde{\mathcal{R}}_{eff} \leq \frac{S_u^*}{N^*} \leq 1$. □

4.3 Conclusions

Some of the main theoretical findings of the study are:

- Under certain conditions, the model (3.1) undergoes backward bifurcation, when *the reproduction number* ($\mathcal{R}_{eff}$) is less than unity. The

backward bifurcation phenomenon resulted from the imperfect nature of the public health education program.

- For the case when the public health education program is 100% effective, the disease-free equilibrium of the model (3.1) is globally-asymptotically stable whenever the *associated reproduction number* is less than or equal to a quantity less than unity.

Chapter 5

Travelling waves for an SIR model with nonsmooth treatment rates

5.1 Introduction

Since the pioneering work of Kermack and McKendrick (1927), mathematical epidemiology developed an extensive body of literature and SIR models have been playing an important role in modelling epidemics of infectious diseases (such as measles, chickenpox, SARS, HIV, flu and poliomyelitis). The SIR model is suitable for: (i) a directly transmitted disease such as measles, rubella, or mumps, for which an infection confers permanent immunity (i.e., the individual once recovered is not susceptible to infection again) (Hethcote, 1989, 2000; Fuentes and Kuperman, 1999), (ii) diseases that allow permanent removal some of the infectives from the infectious class due to quarantine,

isolation, treatment, etc (Wang and Ruan, 2004; Altmann, 1995; Gul et al., 2009). Many researchers have studied the classical SIR model (e.g., Wang and Ruan, 2004; Altmann, 1995; Wang, 2006; d'Onofrio et al., 2007; Anderson and May, 1991, and the references therein), which describes the infection and removal process of individuals during an epidemic of an infectious disease. The SIR model is one of the simplest and yet most accurate of all biological models (May and Anderson, 1979; Keeling et al., 2001). Deterministic models for studying dynamics of epidemics are based on ordinary differential equations.

In recent years, some mathematical models incorporating treatment have been studied by many researchers (e.g., Wang and Ruan, 2004; Wang, 2006; Arino et al., 2008; Brauer, 2008; Gul et al., 2009). We define treatment as an act or manner of managing patients medically which may include isolation or quarantine. Further, this type of treatment has been successful in reducing the burden and spread of diseases such as HIV/AIDS, TB, and SARS (Hyman and Li, 1998; Jung et al., 2002; Gumel et al., 2004; Yan and Zou, 2008). Thus, in this Chapter, the infected individuals are removed from the infected class due to the treatment at a certain rate.

In mathematical epidemiology, some models for spatial spread of epidemics have been analyzed (Mulone et al., 2007; Mulone and Straughan, 2009; Murray, 2003; Rass and Radcliffe, 2003; van den Bosch et al., 1990; Webb, 1982; Marcati and Pozio, 1980). A fascinating question is whether a disease could remain endemic by the geographic motion of individuals. Mobility formulation as a random diffusion process in epidemic models takes the form of reaction-diffusion equations, which have been successful in modelling the

spatial spread of diseases as illustrated in Murray (2003). In the theory of reaction-diffusion equations, travelling waves play an important role and many techniques have been developed to prove existence or stability of such waves (see, Conley (1975); Conley and Gardner (1984); Dunbar (1984); Gardner and Smoller (1983) for their existence, and stability results can be found in Volpert et al. (1994); Rauch and Smoller (1978) and references therein). In general, Murray (2003), Gardner (1995), Fife (1979) and Volpert et al. (1994) provide a great detail on the subject. The investigations on travelling wave solutions for epidemic models are attracting more and more attention (Rass and Radcliffe, 2003).

In this Chapter, we consider epidemiological models introduced by Wang and Ruan (2004) and Wang (2006) which have certain non-smooth nonlinearities. After adding diffusion terms to the system like in Liu and Jin (2007), we analyze travelling-wave solutions. We consider two different cases for nonlinear and non-smooth treatment terms: (i) piecewise linear treatment rate with saturation effect, (ii) piecewise constant treatment rate with jump (Heaviside function). In Case (i), we observe some effects which are not present for travelling waves in classical SIR systems with constant coefficients such as non-monotone profiles for both susceptible individuals and infectives, oscillations of the profiles due to complex eigenvalues. In Case (ii), we observe a profile for which the susceptible individuals tend to infinity, the infectives converge to zero and their product approaches a constant at the forward end of the profile. Finally, numerical simulations are presented which confirm these analytical results.

5.2 Basic Model

Following Liu and Jin (2007); Wang and Ruan (2004) and Wang (2006), we consider, as basic model because of its interesting dynamical behaviour, the following deterministic system of nonlinear differential equations which represent an SIR model with nonlinear and non-smooth treatment rate:

$$\begin{aligned} \frac{dS}{dt} &= A - dS - \lambda SI, \\ \frac{dI}{dt} &= \lambda SI - dI - T(I), \\ \frac{dR}{dt} &= T(I) - dR, \end{aligned} \tag{5.1}$$

where $S(t)$, $I(t)$ and $R(t)$ denote three classes, namely, susceptible to disease, infected and infectious, and removed (infected, but no longer infectious due to treatment) individuals at time t, respectively. The constant A is the recruitment rate of the population, d is the natural death rate of the population and λ is the force of infection associated with the transmission of the disease by the infectives, $T(I)$ is the treatment rate of infected individuals. In most epidemic models it is assumed that $T(I) = cI$ for some constant $c > 0$. To take into account the limited capacity of treatment facilities, Wang (2006) considers a treatment rate which is proportional to the number of the infectives below the maximal capacity and remains constant otherwise. Furthermore, Wang and Ruan (2004) adopts a piecewise constant treatment rate with a jump. Thus,

we consider both cases with regard to the definition of $T(I)$ as follows;

$$(i) \quad T(I) = \begin{cases} rI, & \text{if } 0 \leq I \leq I_0, \\ \\ k, & \text{if } I \leq I_0, \end{cases} \qquad (ii) \quad T(I) = \begin{cases} m, & \text{if } I > 0, \\ \\ 0, & \text{if } I \leq 0, \end{cases} \tag{5.2}$$

as defined in Wang and Ruan (2004) and Wang (2006) respectively, where the constants $r > 0$, $m > 0$, $k = rI_0$ and I_0 is the capacity of treatment resources. Note that for (i) we have a piecewise linear treatment rate with saturation effect and for (ii) a piecewise constant treatment rate with jump (Heaviside function).

5.3 Spatial SIR Model

Following Liu and Jin (2007), we add diffusion effects to the basic model. Whereas Liu and Jin (2007) analyze Turing instability and simulate stripy patterns, we are interested in travelling waves. Random movement of individuals in space was further incorporated into model (5.1) by adding some diffusion terms, so that Fick's law holds. Letting $S(x,t)$ and $I(x,t)$ be the respective densities at a spatial position x and time t, this results in the following system of PDEs:

$$S_t = A - d\,S - \lambda S\,I + D_s\,S_{xx}, \tag{5.3a}$$

$$I_t = \lambda S\,I - d\,I - T(I) + D_i\,I_{xx}, \tag{5.3b}$$

$$R_t = T(I) - d\,R + D_r\,R_{xx}, \qquad x \in \mathbb{R}, \quad t > 0, \tag{5.3c}$$

where D_s, D_i and D_r are the diffusion rates for the susceptible, infected and recovered individuals, respectively. Since the first two equations of system (5.3) are independent of the last one, it suffices to consider the following reduced reaction diffusion model:

$$\begin{aligned} S_t &= A - d\,S - \lambda S\,I + D_s\,S_{xx}, \\ I_t &= \lambda S\,I - d\,I - T(I) + D_i\,I_{xx}, \qquad x \in \mathbb{R}, \quad t > 0. \end{aligned} \tag{5.4}$$

After solving system (5.4), R can be determined from (5.3c) which is a linear equation for R. It is assumed that the parameters A, d, λ, D_s, D_i are all positive constants. The system (5.4) has a disease-free equilibrium $\mathcal{E}_0 = (A/d, 0)$. For Case (i), the basic reproduction numbers are given by $\mathcal{R}_0 = \dfrac{\lambda A}{d(d+r)}$ if $0 \le I \le I_0$ and $\mathcal{R}'_0 = \dfrac{\lambda A}{d^2}$ if $I > I_0$, which measure the average number of new infections generated by a single infected person in a community. For Case (ii), $\mathcal{R}'_0$ is always used. Note that $\mathcal{R}_0 = \dfrac{\lambda A}{d(d+r)} < \mathcal{R}'_0 = \dfrac{\lambda A}{d^2}$. The number of infected individuals is expected to decline towards zero whenever $\mathcal{R}'_0 < 1$, because each infected individual on average infects less than one susceptible person. The disease will persist whenever $\mathcal{R}_0 > 1$.

We now consider homogeneous equilibria of system (5.4). For Case (i) there will be a positive endemic equilibrium $\mathcal{E}_1 = (S_1, I_1)$ of the system (5.4) provided $1 < \mathcal{R}_0 \leq 1 + \dfrac{\lambda\, k}{d\, r}$, where

$$S_1 = \frac{d + r}{\lambda}, \qquad I_1 = \frac{d(\mathcal{R}_0 - 1)}{\lambda} < I_0.$$

Further, define $b = d^2 + (k - A)\,\lambda$ and $\Delta = b^2 - 4\, d^2\, k\, \lambda$. Following Wang (2006), if $\Delta \geq 0$ then we have positive endemic equilibria of system (5.4), namely, $\mathcal{E}_2 = (S_2, I_2)$ and $\mathcal{E}_3 = (S_3, I_3)$, where

$$S_2 = \frac{A}{(d + \lambda I_2)}, \qquad I_2 = \frac{-b - \sqrt{\Delta}}{2d\lambda} > I_0,$$

$$S_3 = \frac{A}{(d + \lambda I_3)}, \qquad I_3 = \frac{-b + \sqrt{\Delta}}{2d\lambda} > I_0.$$

From Theorems 2.1 and 2.2 of Wang (2006), we deduce the following result.

Proposition 1. *Consider the system (5.4), where $T(I)$ is given by Case (i), and define $p_0 = 1 + \dfrac{\lambda\, k - d\, r}{d(d + r)} + \dfrac{2\sqrt{\lambda\, k}}{(d + r)}$, $p_1 = 1 + \dfrac{\lambda\, k - d\, r}{d(d + r)} + \dfrac{2\lambda\, k}{r(d + r)}$ and $p_2 = 1 + \dfrac{\lambda\, k}{d\, r}$. Suppose that $\mathcal{R}_0 \geq p_0$ and $\mathcal{R}_0 > 1$ then*

(a) $\mathcal{E}_1$ is the unique endemic equilibrium if $\mathcal{R}_0 \leq p_2$ and $\mathcal{R}_0 < p_1$.

(b) The endemic equilibrium points $\mathcal{E}_2$ and $\mathcal{E}_3$ co-exist whenever

$p_1 < \mathcal{R}_0 < p_2$.

We will investigate travelling wave solutions whose profiles are heteroclinic orbits connecting different equilibrium points of system (5.4) in Section 5.4.

5.3.1 Stability of Disease-free Equilibrium

Here, we are concerned with the stability of the disease-free equilibrium $\mathcal{E}_0 = (A/d, 0)$ of the system (5.4). Therefore, we claim the following result.

Theorem 25. *Suppose that $\mathcal{R}_0 < 1$ in the system (5.4), where the nonlinearity $T(I)$ is given in Case (i) of equation (5.2). Then the disease-free equilibrium $\mathcal{E}_0 = (A/d, 0)$ is locally asymptotically stable.*

Proof. Consider the vector field

$$(f_1(S, I), f_2(S, I)) = (S\,M(S, I), I\,N(S, I)),$$

where

$$f_1(S, I) = A - d\,S - \lambda S\,I, \quad f_2(S, I) = \lambda S\,I - d\,I - T(I),$$

$$M(S, I) = A/S - d - \lambda I \quad \text{and} \quad N(S, I) = \lambda S - d - T(I)/I.$$

Note that $M_I(S, I) < 0$ and $N_S(S, I) > 0$ (where subscripts denote differentiation). The Jacobian J of the vector field $(S\,M(S, I), I\,N(S, I))$ around the disease-free equilibrium $\mathcal{E}_0$ is given by

$$J = \begin{pmatrix} -d & -\frac{\lambda A}{d} \\ \\ 0 & \frac{\lambda A}{d} - (d + r) \end{pmatrix}.$$

Thus, the eigenvalues of J are both negative if $\mathcal{R}_0 < 1$. From Theorem 4.1 of Conway and Smoller (1977), there exists an open neighourhood Σ of $\mathcal{E}_0$ which

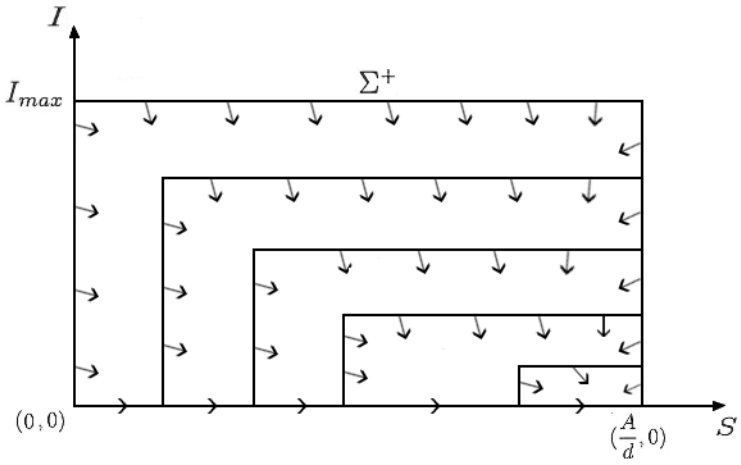


Figure 5.1: Semi-contracting rectangle.

is contained in $\{(S,I):\ S\geq 0,\ I\geq 0\}$ such that every solution to the system (5.4) with initial conditions in Σ decays exponentially to $\mathcal{E}_0$ as $t\to\infty$. □

Under slightly stronger assumptions (replacing $\mathcal{R}_0<1$ by $\mathcal{R}_0^{'}<1$) we are able to prove a result which includes both Cases (i) and (ii) for $T(I)$ and explicitly locates a set of initial conditions for which asymptotic stability holds.

Theorem 26. *Suppose that $\mathcal{R}_0^{'}<1$, then the disease-free equilibrium $\mathcal{E}_0=(\frac{A}{d},0)$ of the system (5.4) is locally asymptotically stable. More precisely, $(S(t,x),I(t,x))\to(\frac{A}{d},0)$ if $(S(0,x),I(0,x))\in\Sigma^+$ where $\Sigma^+=(0,\frac{A}{d})\times(0,I_{max})$ for all $x\in\mathbb{R}$, and $I_{max}=\frac{d}{2\lambda}$.*

Proof.

Consider the rectangle $\Sigma^+=(0,\frac{A}{d})\times(0,I_{max})$ given in Figure 5.1, where $I_{max}=\frac{d}{2\lambda}$.

Let $f_1(S,I)=A-d\,S-\lambda S\,I$ and $f_2(S,I)=\lambda S\,I-d\,I-T(I)$. We can

easily see that f_1 is negative on the "right edge" of Σ^+, and positive on the "left edge" of Σ^+. On the other hand, on the "top" of Σ^+,

$$f_2(S, I_{max}) = \lambda S\, I_{max} - d\, I_{max} - T(I_{max}).$$

Since $S \leq \frac{A}{d}$ and $\mathcal{R}_0' < 1$ then $f_2(S, I_{max}) < 0$. On the "bottom" of Σ^+, $f_2(S, 0) = 0$. Thus, Σ^+ is a semi-contracting rectangle as defined in Definition 16 (see also Mimura, 1979).

In the same way we now show that

$$\gamma\Sigma^+ + (1-\gamma)(\frac{A}{d}, 0) = [(1-\gamma)\frac{A}{d}, \frac{A}{d}] \times [0, \gamma I_{max}] := [S_l, \frac{A}{d}] \times [0, I_l]$$

is a family of similar semi-contracting rectangles for $0 < \gamma < 1$ centered at the point $(\frac{A}{d}, 0)$. By definition, it is clear that this is a similar family of rectangles. Further, as in the case $I_l = I_{max}$, this is a semi-contracting family if

$$A - d\, S_l - \lambda S_l\, I_l > 0, \tag{5.5}$$

where $S_l = (1-\gamma)\frac{A}{d}$ and $I_l = \gamma I_{max}$ for all $0 < \gamma < 1$. From (5.5), we obtain

$$\frac{\lambda(1-\gamma)}{d} I_{max} < 1 \quad \text{for all } 0 \leq \gamma \leq 1.$$

The condition (5.5) is satisfied if $I_{max} < \frac{d}{\lambda}$. Choosing $I_{max} = \frac{d}{2\lambda}$, we have a similar semi-contracting family of rectangles centered at $(\frac{A}{d}, 0)$.

Finally, by using the same argument as in the proof of Lemma 3.8 of Rauch and Smoller (1978), from the existence of similar semi-contracting fam-

ily of rectangles centered at $(\frac{A}{d}, 0)$ follows the convergence of any solution whose initial condition lies in Σ^+ for all $x \in \mathbb{R}$ to $(\frac{A}{d}, 0)$. □

Remarks:

(1) Theorem 25 considers the non-linearity in Case (i) of equation (5.2) only, while Theorem 26 deals with both non-linearities of equation (5.2).

(2) It is assumed that $\mathcal{R}_0 < 1$ and $\mathcal{R}_0^{'} < 1$ in Theorems 25 and 26, respectively, where $\mathcal{R}_0 < \mathcal{R}_0^{'} < 1$. Thus, the condition in Theorem 25 is stronger.

(3) Σ^+ is located to the left of the point $(\frac{A}{d}, 0)$ in Theorem 26, whilst there exists Σ around $(\frac{A}{d}, 0)$ in Theorem 25.

(4) Mulone et al. (2007) introduced Liapunov functions to prove nonlinear stability of some epidemic models of SI type. Their method is elegant and shows global stability, but it requires special transformations and works only on bounded domains.

5.4 Travelling-wave solutions

The spatial model (5.4) is the starting point of the analysis in this Chapter. We are interested in the question of the existence of travelling wave solutions. Now, we look for travelling wave solutions of the form $S(x,t) = u(x+ct) = u(z)$

and $I(x,t) = v(x+ct) = v(z)$ with $z = x + ct$ and c is the travelling wave speed. We assume that susceptible individuals and infectives diffuse at the same rate (i.e., $D_s = D_i = 1$) and substitute u and v into (5.4). These result in the coupled system of ordinary differential equations below

$$u_{zz} - cu_z + A - du - \lambda uv = 0, \tag{5.6a}$$

$$v_{zz} - cv_z + \lambda uv - dv - T(v) = 0. \tag{5.6b}$$

Biologically speaking, the introduction of few infected individuals at one end of linear habitat (e.g., coastline), which is initially uniformly saturated with susceptible individuals at the carrying capacity of the environment, may result in a "wave of propagation" of infected individuals. Therefore, a zone of transition from one equilibrium point to another is possible and the traveling wave profiles occurs when this transition zone moves across the population (Dunbar, 1984). In order to investigate the existence of such wave (i.e., travelling wave) of system (5.4), let $f = u_z$ and $g = v_z$, so that $f_z = u_{zz}$ and $g_z = v_{zz}$, which leads to the four-dimensional system

$$u_z = f, \tag{5.7a}$$

$$f_z = c\,f - A + d\,u + \lambda\,u\,v, \tag{5.7b}$$

$$v_z = g, \tag{5.7c}$$

$$g_z = c\,g - \lambda\,u\,v + d\,v + T(v). \tag{5.7d}$$

Now we state the following Corollary about the non-existence of certain travelling waves which follows immediately from Theorem 25.

Corollary 1. *Suppose that* $\mathcal{R}_0' < 1$*, then there is no travelling wave profile from the disease-free equilibrium* $\mathcal{E}_0 = (\frac{A}{d}, 0)$ *of the system (5.6) provided the initial sizes of the sub-populations are within the semi-contracting set* $\Sigma^+ = (0, \frac{A}{d}) \times (0, I_{max})$.

Proof. Corollary 1 follows directly from the result of Theorem 25. □

In the following subsections, we consider the Case (i) piecewise linear treatment rate with saturation effect and Case (ii) piecewise constant treatment rate with jump separately.

5.4.1 Piecewise linear treatment rate with saturation effect

In this section, we assume that the treatment rate is proportional to the number of the infected individuals when the capacity of treatment is less than or equal to the number of infected individuals and takes the maximal capacity otherwise (i.e., we are considering Case (i)). We shall first establish the existence of a heteroclinic connection in $\mathbb{R}^4$. In other words, a travelling wave solution must correspond to a trajectory that connects two steady states in $\mathbb{R}^4$. A travelling wave solution of system (5.4) exists if there exists a heteroclinic orbit connecting at least two of the following critical points of (5.7), which are related to the equilibrium points found in Section 5.3.

$$\mathcal{E}'_0 = \begin{pmatrix} 0 \\ A/d \\ 0 \\ 0 \end{pmatrix}, \qquad \mathcal{E}'_1 = \begin{pmatrix} 0 \\ S_1 \\ 0 \\ I_1 \end{pmatrix}, \qquad \mathcal{E}'_2 = \begin{pmatrix} 0 \\ S_2 \\ 0 \\ I_2 \end{pmatrix} \qquad \text{and} \qquad \mathcal{E}'_3 = \begin{pmatrix} 0 \\ S_3 \\ 0 \\ I_3 \end{pmatrix}.$$

Linearization of (5.7) about $\mathcal{E}'_0$ has a characteristic equation

$$\lambda^4 - 2\,c\lambda^3 + \frac{(-2\,d^2 - rd + \lambda\,A + c^2 d)\,\lambda^2}{d} - \frac{c\,(-2\,d^2 - rd + \lambda\,A)\,\lambda}{d} + d^2 + rd - \lambda\,A = 0.$$

Thus, it has the following eigenvalues

$$\Lambda_{1,2} = \frac{c \pm \sqrt{c^2 + 4\,d}}{2} \qquad \text{and} \qquad \Lambda_{3,4} = \frac{c \pm \sqrt{c^2 - 4(r+d)(\mathcal{R}_0 - 1)}}{2\,d}. \quad (5.8)$$

Since $\mathcal{R}_0 > 1$, then for $c > c^*$, where $c^* = 2\sqrt{(r+d)(\mathcal{R}_0 - 1)}$, the stable manifold at $\mathcal{E}'_0$, denoted by $\mathcal{M}_s(\mathcal{E}'_0)$, is three dimensional (that is, $\dim(\mathcal{M}_s(\mathcal{E}'_0)) = 3$) while the dimension of the unstable manifold is one (that is, $\dim(\mathcal{M}_u(\mathcal{E}'_0)) = 1$). If $c \geq c^*$ then all the four eigenvalues in equations (5.8) are real.

However, if $0 < c < c^*$ then Λ_3 and Λ_4 are a pair of complex conjugate eigenvalues with positive real part. From Theorems 6.1 and 6.2 in Hartman (1973), we have a two-dimensional unstable manifold at $\mathcal{E}'_0$ and the disease-free equilibrium point is a spiral point on this unstable manifold. A trajectory approaching $\mathcal{E}'_0$ must have $v(z) < 0$ for some z. This contradicts the fact that the traveling wave solutions are non-negative. Therefore c^* is a minimal wave speed. Hence, we summarize the result as follows.

Theorem 27. *Suppose that $\mathcal{R}_0 > 1$ and $0 < c < c^*$, then the system (5.7) with Case (i) of equation (5.2) has no heteroclinic orbit connecting $\mathcal{E}'_0$ with any of the endemic equilibrium points.*

Let $\mathcal{M}_s(\mathcal{E}'_i)$ and $\mathcal{M}_u(\mathcal{E}'_i)$ denote the local stable and unstable manifolds associated with $\mathcal{E}'_i$, $i = 0, 1, 2, 3$. We claim the following result.

Lemma 6. *Suppose that Case (a) of Proposition 1 holds, then*

$$dim(\mathcal{M}_s(\mathcal{E}'_0)) + dim(\mathcal{M}_u(\mathcal{E}'_1)) = dim(\mathbb{R}^4) + 1.$$

Proof. Let Case (a) of Proposition 1 hold, then $\mathcal{E}'_1$ exists and we linearize (5.7) around $\mathcal{E}'_1$. Thus, we have the following characteristic polynomial

$$\lambda^4 - 2\,c\lambda^3 + \left(c^2 - d\mathcal{R}_0\right)\lambda^2 + c\,d\mathcal{R}_0\lambda + d\,(\mathcal{R}_0 - 1)\,(d + r) = 0,$$

and the corresponding eigenvalues

$$\Lambda_{1,2} = \frac{c \pm \sqrt{c^2 + 2\,d\mathcal{R}_0 - 2\sqrt{\Delta_2}}}{2},$$

$$\Lambda_{3,4} = \frac{c \pm \sqrt{c^2 + 2\,d\mathcal{R}_0 + 2\sqrt{\Delta_2}}}{2},$$

where $\Delta_2 = d^2{\mathcal{R}_0}^2 - 4\,d(d + r)(\mathcal{R}_0 - 1)$. This implies $\dim(\mathcal{M}_s(\mathcal{E}'_1)) = \dim(\mathcal{M}_u(\mathcal{E}'_1)) = 2$. Since $\dim(\mathcal{M}_s(\mathcal{E}'_0)) = 3$ and $\dim(\mathcal{M}_u(\mathcal{E}'_0)) = 1$, then

$$\dim(\mathcal{M}_s(\mathcal{E}'_0)) + \dim(\mathcal{M}_u(\mathcal{E}'_1)) = \dim(\mathbb{R}^4) + 1.$$

□

Lemma 7. *Suppose that Case (b) of Proposition 1 holds, then*

$$dim(\mathcal{M}_s(\mathcal{E}'_0)) + dim(\mathcal{M}_u(\mathcal{E}'_3)) = dim(\mathbb{R}^4) + 1.$$

Proof. Let Case (b) of Proposition 1 hold, then $\mathcal{E}'_3$ exists. By using similar argument above, we linearize around $\mathcal{E}'_3$ and obtain the following eigenvalues

$$\frac{c \pm \sqrt{c^2 + 4d}}{2} \quad \text{and} \quad \frac{c \pm \sqrt{c^2 + \frac{4}{d}\sqrt{\Delta}}}{2},$$

with $\dim(\mathcal{M}_s(\mathcal{E}'_3)) = \dim(\mathcal{M}_u(\mathcal{E}'_3)) = 2$ where $\Delta = b^2 - 4\,d^2\,k\,\lambda$ and $b = d^2 + (k - A)\,\lambda$. Hence,

$$\dim(\mathcal{M}_s(\mathcal{E}'_0)) + \dim(\mathcal{M}_u(\mathcal{E}'_3)) = \dim(\mathbb{R}^4) + 1.$$

□

The Lemmas 6 and 7 show that $\mathcal{M}_s(\mathcal{E}'_0)$ can potentially intersect transversally along a one-dimensional curve with $\mathcal{M}_u(\mathcal{E}'_i)$ in $\mathbb{R}^4$ for $i = 1$ and 3 (Ashwin et al., 2002; Guckenheimer and Holmes, 2002; Beyn, 1990a). If this happens, then the existence of a heteroclinic connection between the equilibrium points $\mathcal{E}'_0$ and $\mathcal{E}'_i$ for $i = 1$ and 3 follows.

The linearization about $\mathcal{E}'_2$ leads to the following eigenvalues

$$\Lambda^4 - 2\,c\Lambda^3 - \gamma_1\Lambda^2 + \gamma_2\Lambda + \frac{\Delta + b\sqrt{\Delta}}{b + \sqrt{\Delta}} = 0,$$

and the corresponding eigenvalues $\frac{c \pm \sqrt{c^2 + 4\,d}}{2}$ and $\frac{c \pm \sqrt{c^2 - \frac{4}{d}\sqrt{\Delta}}}{2}$, where

$$\gamma_1 = \frac{\left(d^2\,b + \Delta - c^2 d^2 (d - \lambda\,k + \lambda\,A) - (c^2 d + \lambda\,k - \lambda\,A)\sqrt{\Delta}\right)}{d\left(b + \sqrt{\Delta}\right)},$$

$$\gamma_2 = \frac{c\left(d^2\,b + \Delta + d^2 b\sqrt{\Delta}\right)}{d\left(b + \sqrt{\Delta}\right)},$$

$\Delta = b^2 - 4\,d^2\,k\,\lambda$ and $b = d^2 + (k - A)\,\lambda$. Therefore,

$$\dim(\mathcal{M}_s(\mathcal{E}'_2)) = 3 \quad \text{and} \quad \dim(\mathcal{M}_u(\mathcal{E}'_2)) = 1,$$

with a critical speed $c^{**} = 2\sqrt{\frac{\sqrt{\Delta}}{d}}$ where $\Delta \geq 0$.

We summarize the result as follows.

Lemma 8. *Suppose that Case (b) of Proposition 1 holds, then*

$$dim(\mathcal{M}_s(\mathcal{E}'_2)) + dim(\mathcal{M}_u(\mathcal{E}'_3)) = dim(\mathbb{R}^4) + 1.$$

It should be noted that $\mathcal{E}'_2 = (0, S_2, 0, I_2)$ does not have zero components corresponding to the subpopulation densities. Therefore, it will be instructive to study oscillation of trajectories around this equilibrium point. For $0 < c < c^{**}$, which means travelling wave fronts travel with a speed smaller than the critical value c^{**}, there are two complex conjugate eigenvalues which lead to small oscillations in the travelling wave profiles around $\mathcal{E}'_2$. Numerical examples of heteroclinic orbits for all cases in lemmas 6, 7 and 8 will be

presented in Section 5.4.3.

5.4.2 Piecewise Constant Treatment Rate with a Jump

Here, we assume that the treatment rate is piecewise constant with a jump, i.e.,

$$T(I) = \begin{cases} m, & \text{if } I > 0, \\ \\ 0, & \text{if } I \leq 0. \end{cases} \tag{5.9}$$

(Case (ii)). Due to the discontinuity of $T(I)$, we cannot use our approach in Section 5.4.1 to construct travelling waves. Further, we will see that the jump of $T(I)$ creates a jump in the second derivative of $v(z)$ and in the fourth derivative of $u(z)$ at $z = 0$. We claim the following result.

Theorem 28. *Suppose that we have Case (ii) for the treatment rate and that*

$$(\frac{\lambda A}{d} - d)v(z_0) > m \quad \textit{for some } z_0 > 0. \tag{5.10}$$

Then a positive travelling front solution $(u(z), v(z))$ of (5.7), if it exists, has the following properties: for all $c < 0$, $u(z)$ is monotone increasing for all $z \in (0, \infty)$ and $v(z)$ has at least one local maximum point $z_0 \in (0, \infty)$.

Proof. We first show that $u(z)$ is monotone increasing. Considering (5.7), we derive from the fact that $T(v)$ has a jump at $v = 0$, that v_{zz} has a jump where $v = 0$ and v, v_z are both smooth functions. Because of the jump for v_{zz} there is also a jump for u_{zzzz} and u, u_z, u_{zz}, u_{zzz} are all smooth

functions.

Since $u(z) = \frac{A}{d}$ for $z < 0$, we derive $u(0) = A/d$ and $u_z(0) = u_{zz}(0) = u_{zzz}(0) = 0$. Using again (5.7), we derive $u_{zzzz}(0^+) = \dfrac{\lambda\, A\, m}{d}$. Thus,

$$u(z) = \frac{A}{d} + \frac{\lambda\, A\, m}{d}\frac{z^4}{24} + O(z^5) \text{ for } z > 0 \text{ small.}$$

This implies that $u(z) > \frac{A}{d}$ and $u(z)$ is increasing for z small enough. Suppose that $u(z)$ has a local maximum point z_0 with $u(z_0) > \dfrac{A}{d}$, then $u_z(z_0) = 0$ and $u_{zz}(z_0) \leq 0$. This implies that $f(z_0) = 0$ and $f_z(z_0) \leq 0$, but the right-hand side of (5.7b) is strictly positive (i.e., $c\, f - A + d\, u + \lambda\, u\, v > 0$) which is a contradiction. Hence, $u(z)$ has no local maximum.

Next we show that $v(z)$ has at least one local maximum. Using again (5.7), we derive $v(0) = v_z(0) = 0$ and $v_{zz}(0^+) = m$. Therefore,

$$v(z) = m\frac{z^2}{2} + O(z^3) \quad \text{for } z > 0 \text{ small.}$$

Hence, $v(z)$ is monotone increasing for $z > 0$ small.

Assuming that $v(z)$ is monotone increasing for all $z > 0$ (i.e., $v(z_2) > v(z_1)$ for all $z_2 > z_1 > 0$) we will derive a contradiction. Then from (5.6b) we

have for $z > z_0$

$$\begin{aligned}
v_{zz} - c\,v_z &= -\lambda\,u\,v + d\,v + m \\
&\leq -\lambda\tfrac{A}{d}v + d\,v + m \quad \text{since } u \text{ is increasing (implying } u(z) \geq A/d) \\
&= v\left(-\lambda\tfrac{A}{d} + d\right) + m \\
&\leq v(z_0)\underbrace{\left(-\lambda\frac{A}{d} + d\right)}_{<0 \text{ by (5.10)}} + m \quad \text{since } v(z) > v(z_0) \text{ for all } z > z_0 \\
&\leq L < 0, \quad \text{where } L \text{ is a negative constant by (5.10).}
\end{aligned}$$

Using that $v_{zz} - c\,v_z \leq L < 0$ for all $z > z_0$, we derive $g_z - cg \leq L$, where $g = v_z$. Setting $g(z) = \exp(cz)h(z)$, we have $h_z \exp(cz) \leq L$. Integrating this inequality gives $h(z) \leq -\frac{L}{c}\exp(-cz) + D$ for some real constant D. This implies $g(z) \leq -\frac{L}{c} + D\exp(cz) < 0$ for z large enough since $L < 0$. Integrating again, we get $v(z) = B_1 \exp(c\,z) + B_2 - \dfrac{L}{c}z$ for some constants B_1, B_2. This implies that $v(z) < 0$ if z is large enough. This is a contradiction to the positivity of v. Therefore v is not monotone.

Since v is a continuously differentiable function which is monotone increasing for small enough $z > 0$ and monotone decreasing for some other $z > 0$, it must have a local maximum somewhere in between by the Intermediate Value Theorem for the derivative of $v(z)$.

□

Remark: The technical assumption (5.10) seems quite strong. However, we have not been able to prove the non-monotonicity or the existence of a local maximum for v without it.

Next we state a result about the behavior of the solution as $z \to \infty$.

Theorem 29. *If $u(z) \to \infty$ and $v(z) \to 0$ as $z \to \infty$, then $u(z)\,v(z)$ approaches a constant.*

Proof. Let $u(z) \to \infty$ and $v(z) \to 0$, then $u(z)\,v(z) >> v(z)$, $u(z) >> u(z)\,v(z)$ and $u(z) >> A$ as $z \to \infty$. Thus, (5.7) in leading order reads

$$u_z = f, \tag{5.11a}$$

$$f_z = c\,f + d\,u \tag{5.11b}$$

$$v_z = g, \tag{5.11c}$$

$$g_z = c\,g - \lambda\,u\,v + d\,v + m. \tag{5.11d}$$

From (5.11a) and (5.11b), we have $u_{zz} - cu_z - d\,u = 0$. Solving this linear equation for u, leads to the characteristic equation $\mu^2 - c\,\mu - d = 0$ which has the solutions

$$\mu_{\pm} = \frac{c \pm \sqrt{c^2 + 4\,d}}{2}.$$

Since $u(z) \to \infty$, we take

$$\mu_{+} = \frac{c + \sqrt{c^2 + 4\,d}}{2}.$$

Further, considering the original system (5.7) we arrive at

$$u(z) = u_0 \exp(\mu_+ z) + O(1) \quad \text{as} \quad z \to \infty \tag{5.12}$$

since all the terms neglected when going from (5.7) to (5.11) are of order $O(1)$. This requires the estimate $v(z) = O(\exp(-\mu_+ z))$ which will be shown below.

We now determine the decay for v, assuming that $v(z) \to 0$ as $z \to \infty$. From (5.11c) and (5.11d), we obtain

$$v_{zz} - c\, v_z - d\, v + \lambda\, u\, v - m = 0. \tag{5.13}$$

Using asymptotic expansion, we consider the following estimate:

$$v(z) = H_0 \exp(-\mu_+ z) + O(\exp(-2\mu_+ z)).$$

Substituting $u(z)$ and $v(z)$ into (5.13) gives, at order 1,

$$\lambda\, u_0\, H_0 - m = 0; \quad \Longrightarrow \quad H_0 = \frac{m}{\lambda\, u_0}.$$

Thus, for the solution of (5.7) we have the estimate

$$v(z) = \frac{m}{\lambda\, u_0} \exp(-\mu_+ z) + O(\exp(-2\mu_+ z)).$$

Hence, for the solution (u, v) of (5.7) we have derived the estimate

$$u(z)v(z) = \frac{m}{\lambda} + O(\exp(-\mu_+ z)).$$

□

5.4.3 Numerical simulations

In this section, before mentioning our numerical results with regard to sections 5.4.1 and 5.4.2, it will be instructive to briefly describe the numerical methods used. For Case (i), since $T(I)$ is continuous, let $\xi = (\xi_1, \xi_1)$ and $\Phi = (\Phi_1, \Phi_1)$ be two equilibrium points we are interested in connecting. Then the travelling wave solutions, if exist, must satisfy the following asymptomatic boundary conditions: $u(-\infty) = \xi_1$, $u(\infty) = \xi_2$ and $v(-\infty) = \Phi_1$, $v(\infty) = \Phi_2$. We truncate the interval $\mathbb{R} = (-\infty, \infty)$ by a finite interval $[Z_-, Z_+]$ where $Z_- < 0 < Z_+$ and $Z_\pm \in \mathbb{Z}$. We obtain the travelling wave solutions by simulating system (5.7) with $T(I)$ as defined in Case (i) as a Boundary Value Problem (BVP). We implement this on MATLAB using solver *bvp4c* together with the projected boundary and phase conditions given by (Beyn, 1990a,b; Champneys et al., 1996; Bai et al., 1993). By setting the truncated domain to be $[-30, 30]$, we use the following piecewise functions as initial conditions:

$$u(z) = \begin{cases} \xi_1, & \text{if } -30 \leq z \leq 0, \\ \\ \xi_2, & \text{if } 0 \leq z \leq 30, \end{cases} \qquad v(z) = \begin{cases} \Phi_1, & \text{if } -30 \leq z \leq 0, \\ \\ \Phi_2, & \text{if } 0 \leq z \leq 30. \end{cases} \tag{5.14}$$

Here, however, we do not fix the model variables and parameters throughout the simulations due to the existence conditions of the equilibrium points mentioned in Proposition 1. At first, we demonstrate the results for Theorem 27

with the following set of parameter values:

$$A = 2.8,\ \lambda = 0.001,\ r = 0.001,\ d = 0.02,\ k = 1. \tag{5.15}$$

This leads to $\mathcal{E}'_0 = (0, 140, 0, 0)$ and $\mathcal{E}'_1 = (0, 21, 0, 113.3333)$. Further, the condition for the existence of $\mathcal{E}'_1$ is fulfilled (i.e., $p_0 = 6.345 < \mathcal{R}_0 = 6.6667 < p_2 = 51\ \mathcal{R}_0 = 6.6667 < p_1 = 98.5714$). Figure 5.2 shows that there is no travelling wave front connecting the disease-free equilibrium $\mathcal{E}'_0$ and the endemic equilibrium $\mathcal{E}'_1$ with speed $c = 0.1099 < c^* = 0.6899$, because $v(z)$ takes negative values, which is unrealistic, and oscillates around the disease-free equilibrium $\mathcal{E}'_0$. Hence, the simulation agreed with Theorem 27.

The subpopulation densities of susceptible individuals and infected individuals are represented as Subfigures $A1$ and $A2$ respectively, for most of the simulation. Figures 5.3 and 5.2 indicate that as c decreases from c^* more and more oscillations observed.

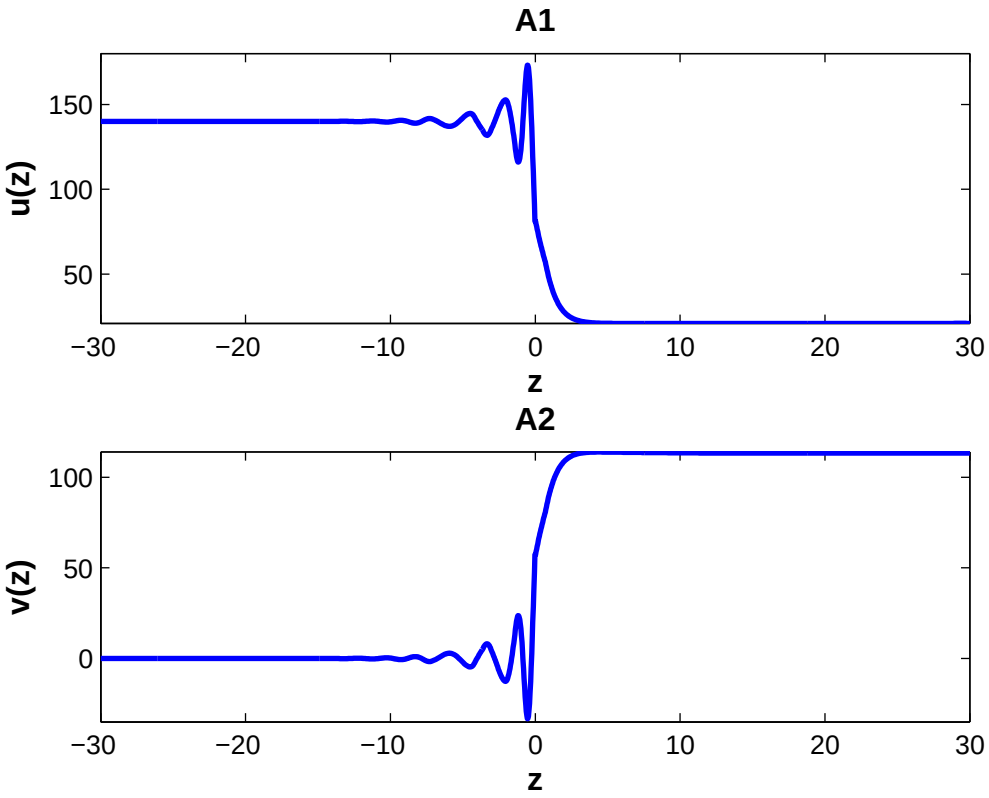


Figure 5.2: Assuming (5.15) with $c^* = 0.6899 > c = 0.1099$.

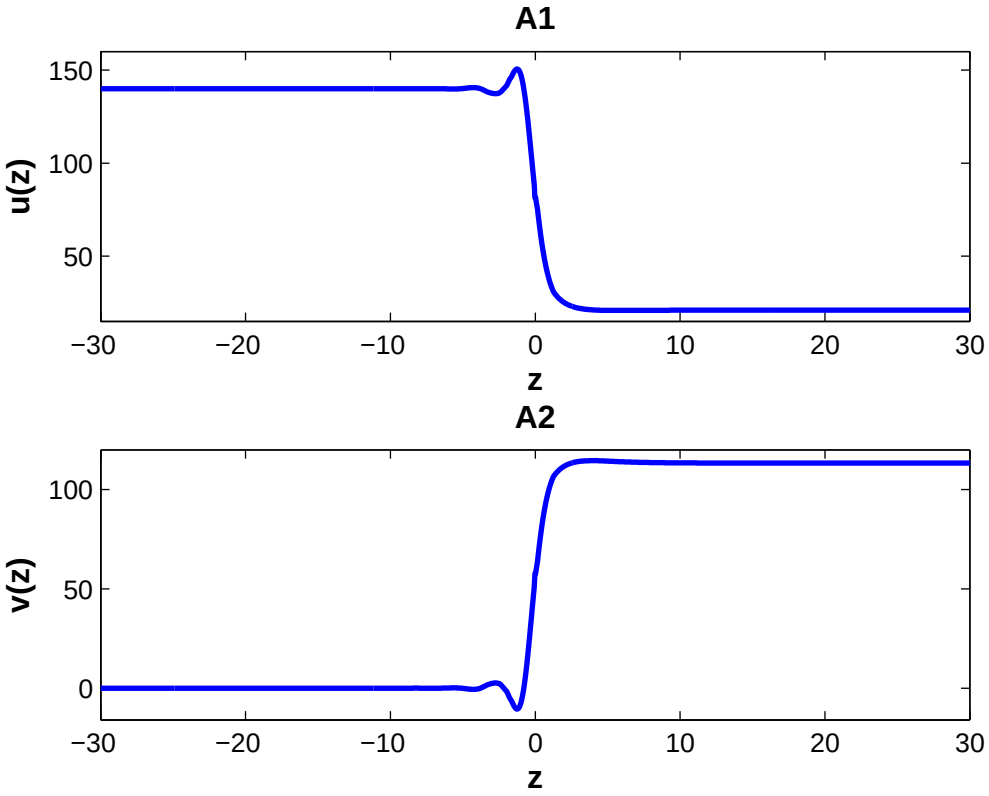


Figure 5.3: Assuming (5.15) with $c^* = 0.6899 > c = 0.2899$.

Now, we numerically illustrate the results obtained in Lemmas 6, 7 and 8, by carrying out some simulations. Lemma 6 suggests the connection between $\mathcal{E}'_0$ and $\mathcal{E}'_1$ and we have the following:

$\Delta_2 \geq 0$: all the eigenvalues of the jacobian evaluated at $\mathcal{E}'_1$ are strictly real and hence a smooth travelling wave profiles, corresponding to the system (5.7) with $T(I)$ as defined in Case (i), connecting $\mathcal{E}'_0$ and $\mathcal{E}'_1$ are obtained as depicted in Figure 5.4.

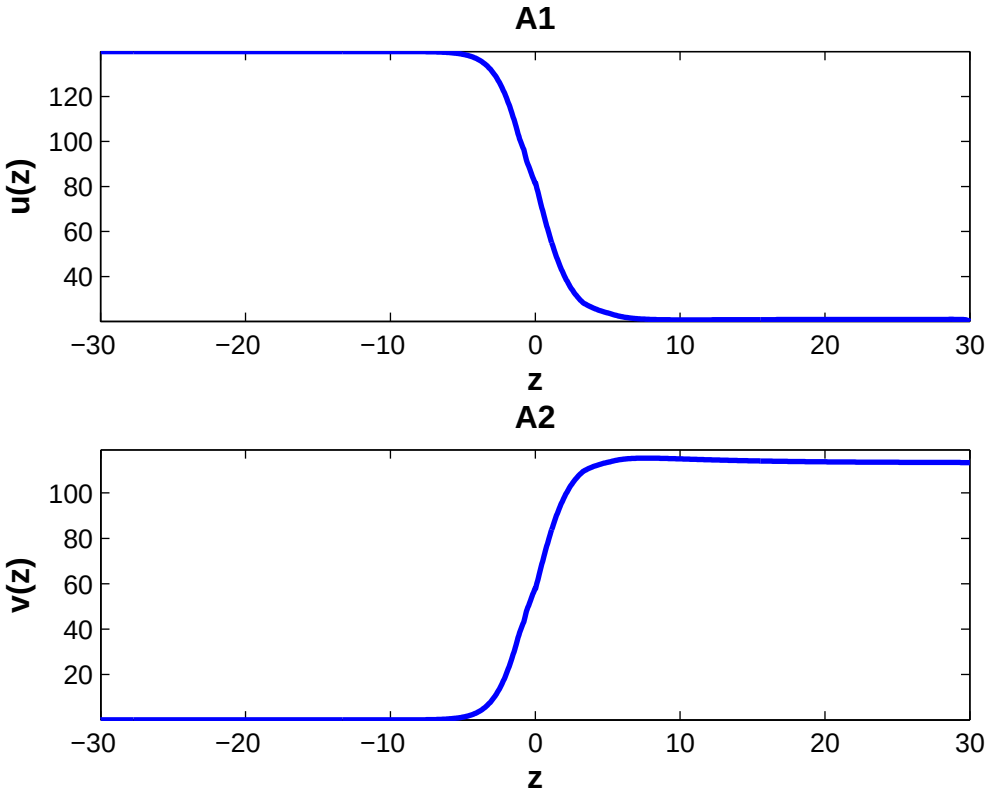


Figure 5.4: Assuming (5.15) with $\Delta_2 = 0.0083$ and $c = 0.9899$.

$\Delta_2 < 0$: non-monotone travelling wave solutions connecting $\mathcal{E}'_0 = (0, 140, 0, 0)$ and $\mathcal{E}'_1 = (0, 30, 0, 73.3333)$ are obtained as shown in Figure 5.5. Here, we observed a hump in the wave profile for $v(z)$ and a corresponding dip in that for $u(z)$.

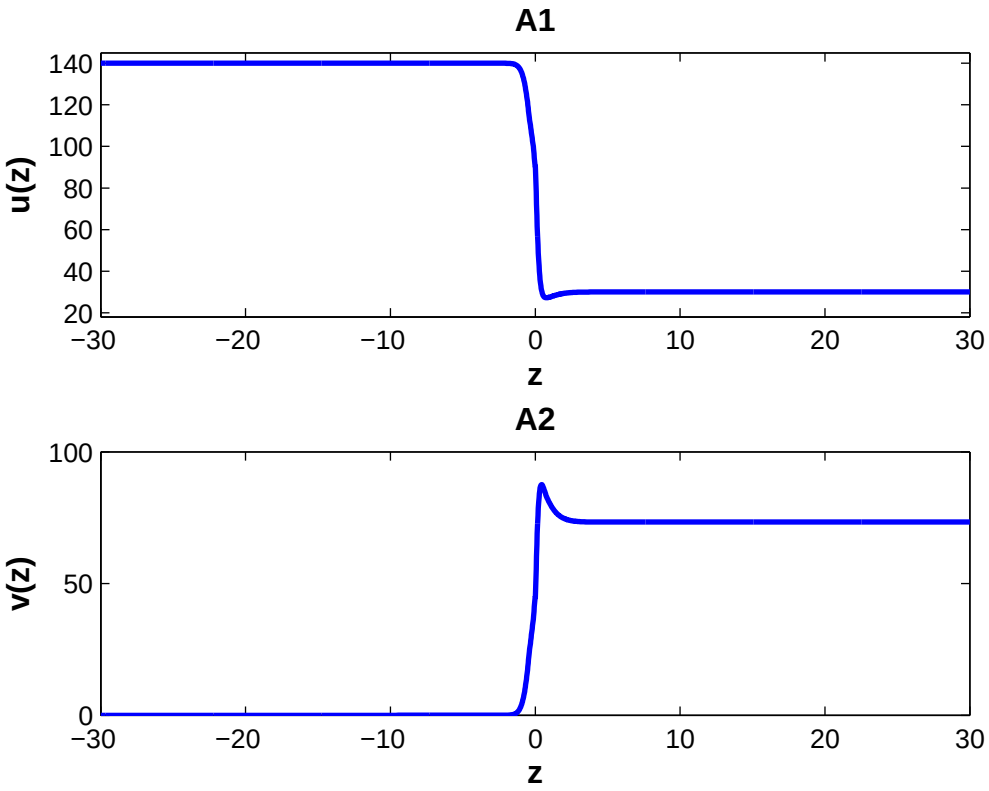


Figure 5.5: Assuming (5.15) with $r = 0.01$ and $c = 0.6643$. This leads to $\Delta_2 = -8.8889 \cdot 10^{-5}$, $p_0 = 4.4415 < \mathcal{R}_0 = 4.6667 < p_2 = 6$, $\mathcal{R}_0 = 4.6667 < p_1 = 9$.

Lemma 7 suggests the connection between $\mathcal{E}'_0$ and $\mathcal{E}'_3$ and Figure 5.6 depicts non-monotone wave fronts connecting the two equilibria. This shows a zone of transition from the disease-free equilibrium $\mathcal{E}'_0$ to the endemic equilibrium $\mathcal{E}'_3$ where the level of susceptible individuals decreased and that of infected individuals first increased then decreased.

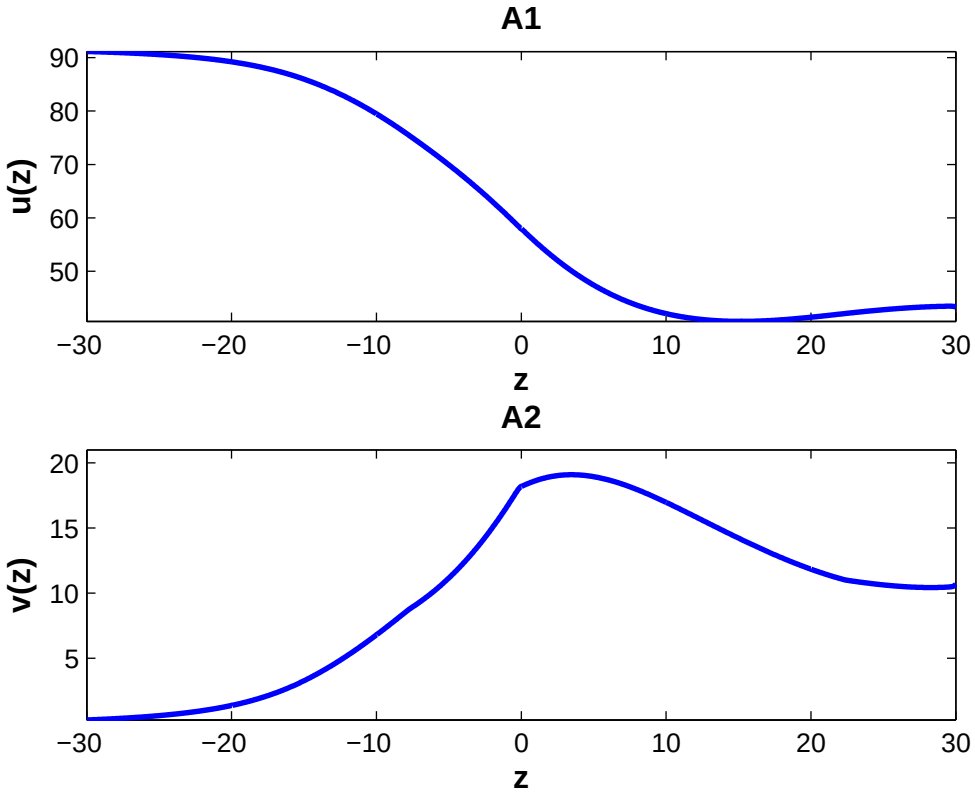


Figure 5.6: $\mathcal{E}'_0 = (0, 91.6, 0, 0)$, $\mathcal{E}'_3 = (0, 44.4788, 0, 11.7712)$, $\mathcal{R}_0 = 1.8320$, $\Delta = 3.7779 \cdot 10^{-8}$, $p_0 = 1.7220$, $p_1 = 1.3332$, $p_2 = 1.9090$, $A = 0.916$, $\lambda = 0.0009$, $r = 0.035$, $d = 0.01$, $I_0 = 10.1$.

Lemma 8 suggests the connection between $\mathcal{E}'_2$ and $\mathcal{E}'_3$ if Case (b) of Proposition 1 holds (i.e., $\mathcal{E}'_2$ and $\mathcal{E}'_3$ exist simultaneously). Thus, the model parameters and variables are fixed as follows:

$$A = 0.916,\ \lambda = 0.003,\ r = 0.035,\ d = 0.02,\ k = 0.35. \tag{5.16}$$

The conditions for the existence of $\mathcal{E}'_3$ and $\mathcal{E}'_3$ are satisfied (i.e., $p_0 = 2.4965 < \mathcal{R}_0 = 2.4982 < p_2 = 2.5$ $\mathcal{R}_0 = 2.4982 > p_1 = 2.4091$). We investigate the

travelling wave solutions connecting $\mathcal{E}'_2 = (0, 18.0609, 0, 10.2391)$ and $\mathcal{E}'_3 = (0, 16.9057, 0, 11.3943)$ as follows:

If $c \geq c^{**}$ then there are travelling wave profiles which connect $\mathcal{E}'_2$ and $\mathcal{E}'_3$ without any oscillations as depicted in Figure 5.7. The wave profiles for both $u(z)$ and $v(z)$ are monotone and smooth.

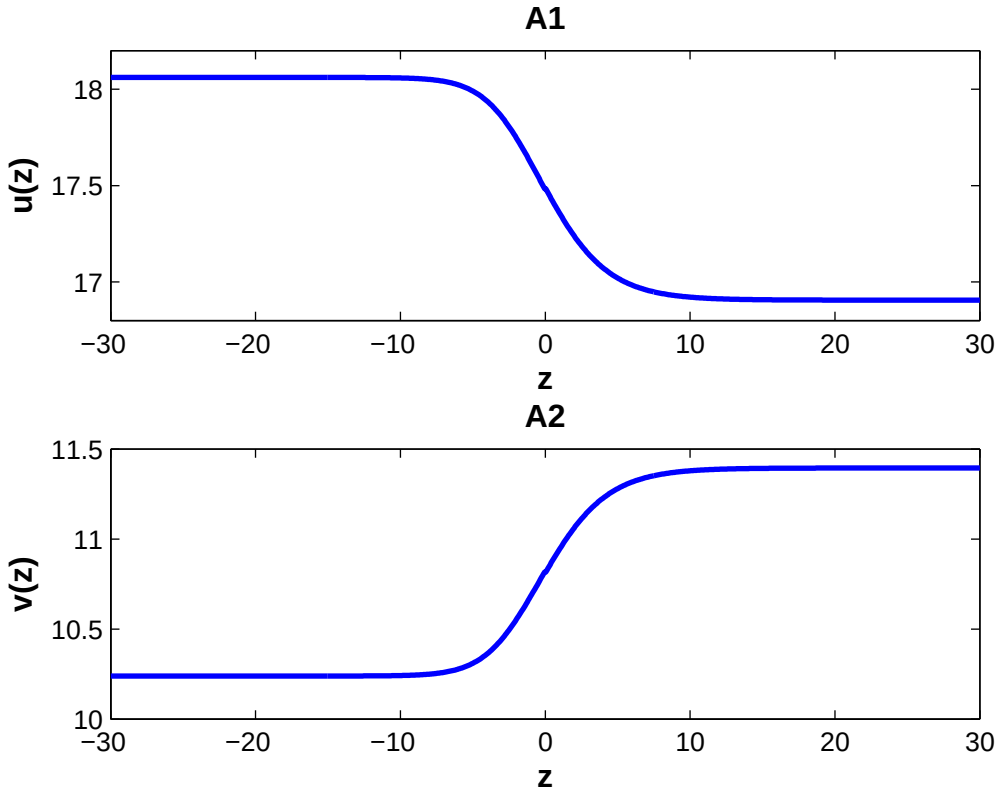


Figure 5.7: Assuming (5.16) with $\Delta = 4.8040 \cdot 10^{-9}$, $c^{**} = 0.1177 < c = 0.1277$

If $c < c^{**}$ then there is a travelling wave profile connecting $\mathcal{E}'_2$ and $\mathcal{E}'_3$ which oscillates near $\mathcal{E}'_2$ as shown in Figure 5.8.

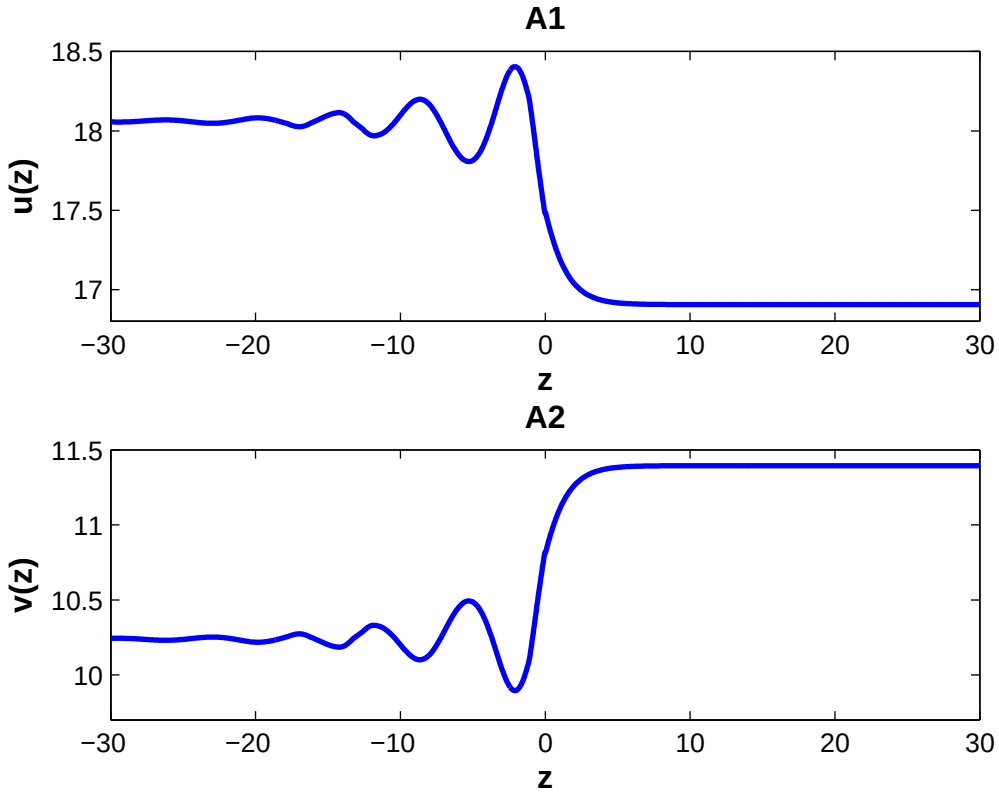


Figure 5.8: Assuming (5.16) with $\Delta = 4.8040 \cdot 10^{-9}$, $c^{**} = 0.1177 > c = 0.0176$.

Finally, we consider system (5.7), with $T(I)$ defined in *Case (ii)*, as Initial Value Problem (IVP) with condition $(A/d, 0, 0, 0)$ due to the discontinuity of $T(I)$. We show the results obtained in Theorems 28 and 29, by carrying out some simulations as depicted in Figures 5.9(A & B) and 5.9C respectively. The observed behaviour of the system is qualitatively different from that of the case analysed previously, and the travelling wave connects the disease-free equilibrium state to another disease-free state for which $u \to \infty$. In the last part of Figure 5.9 it can be seen that $u(z)v(z) \to \frac{m}{\lambda} = 110$ (compare with the

proof of Theorem 5).

It is evident from Figure 5.10 that travelling wave profile for the density of the infected individuals $v(z)$ oscillates in the initial phase as the removal rate of the infected individuals m increases. Furthermore, the decay rate of $v(z)$, as calculated in Theorem 29, is independent of the removal rate m. It can also be seen that the gradient of $\log(v(z))$ approaches approximately 0.03 which corresponds reasonably well with the value $\mu_+ \approx 0.06$ for the approximate solution (see the proof of Theorem 29).

With increasing removal rate m of the infected individuals, the region where the disease presents high incidence shrinks, and the maximum of $v(z)$ increases with m.

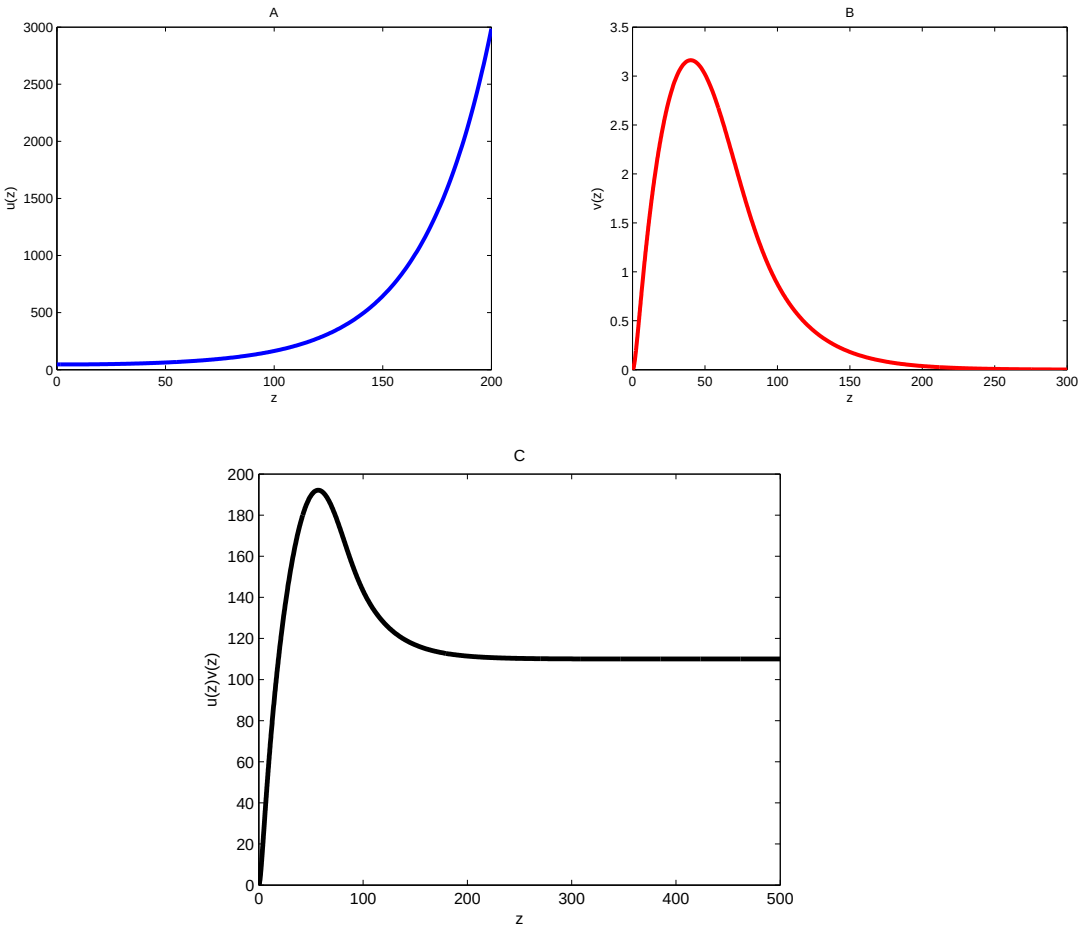


Figure 5.9: $A = 0.916$, $d = 0.02$, $\lambda = 0.001$, $m = 0.11$, $c = -0.6$.

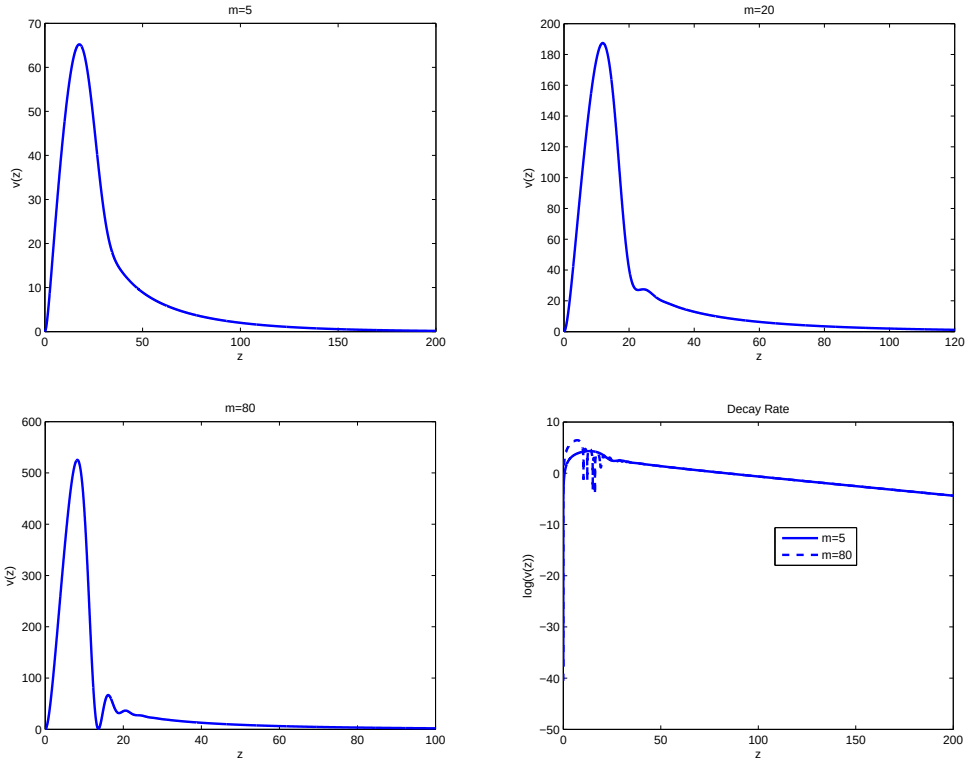


Figure 5.10: $A = 1$, $d = 0.02$, $\lambda = 0.001$, $c = -0.5$

5.5 Conclusion

In this Chapter, we incorporate reaction-diffusion terms in a simplified form of the systems in Wang and Ruan (2004) and Wang (2006) to model the spatial spread of an epidemic in the presence of a treatment in a given populations. This work has been motivated by our effort to analyze the effect of the nature of treatment rate in model (5.1). That is, nonlinear and non-smooth treatment terms; namely, (i) piecewise linear treatment rate with saturation effect, (ii) piecewise constant treatment rate with jump (Heaviside function).

We have analyzed the linear stability of the disease-free equilibrium of the model with both treatment terms. Travelling waves are constructed and their existence is numerically shown in both cases. Furthermore, when treatment rate is piecewise-linear with saturation effect we have shown that the travelling wave trajectory that connects the disease-free state to an infected state and also between two endemic states, while with piecewise constant rate of treatment, which has a jump at the disease-free state, we can only connect the disease-free state to itself. Biologically, the latter is indeed of public health importance because it shows that if few infecteds are introduced into a completely susceptible population, then there will be a moving transition zone of the infected individuals only for a while and then returns to the initial state at the end of the wave front. However, the former demonstrates the conditions of reaching the endemic state from the disease-free state and how two infected states are connected. For piecewise linear treatment rate with saturation effect, we observe some phenomena which are not present for travelling-waves in classical SIR systems with constant coefficients such as non-monotone profiles for both susceptible individuals and infectives, or oscillations of the profiles due to complex eigenvalues. If the treatment rate is piecewise constant and has a jump, the wave profile for susceptible individuals tends to infinity, whilst the infecteds converge to zero and their product approaches a constant at the forward end of the profile. Furthermore, we have shown that if the removal rate m of the infected individuals increases, oscillations of the wave profile occur and their amplitude also increases.

Chapter 6

Discussion and Suggestions for Further Development

6.1 Discussion

This thesis provides some useful epidemiological insights about the impact public health education campaign as a sole intervention strategy for HIV/AIDS prevention in chapters 3 and 4. Amongst other things, the measure of increase or decrease in risky behaviour (or negative attitude) of the individuals in the community who received public health education is calculated and an alternative measure called an impact factor is also provided. Furthermore, it is shown that an optimal strategy for administering public health education campaign is universal strategy. It is also shown that the backward bifurcation phenomenon existed and caused by imperfect efficacy of the public health education program. However, the overall result of chapters 3 and 4 shows that an effective public health education campaign which focuses on change of risky behaviour

with a reasonable coverage level could help in stemming HIV/AIDS in the countries studied. This requires a concerted effort from all the stake holders especially the governments of the respective countries.

In chapter 5, we search for travelling wave solutions for a model with nonlinear and non-smooth treatment terms. We found that when treatment rate is piecewise-linear with saturation effect there is a travelling wave trajectory that connects the disease-free state to an infected state and also between two endemic states and we observe oscillations of the profiles due to complex eigenvalues and non-monotone profiles for both susceptible individuals and infectives. However, if the treatment rate is piecewise constant the wave profile for susceptible individuals tends to infinity, whilst the infecteds converge to zero and their product approaches a constant at the forward end of the profile. Furthermore, if removal rate m of the infected individuals increases then the wave profile oscillates, its amplitude increases and the region where the disease presents high incidence shrinks.

6.2 Future Directions

Although we have shown that an optimal strategy for administering public health education campaign is universal strategy, this result could change if we consider the cost of implementing the public health education campaign policy. Thus, it would be instructive to study the cost effectiveness of public health education campaign policy implementation. This is particularly important for developing countries.

Several interesting mathematical questions still remain wide open. For instance, what is the impact public health education in relation to sexually transmitted diseases (STD) on HIV transmission, since there is evidence in the literature that the presence of STD increases the probability of HIV transmission (Rottingen et al., 2001). Similarly, European Study Group on Heterosexual Transmission of HIV (1992) reported that the probability of transmitting HIV from male-to-female is greater than female-to-male. Thus, it would be prudent to assess the effects of gender-wise public health education campaign against HIV. Furthermore, pharmaceutical interventions (such as vaccine and ARVs) could be incorporated into our model for further study.

In model (5.1), it would be desirable and instructive to study the stability and instability (such as bifurcations to see more complicated profiles) of travelling waves and to investigate the spatial spread in higher-dimensional space. The mathematical analysis for the resulting model is considerably more complicated and so, we leave it for future work. The assumption that susceptible individuals and infectives diffuse at the same rate is not necessary, one could also study the effects of different diffusion rates on the travelling wave profile.

Bibliography

M. Altmann. Susceptible-infected-removed epidemic models with dynamic partnerships. *J. Math. Biol.*, 33:661–675, 1995.

R.M. Anderson. The role of mathematical models in the study of HIV transmission and the epidemiology of AIDS. *J. Acquir. Immune Defic. Syndr.*, 1:241–256, 1988.

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

J. Arino, F. Brauer, P. van den Driessche, J. Watmough, and J. Wu. A model for influenza with vaccination and antiviral treatment. *Math. Biosci. Eng.*, 5:118–130, 2008.

P. Ashwin, M.V. Bartuccelli, T.J. Bridges, and S.A. Gourley. Travelling fronts for the KPP equation with spatio-temporal delay. *Z. Angew. Math. Phys.*, 53(1):103–122, 2002.

F. Bai, A. Spence, and A.M. Stuart. The numerical computation of heteroclinic connections in systems of gradient partial differential equations. *SIAM J. Appl. Math.*, 53:743–769, 1993.

E.A. Barbashin. *Introduction to the theory of stability*. Wolters-Noordhoff, 1970.

M.H. Berker and J.G. Joseph. AIDS and behavioral change to reduce risk: A review. *American Journal of public health*, 78:394–410, 1988.

W.J. Beyn. The numerical computation of connecting orbits in dynamical systems. *IMA Journal of Numerical Analysis*, 9:379–405, 1990a.

W.J. Beyn. Global bifurcation and their numerical computation. In D. Rossed, B.D. Dier, and A. Spence, editors, *Bifurcation: Numerical Techniques and Applications*, pages 169–181. Kluwer, Dordrecht, 1990b.

S.M. Blower and H. Dowlatabadi. Sensitivity and uncertainty analysis of complex models of disease transmission. *Internat. Stat. Rev.*, 62:229–243, 1994.

F. Bortolotti, A. Stivanello, F. Noventa, G. Forza, N. Pavanello, and A. Bertolini. Sustained AIDS education campaigns and behavioural changes in italian drugs abusers. *Eur. J. Epidemiol.*, 8:264–267, 1992.

F. Brauer. Epidemic models with heterogeneous mixing and treatment. *Bulletin of Mathematical Biology*, 70(7):1869–1885, 2008.

F. Brauer and C. Castillo-Chavez. *Mathematical Models in Population Biology and Epidemiology*. Springer-Verlag New York, Inc., 2001.

J. Carr. *Applications Centre Manifold Theory*. Springer-Verlag, 1981.

M.M. Cassell, D.T. Halperin, J.D. Shelton, and D. Stanton. Risk compensation: the Achilles heel of innovations in HIV prevention? *British Medical Journal*, 332:605–607, 2006.

C. Castillo-Chavez and B. Song. Dynamical models of tuberculosis and their applications. *Math. Biosci. Eng.*, 1:361–404, 2004.

C. Castillo-Chavez, K. Cooke, W. Huang, and S.A. Levin. Results on the dynamics for models for the sexual transmission of the human immunodeficiency virus. *Applied Mathematical Letters*, 2:327–331, 1989a.

C. Castillo-Chavez, H. Hethcote, V. Andreason, S.A. Levin, and W. Liu. Epidemiolgical models with age sturucture, proportionate mixing, and cross-immunity. *Journal of Mathematical Biology*, 27:233–258, 1989b.

A.R. Champneys, Y.A. Kuznetsov, and B. Sandstede. A numerical toolbox for homoclinic bifurcation analysis. *International Journal of Bifurcation and Chaos*, 6:867–887, 1996.

CIA. World factbook. Technical report, 2002. URL https://www.cia.gov/library/publications/the-world-factbook/index.html.

CIA. World factbook. Technical report, 2008. URL https://www.cia.gov/library/publications/the-world-factbook/index.html.

C. Conley. *Traveling wave solutions of nonlinear diffusion equations: Lecture Notes in Physics*. Number 38. Springer-Verlag, 1975.

C. Conley and R. Gardner. An application of the generalized morse index to traveling wave solutions of a competitive reaction diffusion model. *Indiana Univ. Math. J.*, 44:319–343, 1984.

E.D. Conway and J.A. Smoller. Diffusion and the predator-prey interaction. *SIAM Journal on Applied Mathematics*, 33(4):673–686, 1977.

B.O. Dane and S.O. Miller. AIDS and dying: The teaching challenge. *Journal of Teaching in Social Work*, 4:85–100, 1990. URL http://www.informaworld.com/10.1300/J067v04n01_07.

L. Daniel and S.L. Rand. Behaviour and communication change in reducing HIV: is Uganda unique? *African Journal of* AIDS *Research*, 2:9–21, 2003.

D. De Walque. How does the impact of an HIV/AIDS information campaign vary with educational attainment? Evidence from rural Uganda. *African Journal of* AIDS *Research*, 84:686–714, 2007.

S. Del Valle, A.M. Ecangelista, M.C. Velasco, C.M. Kribs-Zaleta, and S.-F. Hsu Schmitz. Effects of education, vaccination and treatment on HIV transmission in homosexuals with genetic heterogeneity. *Math. Biosci.*, 187: 111–133, 2004.

O. Diekmann and J.A.P. Heesterbeek. Mathematical epidemiology of infectious diseases: model building, analysis and interpretation. 2000.

O. Diekmann, J.A.P. Heesterbeek, and J.A.J. Metz. On the definition and the computation of the basic reproduction ratio $\mathcal{R}_0$ in models for infectious diseases. *J. Math. Biol.*, 35:503–522, 1990.

A. d'Onofrio, P. Manfredi, and E. Salinelli. Vaccinating behaviour, information, and the dynamics of SIR vaccine preventable diseases. *Theoretical Population Biology*, 71(3):301–317, 2007.

S. R. Dunbar. Travelling wave solutions of diffusive lotka-volterra equations: a heteroclinic connection in R^4. *Trans. Amer. Math. Soc.*, 268:557–594, 1984.

E.H. Elbasha and A.B. Gumel. Theoretical assessment of public health impact of imperfect prophylactic HIV-1 vaccines with therapeutic benefits. *Bull. Math. Biol.*, 68:577–614, 2006.

European Study Group on Heterosexual Transmission of HIV. Comparison of female to male and male to female transmission of hiv in 563 stable couples. *British Medical Journal*, 304(6830):809–813, 1992.

P.C. Fife. *Mathematical Aspects of Reaction and Diffusion System Lecture Notes in Biomathematics*, volume 28. Springer-Verlag, 1979.

M.A. Fuentes and M.N. Kuperman. Cellular automata and epidemiological models with spatial dependence. *Physica A*, 267:471–486, 1999.

M.T. Fullilove, J. Wiley, R.E. Fullilove, E. Golden, J. Catania, J. Peterson, K. Garrett, D. Siegel, B. Marin, and S. Kegeles. Risk for AIDS in multiethnic neighborhoods in San Francisco, California. *West J Med.*, 157(1): 32–40, 1992.

K. Fylkesnes, R.M. Musonda, M. Sichone, Z. Ndhlovu, F. Tembo, and M. Monze. Declining HIV prevalence and risk behaviours in Zambia: evidence from surveillance and population-based surveys. *AIDS*, 15:907–916, 2001.

S.M. Garba and A.B. Gumel. Mathematical recipe for HIV elimination in nigeria. *Journal of Nig. Math. Soc.*, 15, 2010.

J.M. Garcia-Calleja, E. Gouws, and P.D. Ghys. National population based HIV prevalence surveys in sub-saharan Africa: results and implications for HIV and AIDS estimates. *Sexually Transmitted Infections*, 82:64–70, 2006.

R. Gardner. Review on traveling wave solutions of parabolic systems. *Bull. Am. Math. Soc.*, 32:446–452, 1995.

R. Gardner and J. Smoller. The existence of periodic travelling waves for singularly perturbed predator-prey equations via the conley index. *Journal of Differential Equations*, 47(1):133–161, 1983.

P. Glendinning. *Stability, instability and Chaos: an introduction to the theory of nonlinear differential equations*. Cambridge University Press, 1994.

E.C. Green, D.T. Halperin, V. Nantulya, and J.A. Hogle. Uganda's HIV prevention success: the role of sexual behavior change and the national response. *AIDS Behav.*, 10:335–346, 2006.

J. Guckenheimer and P. Holmes. *Nonlinear Oscillations, Dynamical Systems, and Bifurcations of Vector Fields, Applied Mathematical Sciences*. Springer-Verlag, 2002.

Z. Gul, Y.H. Kang, and I.H. Jung. Optimal treatment of an SIR epidemic model with time delay. *Biosystems*, 98(1):43–50, 2009.

A.B. Gumel, S. Ruan, T. Day, J. Watmough, F. Brauer, P. van den Driessche, D. Gabrielson, C. Bowman, M.E. Alexander, S. Ardal, J. Wu, and B.M. Sahai. Modelling strategies for controlling SARS outbreaks. *Proc. R. Soc. B*, 271:2223–2232, 2004.

A.B. Gumel, C.C. Mccluskey, and P. van den Driessche. Mathematical study of a staged-progression HIV model with imperfect vaccine. *Bull. Math. Biol.*, 68:2105–2128, 2006.

K.P. Hadeler and C. Castillo-Chavez. A core group model for disease transmission. *Math. Biosci.*, 128:41–55, 1995.

K.P. Hadeler and P. van den Driessche. Backward bifurcation in epidemic control. *Math. Biosci.*, 146:15–35, 1997.

J.K. Hale and H. Koçak. *Dynamics and Bifucations*. Springer-Verlag New York, Inc., 1991.

H. Hansen and N. Groce. HIV/AIDS treatment and HIV vaccines for Africa. *J. American Medical Association*, 290(21):28–75, 2003.

P. Hartman. *Ordinary Differential Equations*. Wiley, NewYork, 1973.

J.A.P. Heesterbeek and K. Dietz. The concept of $\mathcal{R}_0$ in epidemic theory. *Stat. Neerl.*, 50:89–110, 1996.

J.M. Heffernan, R.J. Smith, and L.M. Wahl. Perspectives on the basic reproductive ratio. *J. R. Soc. Interface*, 2:281–293, 2005.

H.W. Hethcote. The mathematics of infectious diseases. *SIAM Rev.*, 42:599–653, 2000.

H.W. Hethcote. Three basic epidemiological models. In L. Gross S.A. Levin, T.G. Hallam, editor, *Applied Mathematical Ecology*, volume 18, pages 119–144. Springer-Verlag Berlin, 1989.

E.J. Hobsbawm. *Industry and Empire*. Penguin Books, Harmondsworth, 1969.

P.-F. Hsieh and Y. Sibuya. *Basic Theory of Ordinary Differential Equations*. Springer-Verlag, New York Inc., 1999.

J.M. Hyman and J. Li. Modeling the effectiveness of isolation strategies in preventing STD epidemics. *SIAM J. Appl. Math.*, 58:912–925, 1998.

J.M. Hyman, J. Li, and E.A. Stanley. The differential infectivity and staged progression models for the transmission of HIV. *Math. Biosci.*, 208:227–249, 1999.

E. Jung, S. Lenhart, and Z. Feng. Optimal control of treatments in a two-strain tuberculosis model. *Discrete and Continuous Dynamical Systems-Series B*, 4:473–482, 2002.

R.D. Karen and C.W. Susan. The effectiveness of condoms in reducing heterosexual transmission of HIV. *Family Planning Perspectives*, 31:272–279, 1999.

M.J. Keeling, P. Rohani, and B.T. Grenfell. Seasonally forced disease dynamics explored as switching between attractors, part ii. *Physica D*, 148:317–335, 2001.

M.D. Keitshokil, S. Naomi, B.S. Marie, N. Miriam, and S. Motshedisi. HIV/AIDS education, prevention and control course (BNS101): The way forward. *JANAC*, 18:22–31, 2007.

M.G. Kendall and A. Stuart. *The Advanced Theory of Statistics*, volume 2. Inference and Relationship London:Charles Griffin, 1979.

W.O. Kermack and A.G. McKendrick. A contribution to the mathematical theory of epidemics. *Proc. R. Soc. Lond. A*, 115:700–721, 1927.

M. Kgosimore and E.M. Lungu. The effects of vertical transmission on the spread of HIV/AIDS in the presence of treatment. *Mathematical Biosciences and Engineering*, 3(2):297–312, 2006.

J.J. Koob and J.S. Harvan. AIDS instruction in US schools of social work: 20 years into the epidemic. *Social Work Education*, 22:309–319, 2003.

C. Kribs-Zaleta and J. Halesco-Hernandez. A simple vaccination model with multiple endemic states. *Math. Biosci.*, 164:183–201, 2000.

V. Lakshmikantham, S. Leela, and A.A. Martynyuk. *Stability Analysis of Nonlinear Systems*, volume 164. Marcel Dekker, Inc., New York and Basel, 1989.

W.R. Lange, F.R. Snyder, D. Lozovsky, V. Kaistha, M.A. Kaczaniuk, and J.H. Jaffe. Geographic distribution of human immunodeficiency virus markers in parenteral drug abusers. *Am J Public Health*, 78(4):443–446, 1988.

J.P. LaSalle. *The Stability of Dynamical Systems*, volume 25. SIAM, 1976.

J.P. LaSalle. Stability theory for ordinary differential equation. *J. Diff. Eq.*, 4:57–65, 1968.

C. Lindan, S. Allen, M. Carael, F. Nsengumuremyi, P. van de Perre, A. Serufilira, J. Tice, D. Black, C. Thomas, and S. Hulley. Knowledge, attitudes, and percieved risk of AIDS among urban Rwandan women- relationship to HIV-infection and behaviour change. *AIDS*, 5:993–1002, 1991.

Q.X. Liu and Z. Jin. Formation of spatial patterns in an epidemic model with constant removal rate of the infectives. *Journal of Statistical Mechanics: Theory and Experiment*, page P05002, 2007.

P. Marcati and M.A. Pozio. Global asymptotic stability for a vector disease model with spatial spread. *Journal of Mathematical Biology*, 9:179–187, 1980.

R.M. May and R.M. Anderson. Population biology of infectious diseases, part ii. *Nature*, 280:455–461, 1979.

H.V. McCoy, R. Correa, and E. Fritz. HIV diffusion patterns and mobility: Gender differences among drug users. *Population Research and Policy Review*, 15:249–264, 1996.

M. Mimura. Asymptotic behaviors of a parabolic system related to a planktonic prey and predator model. SIAM *Journal on Applied Mathematics*, 37 (3):499–512, 1979.

M. Morton, L. Nelson, C. Walsh, S. Zimmerman, and R.M. Coe. Evaluation of a HIV/AIDS education program for adolescents. *J. Community Health*, 21:23–35, 1996.

Z. Mukandavire and W. Garira. Effects of public health educational campaigns and the role of sex workers on the spread of HIV/AIDS among heterosexuals. *Theor. Popul. Biol.*, 72:346–365, 2007.

Z. Mukandavire, W. Garira, and J.M. Tchuenche. Modelling effects of public health educational campaigns on HIV/AIDS transmission dynamics. *Applied Mathematical Modelling*, 33:2084–2095, 2009.

G. Mulone and B. Straughan. Nonlinear stability for diffusion models in biology. SIAM *Journal on Applied Mathematics*, 69(6):1739–1758, 2009.

G. Mulone, B. Straughan, and W. Wang. Stability of epidemic models with evolution. *Studies in Applied Mathematics*, 118:117–132, 2007.

J.D. Murray. *Mathematical Biology II, 3rd ed.* Springer-Verlag Berlin Heidelberg, 2003.

J.D. Murray. *Mathematical Biology I, 3rd ed.* Springer-Verlag Berlin Heidelberg, 2002.

A.S. Perelson and P.W. Nelson. Mathematical analysis of HIV-I: Dynamics in vivo. SIAM *Review*, 41(1):3–44, 1999.

V.R. Pérez, C.I. Barrales, P.J. Jara, R.V. Palma, and M.A. Ceballos. Knowledge of HIV/AIDS among adolescents in Chillán Chile. *Midwifery*, 24: 503–508, 2008.

E. Perez-Stable. Cuba's response to the HIV epidemic. *Am J Public Health*, 81:563–567, 1991.

L. Perko. *Differential Equations and Dynamical Systems.* Springer-Verlag New York, Inc., 2001.

L. Rass and J. Radcliffe. Spatial deterministic epidemics, in: Mathematical surveys and monographs. *American Mathematical Society (Providence, R.I.)*, 102, 2003.

J. Rauch and J. Smoller. Qualitative theory of the fitzhugh-nagumo equations. *Advances in Mathematics*, 27(1):12–44, 1978.

J. Richens, J. Imrie, and A. Copas. Condoms and seat belts: the parallels and the lessons. *The Lancet*, 355:400–403, 2000.

J.A. Rottingen, D.W. Cameron, and G.P. Garnett. A systematic review of the epidemiologic interactions between classic sexually transmitted diseases and hiv: how much really is known? *Sex Transm Dis.*, 28(10):579–597, 2001.

D. Ruelle. *Elements of Differentiable Dynamics and Bifurcation Theory.* Academic Press New York, 1989.

O. Sharomi and A.B. Gumel. Dynamical analysis of a multi-strain model of HIV in the presence of antiretroviral drugs. *Journal of Biological Dynamics*, 2:503–508, 2008.

O. Sharomi, C.N. Podder, A.B. Gumel, E.H. Elbasha, and J. Watmough. Role of incidence function in vaccine-induced backward bifurcation in some hiv models. *Mathematical Biosciences*, 210:436–463, 2007.

V. Simon, D.D. Ho, and Q. Abdool-Karim. HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. *The Lancet*, 368:489–504, 2006.

R.J. Smith and S.M. Blower. Could disease-modifying HIV vaccine cause population-level perversity? *Lancet. Infect. Dis.*, 4:636–639, 2004.

Uganda Bureau of Statistics Census. Population and social statistics. Technical report, 1991. URL http://www.ubos.org/?st=pagerelations2id=17p=related20pages202:Population.

UNAIDS. AIDS epidemic update. Technical report, 2007. URL http://data.unaids.org/pub/EPISlides/2007/2007epiupdateen.pdf.

UNAIDS. Report on the global HIV/AIDS epidemic. Technical report, 2008. URL http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp.

UNAIDS. AIDS epidemic update. Technical report, 2009. URL http://www.unaids.org/en/KnowledgeCentre/HIVData/EpiUpdate/EpiUpdArchive/2009/default.asp.

UNAIDS/WHO/Unicef. Epidemiological fact sheets on HIV/AIDS and STI: Core data on epidemiology and response, uganda. Technical report, 2008. URL www.apps.who.int/globalatlas/predenedReports/EFS2008/full/EFS2008-NG.pdf.

United Nations. World population monitoring 2002: Reproductive rights and reproductive health. Technical report, 2004. URL http://www.un.org/esa/population/publications/2003monitoring/WorldPopMonitoring_2002.pdf.

J.X. Valesco-Hernandez and Y.H. Hsieh. Modelling the effect and behavioral change in HIV transmission dynamics. *J. Math. Biol.*, 32:233–249, 1994.

F. van den Bosch, J.A.J. Metz, and O. Diekmann. The velocity of spatial population expansion. *J. Math. Biol.*, 28:529–565, 1990.

P. van den Driessche and J. Watmough. Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission. *Math. Biosci.*, 180:29–48, 2002.

A.I. Volpert, V.A. Volpert, and V.A. Volpert. *Traveling Wave Solutions of Parabolic Systems, in: Translations of Mathematical Monographs*, volume 140. 1994.

R. Wallace. Traveling waves of HIV infection on a low dimensional socio-geographic network. *Social Science and Medicine*, 32(7):847–852, 1991.

W. Wang. Backward bifurcation of an epidemic model with treatment. *Mathematical Biosciences*, 201(1-2):58–71, 2006.

W. Wang and S. Ruan. Bifurcations in an epidemic model with constant removal rate of the infectives. *Journal of Mathematical Analysis and Applications*, 291(2):775–793, 2004.

G.F. Webb. A recovery-relapse epidemic model with spatial diffusion. *Journal of Mathematical Biology*, 14:177–194, 1982.

P.J. Weidle, T.D. Mastro, A.D. Grant, J. Nkengasong, and D. Macharia. HIV/AIDS treatment and HIV vaccines for Africa. *The Lancet*, 359(9325): 2261–2267, 2002.

T. Welz, V. Hosegood, S. Jaffar, J. B$^{'}$atzing-Feigenbaum, K. Herbst, and M.L. Newell. Continued very high prevalence of HIV infection in rural KwaZulu-Natal, South Africa: a population-based longitudinal study. *AIDS*, 21: 1467–1472, 2007.

S. Wiggins. *Introduction to Applied Nonlinear Dynamical Systems and Chaos*. Springer-Verlag, New York Inc., 2003.

D. Wilson. Partner reduction and the prevention of HIV/AIDS. *British Medical Journal*, 328:848–849, 2004.

X. Yan and Y. Zou. Optimal and sub-optimal quarantine and isolation control in SARS epidemics. *Mathematical and Computer Modelling*, 47(1-2):235–245, 2008.