MODELING THE TRANSMISSION AND SURVIVAL RATE OF HIV/AIDS IN GHANA

BY

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DECLARATION

This thesis is a true work of the undersigned candidate and that it has not been submitted in any form to any organization, institution or body for the award of any degree. All inclusions as well as references from works of previous authors have been duly acknowledged.

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ABSTRACT

A comprehensive deterministic HIV/AIDS transmission model incorporating treatment strategies is presented and rigorously analyzed. Two structures of the model are considered with preliminary one consisting of eight differential equations of the state variables and the expanded one also consisting of twenty differential equations involving parameters which determine the transmission rate and treatment HIV/AIDS of the model. A compartment model that tracks the spread of HIV in multiple two-sex populations over time in the presence of limited treatment was investigated. In this study we investigate the effects of treatment and the future spread of HIV in all populations. Treatment simulations shows that when the probability of transmission is high, it is harder to prevent the future spread of HIV, even with treatment .ARTdistribution methods are introduce to prevent the largest number of future HIV infections. The model has been fit to represent the HIV epidemic in rural and urban areas in Ghana. With the model, the spread of HIV among urban and rural regions were examined and observed the effects of preferential treatment to rural areas on the spread of HIV in the country as a whole. The researcher investigated the effects of preferentially treating women on the spread of HIV. It was observed that, preferentially treating urban women produces the most dramatic effect in reducing the number of infected male and females in rural and urban areas.

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DEDICATION

I dedicate this thesis to my mother, Madam Gladys Donkor, my father, Mr.C.K Asiedu, my wife, Mrs.Patience Sackey and my lovely daughters, Christlove Asiedu Finwaa and Nana Sakyiwaa Asiedu and also to all my siblings for their moral and financial support.

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CHAPTER ONE

INTRODUCTION

1.1 Background of the study

Human immunodeficiency virus and acquired immune deficiency syndrome (HIV/AIDS) is currently the largest health problem the world faces and is going to continue facing throughout the next generation. We seek to mathematically explore rationing, an issue inherent in the treatment of this devastating disease, and the effects of various rationing strategies. Every country and racial group has been affected by HIV and is dealing with the severe ramifications of this infection. HIV is a global problem that affects and is affected by many facets of sexuality, drug use, and health care. It is estimated that 33 million people were living with HIV in 2007, majority of which were from sub-Saharan Africa (UNAIDS, 2007). The human immunodeficiency virus (HIV) can be transmitted through contact with some bodily fluids. The three known modes of transmission are sexual contact, mother to child transmission (vertical transmission), and sharing contaminated blood or blood products. Unprotected heterosexual contact is the main transmission route across the world, especially in developing nations (UN- AIDS, 2005). Most new infections in developed countries occur in those sharing needles in injection drug use or in men having sex with men (UNAIDS, 2008). The origin of HIV and the mode through which it was introduced to humans is largely accepted to have occurred through humans' interaction with chimpanzees, who suffered from an older form of the disease (Royce, 1997). Many researchers are getting closer to finding the date that the transmission from chimpanzees to humans occurred (Worobey, 2008). HIV is a

"retrovirus," a virus that is able to incorporate its own genome into the DNA of a cell it is infecting, thereby reversing the process of deoxyribonucleic acid (DNA) replication (Okware, 2001). As a robust retrovirus, HIV is able to incorporate its ribonucleic acid (RNA) into cells even in stressful environments. HIV infection occurs over the course of a number of different stages. After the initial transfer of HIV through bodily fluids, the period that follows is called acute HIV infection (Powers, 2008). During this stage the virus rapidly replicates and the RNA viral levels rise.

At this stage, an individual is most infectious and is most likely to pass the disease onto others. Also in this stage, the number of cluster of differentiation (CD+T) cells in the body, an important component of the immune system, is dramatically reduced (Vernazza, 1999).

The latency stage that follows is a result of the immune system's ability to reduce the number of viral particles in the blood stream. This period is marked by a reduced number of symptoms, although individuals are still infectious (Vernazza, 1999). Once the disease has progressed and the CD4+ count in the body falls below 200 cells, a person is diagnosed with AIDS, and immunity to infection is lost (Vernazza, 1999). Symptoms at this stage include moderate weight loss, respiratory-tract infections, skin rashes, and oral ulcerations (Powers, 2008), untreated, AIDS ultimately leads to death.

HIV often affects the most biologically and socially productive members in society. Because the disease is transmitted sexually, young adults who are having unprotected sex are most at risk for contracting the disease just as they are beginning their careers or finishing their education (MOH, 2006). Because the disease can remain latent (without obvious symptoms) for up to 15 years, people who contract HIV at a young age are often affected during their working years and when their children need them most.

Besides being a problem to children who lose their parents and become AIDS orphans," the disease carries with it enormous public health implications.

About 39 million people will have been infected with HIV worldwide by the end of 2008 (UNAIDS, 2007). The United States currently has an HIV prevalence rate (the proportion of the population that is infected with HIV) of about 0.58 percent (Scott, 2008).

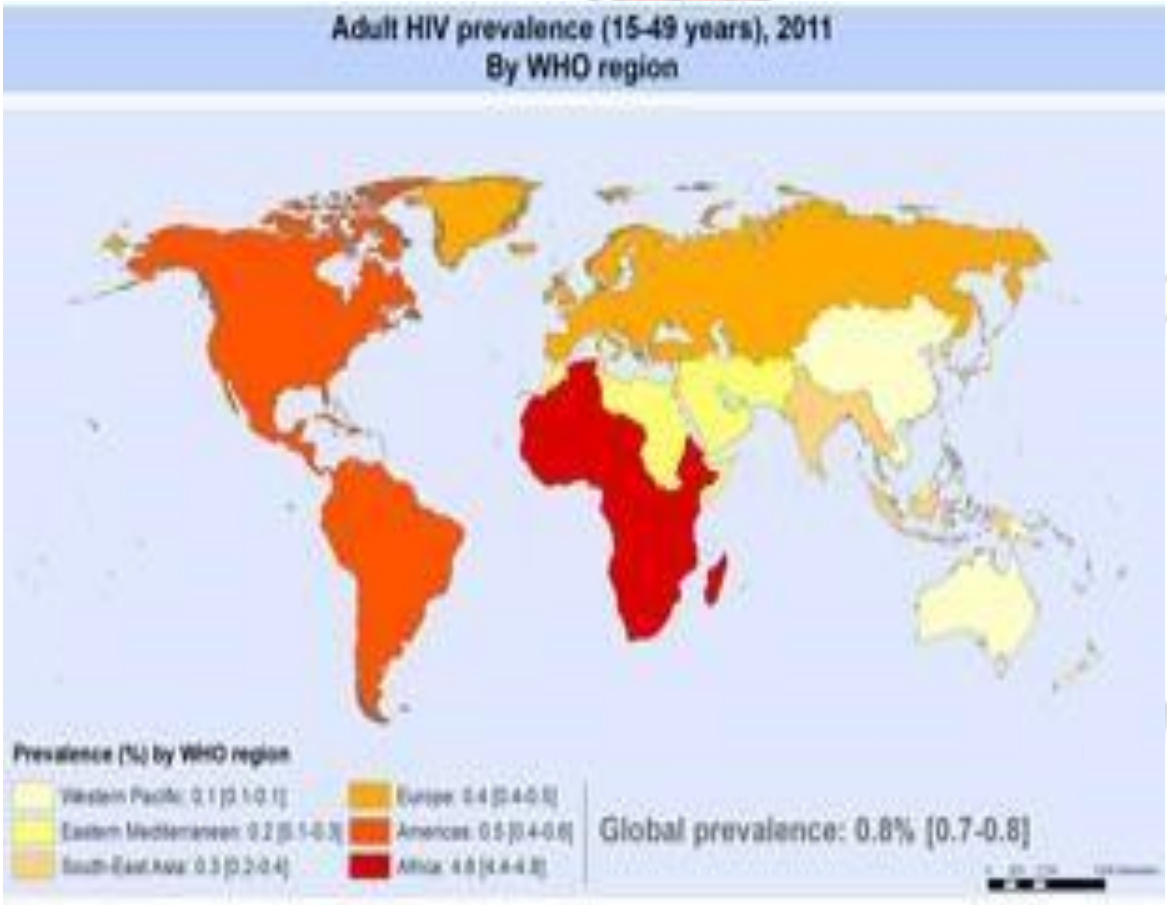


Figure 1.1*: Number of HIV infected people living around the world in 2007, the majority of which are in sub-Saharan Africa (taken from UNAIDS (2008))*

The hardest hit communities within the United States are gay males, injection drug users, and black females. Haiti is the most devastated country in the western hemisphere, where HIV is currently the number one cause of death among young adults between the ages of 18-25 (UNAIDS, 2005). Haiti's pandemic is fast approaching the severity of the sub-Saharan Africa crisis. Currently sub- Saharan Africa contributes less than 10 percent of the world's population but more than 50 percent of the world's HIV infected people, with an overall HIV prevalence rate of 8.57 percent (UNAIDS, 2005). In some countries, such as Rwanda and Botswana, nearly a quarter of the population (25 percent) is infected with HIV. HIV is difficult to tackle in developing nations, as societal factors and economic conditions often contribute to infection.

1.1.1 Ghana

The HIV/AIDS elimination in Ghana seems to be progressing rapidly. The Government of Ghana estimated the number of adults and children living with HIV as at 2010 as 230,000 and prevalence at 1.3% in 2012. The Joint United Nations Program on HIV/AIDS estimated the HIV prevalence in adults to be 0.9% at the end of 2012, with an estimated 200,000 people living with HIV/AIDS.\Health Profile: Ghana". (UNAIDS, 2012). The reduction in the prevalence rate indicates that Ghana is progressively eliminating HIV/AIDS.

Ghana's system of HIV surveillance for women attending antenatal clinics has functioned well since its establishment in 1994. Sentinel surveys of 21 antenatal clinic sites in 2002 reported a range from 3.2% to 9.1% in prevalence among pregnant women. In 2002, the median HIV prevalence at four of these sites in Accra was 4.1%; elsewhere in Ghana, prevalence in antenatal clinics ranged from 3.2% to 3.4% in 2002

(GAC, 2001)

Ghana earmarked 15% of its health budget for HIV/AIDS activities, and all ministries were asked to create an HIV/AIDS budget line. Available funding to support Ghana's response to the HIV/AIDS epidemic includes about 6.7 million dollars from the Global Fund to fight Aids, Tuberculosis and Malaria(GFATM); about 12 million dollars from multilateral partners, including the World Bank; and about 8 million dollars from bilateral donors. Based on the level of funding already committed by the national government and its donors, WHO estimates a 5 to 12.8 million dollars funding gap for HIV/AIDS activities in Ghana for the period 2004 and 2005 while the number of AIDS deaths in Ghana in 2006 was 22,000 (WHO,2006).

1.1.2 The Anatomy of the HIV Virus

Although HIV circulates throughout the entire body upon initial introduction, the virus will only attach to CD4+ cells. This specificity is due in part to the fact that every somatic cell in the human body has a precise array of glycoprotein markers on their surfaces that serve as identification to each other and similar cells. In HIV's case, the gp120 envelope protein located on the surface of the virus fits a cell-surface marker protein called CD4 on the surfaces of macrophages and T cells. CD4+ T cells are a type of white blood cell that fights infection by rousing other defending cells to action. Unfortunately, the CD4+ T cells are where the virus decides to make its home, and without these crucial components of the immune system, the body cannot mount an effective defense against invading viruses and bacteria. When HIV enters a person's CD4+ T cells, it uses the cells to make copies of itself, and as you lose CD4+ T cells, your immune system becomes weak (R.V.Culshaw,2000)

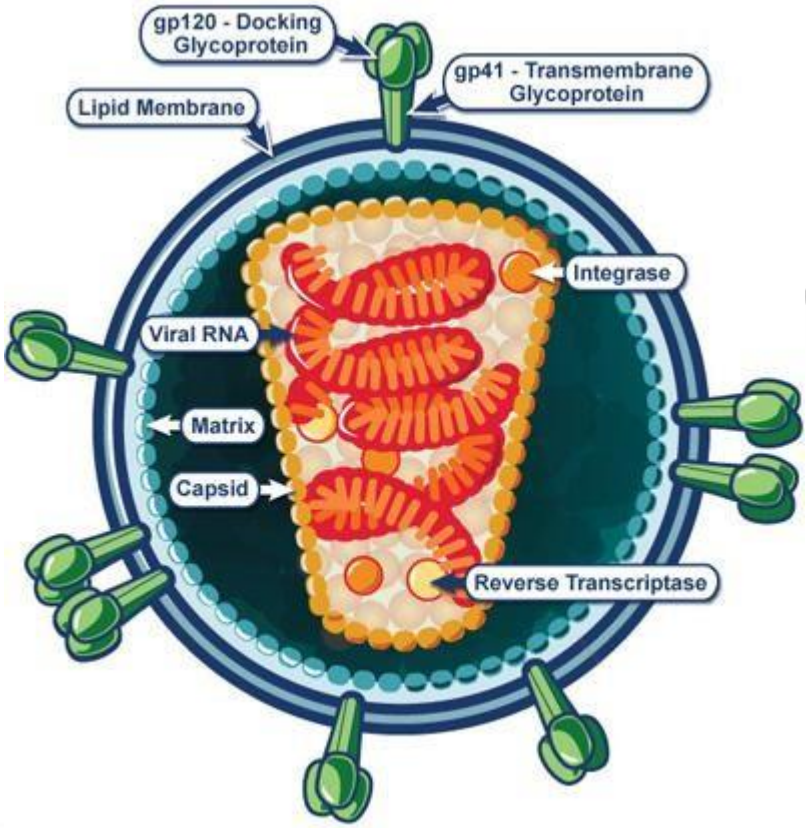


Figure 1.2*: Structure of the HIV virus*

The reverse transcriptase transcribes the single-stranded RNA of the virus into doublestranded DNA, which is in fact a reverse of the original hosts' DNA nucleotide base sequence. During the time of entry into a cell, HIV is constantly mutating and replicating (see Figure 1.2). The significance of these constant mutations is that when it comes to a time for the cell to lyses, a completely new virus will exit the cell, making it difficult for researchers to find an effective treatment for the virus .As stated in R.V Culshaw, (2000), this calculated destruction of the T cells block the immune response and makes it virtually impossible for the body to resist succumbing to AIDS.

An estimated 39.5 million people are infected with the HIV virus worldwide. Though the virus has slowed in some countries, it has escalated or remained unchanged in others. In the U.S., nearly one million people are infected with the HIV virus, and roughly one out

of every 250 has developed into AIDS. At least 40,000 Americans become infected with HIV each year, and it is estimated that half of all people with HIV in the U.S. have not been tested and do not know they are carrying the virus. Being proactive is in fact the best hope for stemming the spread of the virus through preventive health care, education, and treatment.

Mathematical models have proven valuable in understanding the dynamics of the HIV/AIDS virus. The models, if constructed properly, can provide an accurate prediction of the diseases and its output should reflect the results or observations that are made. In this research work, a simple mathematical model will be developed to study the dynamic of the epidemic and the factors associated with the rising intensity of the disease.

1.1.3 The Anti-Retroviral Therapy (ART) Treatment

As stated in the latter part of the anatomy of the HIV virus, being proactive is in fact the best hope for stemming the spread of the virus through preventive healthcare, education, and treatment. However, the creation of anti-retroviral therapy (ART) has been a great stepping stone to allowing people living with HIV/AIDS to lead normal and healthy lives. The "triple cocktail" (three medications taken at the same time) is composed of chemicals that suppress a person's viral load to undetectable levels (Orrell., 2003).

The medications are to be taken every day for the rest of the patient's life and sometimes have debilitating side effects, including nausea, dizziness, pain, and inability to perform everyday functions (Powers, 2008). When these medications were first released, they were too expensive for developing nations to afford.

As such, those most in need of treatment in developing nations were not receiving medication until fairly recently (Scott, 2008). Issues of drug resistance with ART therapy frequently arise for patients who do not take their medication consistently. Because the virus multiplies in the body so rapidly, thousands of genetic variants are created every

minute, and when drugs are taken inconsistently, there is a higher chance of drug resistance developing (Vernazza., 1999). Drug resistance needs to be taken into account when implementing a distribution strategy in developing nations, since distance to health centers has a strong influence on whether people can get their medications on time and thus be compliant (Abuelezam, 2008).

Currently only about 28 percent of individuals worldwide who need treatment are receiving it, even with the creation of generic drugs and the reduction in prices (UNAIDS, 2005). Many countries in sub-Saharan Africa have limited resources and depend on foreign aid and thus are unable to provide their citizens with the drugs they need to survive.

1.2 Problem Statement

The ultimate aim of education, and therefore by implication all aspects of educational management, is the self-actualization of learners (Cangemi, 1984).

This aim may be seriously compromised by the rapid spread of the Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) among all sectors of the Ghana population, and will in all probability have an extremely debilitating impact on the society.

Desmond Cohen (in Porter, 2002), describes the effect of HIV/AIDS on human resources as ―*terrifying*‖ and "*intensifying*". Cohen (in Porter, 2002) maintains that the magnitude of the impact of AIDS on society has been drastically underestimated, and poses the following question: "*How (do you) keep schools functioning, or water supplies functioning, or police services functioning when 20 to 30 percent of the people you have trained are in fact dying of HIV/AIDS?*‖.

While all sectors of society are adversely affected by the impact of HIV/AIDS, the effect on education, which is the cornerstone for the provision of manpower to society, has been devastating. A UNICEF report (2000) on the progress of nations underlines this fact with the following statement: "Although *HIV/AIDS affects all sectors, its most profound effects are concentrated in education. Hardwon gains in school enrolment and educational gains made to improve education are being eroded*". , The effect of AIDS on education and socio-economic development cannot be over emphasised.

Seventy percent of all new HIV infections take place in Africa (UNAIDS,2003) and there can be no doubt that HIV/AIDS is no longer only a public health challenge, and it is having a devastating impact on the continent. Poverty, lack of adequate medical facilities, inadequate education, cultural and social barriers and political inertia are but a few of the complex factors that facilitate the spread of this diseases which is undermining the hard-won economic and social gains that many Africa countries were able to make in the last two to three decades (IBRD/World Bank, 2000).The impact of HIV/AIDS is pervasive and far-reaching, affecting individuals and communities not only psychologically but also economically and socially. Families lose their most productive members to this disease, leaving children and elderly people without means of support. The high cost of the disease wreaks havoc within communities where the already fragile structure are not capable of absorbing further strain

Though Ghana could not be complacent at all in the commitment towards ensuring a record of zero per cent in all areas, there is the need for stakeholders to soberly reflect on and cautiously analyze the trend of infections and the prevalence rate to avoid pitfalls in planning and decision making, hence the need for this research.

1.3 Objectives of the Study

The objectives of the thesis are:

- to formulate a model of Transmission and Treatment of HIV/AIDS using ***SIAT*** (***Susceptible, Infected, Aids class and Treated individuals***) model
- to run simulations on preferential treatment strategies.
- to determine whether or not preferential treatment strategies will affect the future spread of HIV/AIDS.
- to investigate the transmission rate of HIV/AIDS using the ***SIAT*** model

1.4 Methodology

A mathematical model for the transmission of HIV and treatment strategies has been identified and desired to investigate .To achieve the objectives, a system of differential equations preliminary one involving the state variables and the expanded stage which also involve key parameters of transmission and treatment base on the two-sex population compartments would be investigated. The literature review of the various deterministic models of the transmission dynamics of HIV would be examined (Anderson, 1986). Treatment simulations to observe and determine which strategy affects the future spread of HIV would be studied. This simulations would examine statistics of AIDS incidence, prevalence and deaths. It includes a detailed survival analysis of AIDS patients which is used to estimate the transmission parameter for the model (Comiskey, 1992)

Solutions would be analytically obtained with regard to the use of continuous time model. This means that the results of the model can be expressed algebraically, in terms of equations involving the key parameters.

1.5 Significance of the Thesis

HIV/AIDS epidemic has left no part of the world untouched. Notwithstanding the catastrophic effects that are already being experienced, the full consequences of the pandemic are still to be felt. The storm has been gathering for two decades.

While some countries have begun to experience its impact, there are many where it has yet to break with full force. The bleak prospect is that "over the next decade, AIDS will kill more people in Sub-Saharan Africa than the total number of casualties lost in all wars of the 20t h century combined". Across the continent, and in all other severely affected areas, AIDS is already taking a devastating toll in human suffering and death. It is causing untold physical, psychological and emotional sufferings. It is carrying off the most productive members of the society, those in the 15-49 age range. It is disrupting social systems, exacerbating poverty, reducing productivity, wiping out hard won human capacity, and reversing development gains. Although it has only begun to make its way into many communities and economies, its ravages increase by every minute. World-wide, there are 16,000 new HIV infections every day about eleven every minute, or one every four seconds (World Bank, 1999).

However, this study seeks to investigate the rate at which HIV spread rapidly before it weakens immune system of the individual which ultimately leads to death. Focusing on the treatment strategy to investigate which strategy will reduce future spread of HIV/AIDS in Ghana is another line of action that will be analyzed in the study. It is against this back drop that the topic was chosen to create awareness and to educate the society on the devastating effects of HIV and AIDS.

1.6 Scope of the study

The thesis will cover from the individuals who are susceptible to HIV virus through the transmission from one person to another and the analysis of treatment strategies of HIV/AIDS patients.

1.7 Limitation of the Thesis

The thesis is restricted to the objectives of the research. Research work is often characterized by some constraints. Some of these setbacks include resource inadequacy since the project is solely self-sponsored, time constraints and the unavailability of relevant materials such as journals on the study and unpreparedness and unreadiness of personnel to give out information.

1.8 Organisation of the Thesis

The thesis contains five chapters. Chapter 1 discussed the background of study, problem statement, objectives, methodology, significance of the study, scope of study and the limitation of the study. Chapter 2 explores some previous research on HIV and other diseases and some applications. Models based on differential equations for transmission survival rate of HIV/AIDS. Chapter 3 discusses the methodology and its process. Data Analysis and Results are explored in Chapter 4. Chapter 5 deals with the conclusions and recommendations. Preliminary model that accounts only for new infections and an advanced model that accounts for AIDS cases and incorporates treatment.

1.9 Summary

This chapter focused on the background of the study, the statistics of HIV/AIDS in Ghana, the anatomy of HIV virus and the effectiveness of the discharge of the antiretro-viral treatment to the HIV/AIDS patients. The problem statement as well as the objective of the thesis was stated. Not only that but methodology, significant of the thesis, scope and

limitations as well as the organization of the thesis were also presented thoroughly. Literature review would be discussed in chapter two.

CHAPTER TWO LITERATURE REVIEW

2.1 Introduction

The outbreak and spread of disease has been questioned and studied for many years. The ability to make predictions about diseases could enable scientists to evaluate inoculation or isolation plans and may have a significant effect on the mortality rate of a particular epidemic. The modeling of infectious diseases is a tool which has been used to study the mechanisms by which diseases spread, to predict the future course of an outbreak and to evaluate strategies to control an epidemic (Daley, 2005).

2.2 Previous work

The purpose of the review of related literature in a study is to discover findings, concerning the area of study and how they can propel us to explore the unknown Leedy (1989).Again, this review also seeks to investigate the literature on the subject of modeling transmission and survival rate of HIV/AIDS in Ghana using hospital data. Kumekpor (2002), noted that the non-availability of relevant documentary sources poses serious challenge to would-be investigators and rightly so in the West Africa situation. The few of them that exist are normally poorly equipped and it's difficult to get up-to-date information on many topics of interest to the investigator.

This review would actually elaborate on previous research on HIV/AIDS and previous applications of other models. With the success of ART in reducing morbidity and mortality, HIV has become a chronic and manageable disease. Experiences with other chronic illnesses, such as diabetes and hypertension, reveal how challenging chronic disease management is, both for patients and health providers. Medication adherence for chronic diseases, on average, ranges from 50 to 80 percent (WHO, 2003).

Unlike diabetes and hypertension, HIV is an infectious disease and carries the public health risk of transmission of resistant viral strains. To achieve successful treatment outcomes (undetectable viral loads and increasing CD4 counts) and prevent viral

resistance, patients on ART require high levels of adherence-greater than 95 percent (Paterson, 2000). The management of adherence is made more complicated by the fact that multiple, often overlapping factors, such as patient belief in treatment effectiveness, self-efficacy (confidence in managing their own illness), disease stage, medication regimen, patient-provider relationship and health system issues, can influence adherence (Ickovics, 2002; Fogarty, 2002).

Several studies highlight the importance of health literacy (i.e., understanding of basic health concepts), and its relationship to behaviour, including medication taking and health-seeking behaviour, and health outcomes. The WHO Collaborative Fund for HIV Treatment Preparedness defines health or treatment literacy as the possession of scientifically sound knowledge, skills, and attitudes. Kalichman and colleagues report that poor health literacy creates barriers to fully understanding one`s illness and treatment needs, and is associated with poor adherence outcomes in persons receiving combination ART (1999). They found that those with lower health literacy had lower

CD4 counts, had higher viral loads, were less likely to adhere to treatment regimens, and reported more hospitalisations than those with higher levels of health literacy (Kalichman, 2000).

Patients with chronic conditions make day-to-day decisions about managing their illness. Self-management education complements traditional patient education in supporting patients to live with and manage their chronic illness with the best possible quality of life outcomes (Bodenheimer , 2002), and is an integral part of treatment education at the level of the client.

There are a number of mathematical models in the literature that aim to understand different aspects and end goals of HIV prevention and treatment strategies. Although our

developed model is not a direct extension of specific models in the literature, many models are similar in structure, suggesting that we are progressing in the appropriate direction. A number of models that attempt to assess the spread of disease consider interaction between sexes, whereas other models consider interactions between populations. The goal of this research is to combine these two approaches. Doyle, (1998) developed a two-sex, two-population model to better understand the spread of HIV in a heterosexual population and analyzed the model for existence and stability of solutions. Their model did not include treatment, and was concerned with a general
AIDS class for both populations.

Although this work only provides a dynamical systems analysis and not a numerical analysis, understanding the development and justification for this model was useful in developing our own model (Doyle, 1998). Sani, (2007) examined the dynamics of a two-population model while distinguishing between sexes. Although this model is stochastic, it has provided insight into the basic structure of the infection rate, as the infection rate is often the most difficult parameter to estimate and to represent mathematically. Lloyd and May (1996) developed a generalized model for understanding the spread of HIV through multiple populations. The model they develop is analyzed very extensively through dynamical systems techniques.

Keeling, (2002) developed a model to examine spatial coupling and diffusion of individuals from geographically distant populations. In their model they considered the interactions of two populations of susceptible and infected individuals. Because they assume that the populations are far from each other, the length of stay and thus the interaction time between populations is extended when individuals interact with the other population. Their analysis will be useful to our overall goal of incorporating distance

dynamics into our model. The majority of the models in the literature have both age structure and disease-stage structure, allowing for both the tracking of different age groups and the different infectiousness parameters of the different viral loads.

Preferential treatment has been looked at by a number of different authors. Wilson, (2006) developed a spatially explicit partial differential equation (PDE) model that distinguished between urban and rural populations and is the most extensive look at the problem in the literature currently. The model was parameterized to represent dynamics in South Africa, in the KwaZulu-Natal region (Wilson, 2006). The authors found that the distribution strategy that produced the fewest future infections was an urban-only approach where all the treatment was dedicated to the capital. This strategy also produced the highest levels of resistance (Wilson, 2006). A trade-off such as this one would be interesting to observe in our own studies.

2.3 Models

This section outlines current progress in the development of an appropriate model.
Two separate models are going to be developed: one preliminary model that accounts only for new infections, and an advanced model that accounts for AIDS cases and incorporates treatment.

2.4 Preliminary Model

In order to understand better the dynamics expected from the model structure that have been chosen, it is better to develop a preliminary model before expanding the model to include treatment and an AIDS class.

2.4.1 Assumptions

The model has a number of underlying assumptions that will each be discussed in turn and evaluated for legitimacy. The first set of assumptions is based on biological and epidemiological justifications.

Risk of transmission is proportional to the number of sexual encounters.

Although this assumption has previously been assumed to be the standard indicator of risky behavior, many recent studies have shown that the risk of infection is not proportional to the number of sexual encounters someone has, but rather the number of concurrent partnerships an individual is in (Halperin.,2004). We can imagine that in a society with monogamous relationships, if one person became infected with HIV, the disease would not spread but would be contained within the monogamous relationship. In a society in which people maintain concurrent partnerships, if one person is infected with HIV, the rest of society is also at risk, because of the concurrent partnerships occurring (Halperin., 2004). The assumption that risk is proportional to the number of sexual encounters is critical to determining the chosen infection rate.

This second set of assumptions is being made for mathematical expediency.

Infection happens only through unprotected heterosexual contact.

This assumption is valid when considering the model's application to sub- Saharan Africa. According to the Uganda AIDS Commission, heterosexual transmission accounts for nearly 40 percent of all HIV infections in sub-Saharan Africa, with vertical transmission accounting for a large percentage of the rest (UAC, 2003). HIV infections due solely to heterosexual transmission in sub-Saharan Africa are coming into question, and studies are showing that heterosexual transmission is declining in importance (Gisselquist.,2002). Because of these new epidemiological developments, it is necessary to keep this

assumption in mind when validating the model and assessing the basic reproductive number. In attempting to represent dynamics occurring across the globe, we see that about 80 percent of the people infected with HIV are heterosexual (UAC, 2003), suggesting that unsafe heterosexual sex is a relevant mode of transmission.

Risk of transmission is intermediate for all sexual encounters.

There have been a number of studies aimed at determining the average probability of transmission per unsafe sexual encounter. Powers, (2008) performed a meta-analysis in which they claim that a single infection probability is impractical and misleading. Because some interactions produce a large probability of infection due to outside factors, such as the presence of sexually transmitted diseases (STI) (Powers, 2008), the authors suggest that when modeling, one should not use a single infection probability, but rather consider using a range of numbers. The simple infection-force parameter will be used in this model.

2.5 Summary

Many authors work relevant to the formulation of the model were presented while the underlying assumptions were also stated. Chapter three will focus on methodology of the model equations.

CHAPTER THREE

METHODOLOGY

3.1 Introduction

In this chapter we will look at the SIAT model (Susceptible, Infected, Aids class and Treated individuals) for the mathematical modeling of HIV/AIDS and discuss the mathematics behind the model and various tools for judging effectiveness of the control methods. One of the most basic procedures in the modeling of diseases is to use a compartmental model, in which the population is divided into different groups. The SIAT Model is used in epidemiology to compute the amount of susceptible, infected, Aids class and treatment of individuals in a population. It is also used to explain the change in the number of people needing medical attention during an epidemic.

3.2 Model Equations

In developing an appropriate mathematical model that would represent the dynamics of HIV transmission in Ghana, it will have a number of key components. Because the interest is in studying preferential distribution among different subgroups of the population, it will have different compartments for each of these groups.

It is ultimately my decision to focus on women and those living in rural areas, and with this focus the researcher found it necessary to distinguish between men and women, and also between rural and urban populations. Thus, a two-sex, two-population model suited our needs (Figure 3.1). After developing a basic model with two populations, each with two sexes, and two compartments (susceptible and infected) it became apparent that it had to thoroughly understand the interaction term and its elements before proceeding.

The preliminary model is defined by eight differential equations:

$$\frac{dSW_1}{dt} = bNW_1 - dSW_1 - \frac{\beta MWSW_1(C_1IM_1+C_2IM_2)}{NM_1+NM_2}. \quad (1)$$

Susceptible women in population 1 become infected through sexual contacts as,

$$\frac{dIW_1}{dt} = \frac{\beta MWSW_1(C_1IM_1+C_2IM_2)}{NM_1+NM_2} - dIW_1 \quad (2)$$

$$\frac{dSM_1}{dt} = bNW_1 - dSW_1 - \frac{\beta WMSM_1(C_3IW_1+C_4IW_2)}{NW_1+NW_2} \quad (3)$$

Susceptible men in population 1 become infected through sexual contacts as

$$\frac{dIM_1}{dt} = \frac{\beta WMSM_1(C_3IW_1+C_4IW_2)}{NM_1+NM_2} - dIM_1 \quad (4)$$

$$\frac{dSW_2}{dt} = bNW_2 - dSW_2 - \frac{\beta MWSW_2(C_5IM_1+C_6IM_2)}{NM_1+NM_2} \quad (5)$$

Susceptible women in population 2 become infected through sexual contacts as in

$$\frac{dIW_2}{dt} = \frac{\beta MWSW_2(C_5IM_1+C_6IM_2)}{NM_1+NM_2} - dIW_2 \quad (6)$$

$$\frac{dSM_2}{dt} = bNW_2 - dSW_2 - \frac{\beta WMSM_2(C_7IW_1+C_8IW_2)}{NW_1+NW_2} \quad (7)$$

Susceptible men in population 2 become infected through sexual contacts given as

$$\frac{dIM_2}{dt} = \frac{\beta WMSM_2(C_7IW_1+C_8IW_2)}{NW_1+NW_2} - dIM_2 \quad (8)$$

All parameter and state variables are described in **Table 3.1** and **Table 3.2**. In our creation of the model, we were concerned with the dynamics defined by the interaction term. Our first concern was accurately choosing the population to divide by the interaction term. In

the literature, there were models that divided by the size of the entire population (Doyle, 1998; van den Driessche ,2002) and others that divided by only the population that was infecting (Scott., 2008; Sani ., 2007; Baryarama., 2005), such as ours. We decided that since the entire term represents a person's chance of interacting with an infected individual and becoming infected, the denominator would have to be the total population size of the infected population.

Although we considered making the interaction term a mass-action term to match some models in the literature (Sani, 2007), we have decided to stick with the current methodology.

We also referred to the literature to decide on an appropriate method for defining the units of the infection terms (Scott, 2008; Sani, 2007; Baryarama, 2005). The total infection parameter βC can be broken down to the following units: β is the probability of transmission upon a single encounter and C is the total number of sexual encounters in one year.

These definitions of the infection force represent the dynamics we were hoping to see in a two sex multi population model (see Section 4.2). Once we attained appropriate and predicted behavior in this simple model, we decided to move on to a more complex model that incorporated disease stages, including an AIDS stage and a treated stage.

3.3 Model with AIDS Class and Treatment

Because the primary concern of our project is to understand better the dynamics of preferential treatment, it was necessary for us to incorporate both a treated class and an AIDS class into our model.

3.3.1 Assumptions

In addition to the assumptions outlined in Section 2.1.1, we have additional assumptions for the expanded model. As before, this first set of assumptions is based on biological and epidemiological justification. Individuals with AIDS are too sick to have unprotected sexual encounters.

Our model assumes that members of the AIDS class are not being treated. AIDS significantly reduces stamina, health, and physical capacities of those who have developed it. To this extent, it is not unreasonable to assume that people at the AIDS stage are unable to have sexual intercourse (Royce, 1997).

Individuals who receive treatment have only protected sex.

We are assuming that individuals who receive treatment are educated about risky sexual practices at the health center they receive their medications from. To this extent, we would expect them to practice protected sex by using condoms and other methods described to them at health centers. In a recent study by Bunnell, (2008), the authors found that those people who knew their HIV status were three times more likely to use condoms in their last sexual encounter than those who had not been tested.

Other studies and meta-analyses show that interventions, like treatment, reduce the risk of unprotected sex (Crepaz, 2006) and so the assumption holds in most instances. What

is impractical about this assumption, however, is that it assumes that individuals have protected sex 100 percent of the time, which is not what studies have shown (Neumann , 2002).

Individuals with AIDS and with HIV are treated at the same rates.

Treatment levels are not positively correlated with AIDS diagnoses. Treatment in most health organizations is granted on the basis of interviews, as well as a patient's disease progression, and so patients do not often know whether or not they have AIDS before they are put on treatment. The following additional assumption is added for mathematical expediency

Individuals who are treated are compliant with their medication.

We are assuming that no resistant strains of HIV are being created in the population. One could imagine that a different model would take into account individuals who stop treatment, and therefore move to the infected class with a different strain of the disease (Wilson, 2006).

The assumption of compliance is not completely unjustified, as many studies have shown that compliance rates in sub-Saharan Africa are high, and far surpasses the rates predicted in developed countries (Crepaz, 2006).

A study in South Africa of 289 HIV-infected individuals shows that the median adherence levels were 93.5 percent (Orrell, 2003). This result along with many others, suggests that this assumption is not invalid, but maybe impractical in a world of HIV/AIDS.

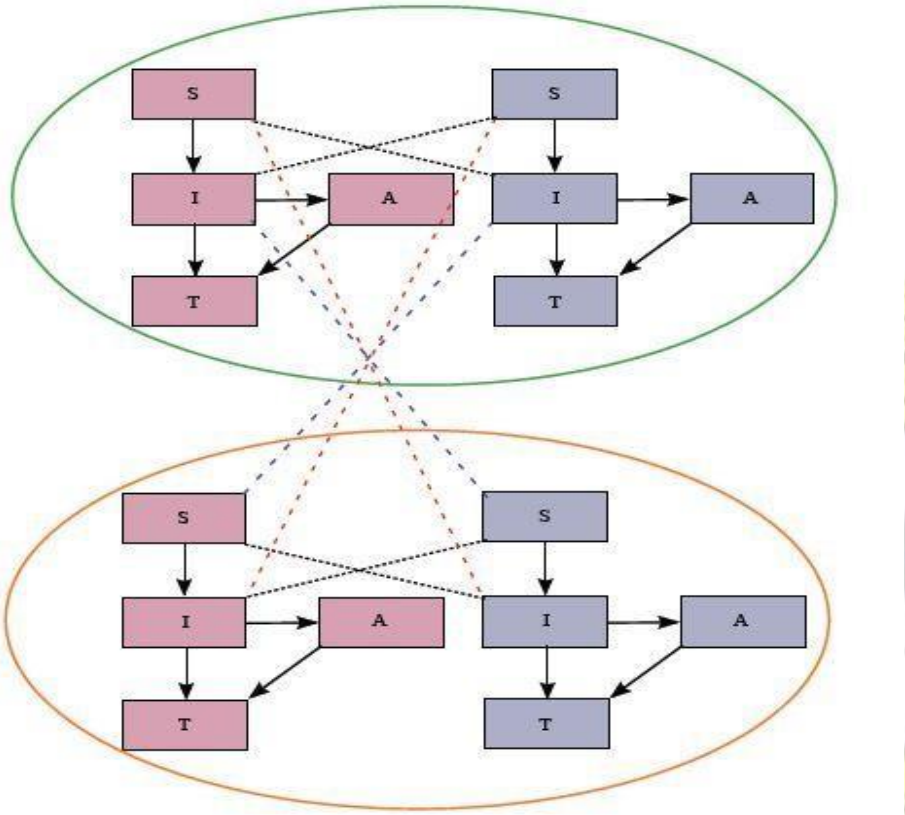
3.3.2 Model Equations

Currently the model is composed of sixteen ordinary differential equations (ODEs), four for each sub-population. Considering two geographically close populations, each with

their own male and female sub-populations, one can imagine that there is a flow of individuals between the two populations and that infection can occur across population lines, as described by the interaction term (Figure 2.2).

In this particular model, we were able to add additional death rates to account for increased death in AIDS and HIV subpopulations. The parameters and state variables are described in **Table 2.3** and **Table 2.**

Figure 3.1 The total dynamics in the expanded treatment and AIDS model.



Each oval represents a distinct population. Within each population there are two sexes, each with susceptible individuals (S), infected individuals (I), treated individuals (T) and those with AIDS (A). The dotted lines account for interactions that lead to HIV infection.

Population 1: Women

$$\frac{dSW_1}{dt} = bNW_1 - dSW_1 - \frac{\beta MWSW_1(C_1IM_1+C_2IM_2)}{NM_1+NM_2}$$

(9)

HIV transmission in population 1 through a simplified heterosexual network, where one male infects one female (male is HIV+)

$$\frac{dIW_1}{dt} = \frac{\beta MWSW_1(C_1IM_1+C_2IM_2)}{NM_1+NM_2} - (d+q)IW_1 - \tau W_1 IW_1 - \alpha IW_1$$

(10)

Infected women in population 1 eventually develop AIDS, become sexually inactive and die at an accelerated rate.

$$\frac{dAW_1}{dt} = \alpha IW_1 - \tau W_1 AW_1 - (l+d)AW_1$$

(11)

$$\frac{dTW_1}{dt} = \tau w_1 IW_1 + \tau w_1 AW_1 - dTW_1$$

(12)

Treatment of women in population 1 eventually reduces rate of transmission per year

$$\frac{dIW_1}{dt} = bNW_1 - dSW_1 - (d+q)IW_1 - (l+d)AW_1 - dTW_1$$

(13)

Population1:Men

$$\frac{dSM_1}{dt} = bNM_1 - dSM_1 - \frac{\beta_{WM}SM_1(C_3IW_1+C_4IW_2)}{NW_1+NW_2}$$

(14)

HIV transmission in population 1 through a simplified heterosexual network, where one female infects one male (female is HIV+)

$$\frac{dIM_1}{dt} = \frac{\beta_{WM} SM_1 (C_3 IW_1 + C_4 IW_2)}{NM_1 + NM_2} - (d+q)IM_1 - \tau_{M1} IM_1 - \alpha IM_1$$

(15)

Infected men in population 1 eventually develop AIDS, become sexually inactive and die at a faster rate

$$\frac{dAM_1}{dt} = \alpha IM_1 - \tau_{M1} AM_1 - (l+d)AM_1$$

(16)

$$\frac{dTM_1}{dt} = \tau_{M1} IM_1 + \tau_{M1} AM_1 - dTM_1$$

(17) Treatment of men in population 1 eventually reduces rate of transmission per year

$$\frac{dNM_1}{dt} = bNM_1 - dSM_1 - (d+p)IM_1 - (l+d)AM_1 - dTM_1$$

(18)

Population2:Women

$$\frac{dSW_2}{dt} = bNW_2 - dSW_2 - \frac{\beta_{MW} SW_2 (C_5 IM_1 + C_6 IM_2)}{NM_1 + NM_2} \quad (19)$$

HIV transmission in population 2 through a simplified heterosexual network, where one male infects one female (male is HIV+)

$$\frac{dIW_2}{dt} = \frac{\beta_{MW} SW_2 (C_5 IM_1 + C_6 IM_2)}{NM_1 + NM_2} - (d+q)IW_2 - \tau_{W2} IW_2 - \alpha_{W2} IW_2 \quad (20)$$

Infected women in population 2 eventually develop AIDS, become sexually inactive and die at an accelerated rate .

$$\frac{dAW_2}{dt} = \alpha IW_2 - \tau_{W2}AW_2 - (l+d)AW_2. \quad (21)$$

$$\frac{dTW_2}{dt} = \tau w_2 IW_2 + \tau w_2 AW_2 - dTW_2 \quad (22)$$

Treatment of women in population 2 eventually reduces rate of transmission per year

$$\frac{dNW_2}{dt} = bNW_2 - dSW_2 - (d+p)IW_2 - (l+d)AW_2 - dTW_2 \quad (23)$$

Population2:Men

$$\frac{dSM_2}{dt} = bNM_2 - dSM_2 - \frac{\beta_{WM}SM_2(C_7IW_1 + C_8IW_2)}{NW_1 + NW_2} \quad (24)$$

HIV transmission in population 2 through a simplified heterosexual network, where one female infects one male (female is HIV+)

$$\frac{dIM_2}{dt} = \frac{\beta_{WM}SM_2(C_7IW_1 + C_8IW_2)}{NW_1 + NW_2} - (d+q)IM_2 - \tau_{M2}IM_2 - \alpha_{M2}IM_2 \quad (25)$$

Infected men in population 2 eventually develop AIDS, become sexually inactive and die at an accelerated rate .

$$\frac{dAM_2}{dt} = \alpha IM_2 - \tau_{M2}AM_2 - (l+d)AM_2 \quad (26)$$

$$\frac{dTM_2}{dt} = \tau_{M2}IM_2 + \tau_{M2}AM_2 - dTM_2 \quad (27)$$

Treatment of men in population 2 eventually reduces rate of transmission per year

$$\frac{dNM_1}{dt} = bNM_1 - dSM_1 - (d+p)IM_1 - (l+d)AM_1 - dTM_1 \quad (28)$$

Table 3.1: Definitions of state variables for expanded model

State Variable	Definition
SWx	susceptible women in population x
SMx	susceptible men in population x
IWx	infected women in population x
IMx	infected men in population x
AWx	women with AIDS in population x
AMx	men with AIDS in population x
TWx	treated women in population x
TMx	treated men in population x
NWx	number of women in population x
NMx	number of men in population x

Table 3.2: **Definitions for parameters in expanded model**

Parameter	Definition
b	birth rate per year
d	death rate per year
q	additional death rate for infected individuals
l	additional death rate for AIDS patients per year
	prob. of transmission from one sexual encounter (male is HIV+)
HIV+)	prob. of transmission from one sexual encounter (female is
	average number of sexual encounter per year
	treatment rate for individual in pop. x per year
α	rate of progression to AIDS per year

3.4 Parameters and State Variables

The system has a large number of parameters that must be estimated. An extensive literature search was undertaken to provide estimates for the parameters defined in **Table 3.2**. Because most of these parameters are estimated from the data, a range of parameter values is provided. These parameters ranges will be explored in the context of a sensitivity analysis, as described in Chapter 4. Many of the parameters that are specific to sexual behaviors rely on data from the Sunyani Regional Hospital.

3.5 Summary

This chapter dealt with the methodology of the model equations for the preliminary and the expanded models of the study. The next chapter would focus on the collection of data and analysis of the results.

CHAPTER FOUR

DATA COLLECTION AND ANALYSIS

4.1 Introduction

A sensitivity analysis will help us better understand which of the twenty two parameters in our model we should focus on estimating most precisely. This section describes both the preliminary and more advanced sensitivity analysis explored and how their results influence our future model simulations.

4.2 Preliminary Sensitivity Analysis

A sensitivity analysis allows us to determine which parameters affect the model results most and thus which will be most important to estimate precisely. Preliminary sensitivity analysis that determines the change of a specific end value when one parameter is changed by a specific percentage is performed. For this sensitivity analysis, it would be used to observe the change in total prevalence with the increase and decrease of parameters by 25 percent.

Again, the sensitivity analysis was used to observe how the total prevalence was affected at different time points, in order to understand whether an outbreak was more likely to occur with certain parameter values. The results of the sensitivity analysis for populations of equal sizes can be visualized in Figure 4.1

From this plot, we see that in the case that the two population sizes are relatively equal, the parameters that seem to have the largest positive effect on the total prevalence are the infection-rate parameters, β_{MW} and β_{WM}. The birth rate b has a negative effect on the total prevalence. From these results it can be concluded that when population sizes are equal we would expect β and b to have the largest effect on the sensitivity of total prevalence. When the simulations were run with one large and one small population, we

see that the parameters associated with the larger population have a larger effect on the outcome of the model.

4.3 Latin Hypercube Sensitivity Analysis

In addition to running a basic sensitivity analysis on the model, a preliminary Latin Hypercube Sensitivity analysis (LHS) has been completed. This analysis allows us to examine a large portion of the parameter space quickly and effectively.

4.3.1 Theory

LHS was first introduced by McKay, (1979). These authors proposed this method of sensitivity analysis because it was both fast and efficient at sampling parameters throughout the entire parameter space. The process has been performed on a number of different epidemiological models modeling HIV (Wilson, 2006; Blower, 1994).

In LHS, each parameter is treated as a random variable defined by a certain probability distribution function (Blower, 1994). Based on the number of samples, N, one wishes to perform, each parameter distribution is split into equal intervals. For each simulation and each parameter, a parameter value is chosen from a randomly selected interval. The intervals are sampled without replacement, ensuring that every part of the parameter space is tested (Blowe, 1994). The model is subsequently run N times. In this way, LHS is able to observe changes in parameter values efficiently, without potentially having redundant sample choices. The process can be visualized in **Figure 4.2.** The LHS design has been compared to simple random sampling and full-factorial sampling and has been found to be the most efficient method to accurately predict the model's sensitivity to parameter changes (Blower, 1994).

The results from LHS can be analyzed using a statistical technique called partial-rank correlation coefficients (PRCC) analysis. PRCC is used to determine the statistical relationship between each input parameter and the output variables while keeping all other

variables at a constant expected value. PRCC is especially useful because it illustrates the independent effects of each parameter. PRCC analysis can only be performed on parameters that cause a monotonic increase or decrease in the outcome variable, since the coefficient indicates the degree of monotonicity between the input and output parameters (Blower, 1994). The partial-rank correlation coefficients can be compared qualitatively for positive or negative relationships and quantitatively with high PRCCs representing stronger monotonicity.

The Sampling and Sensitivity Analysis Tools (SaSAT) were developed at the National Centre in HIV Epidemiology and Clinic Research at the University of New South Wales in Australia (Hoare, 2008). The program they developed produces a parameter table from randomly sampled values from probability distributions input by the user. These parameter values can then be passed through model simulations. Once simulation results have been attained, they can be run through the program for PRCC analysis and the creation of plots (Hoare., 2008). All plots presented as results from LHS have been produced using SaSAT.

4.3.2 Results

Assessment to find the effects of all parameters on a variety of different end points including the prevalence within each population and within each sex, and the total HIV prevalence rate were conducted. This analysis was also run at a variety of different end points in order to determine whether or not sensitivity was time dependent. LHS was run on our model and observe the effects of changing parameter values on total prevalence (**Figure 4.3). The basic sensitivity analysis predicted that the transmission parameters, β_{MW} and β_{WM} should have the largest**

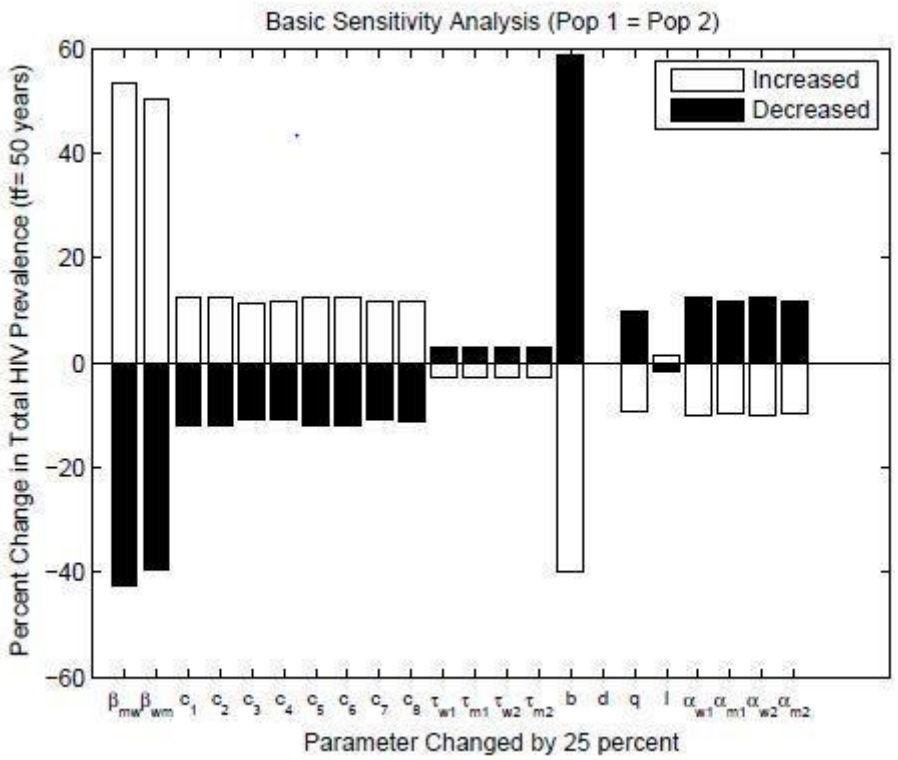


Figure 4.1: *Basic sensitivity analysis for model with treatment and AIDS class. In this simulation, the size of population 1 was set equal to the size of population 2. The seed parameters needed to produce this plot are as follows:* $\beta_{WM} = 0.001$, $\beta_{MW} = 0.003$, $\tau = 0.01$, $\alpha = 0.04$, $C_{1-8} = 60$, $b = 0.05$, $d = 0.02$, $q = 0.01$, *and* $l = 0.03$. *The inital values were chosen as follows: 10 percent infected in all populations; 1 percent on treatment in all populations; 1 percent with AIDS in all populations;* $N_{W1} = 500$, $N_{M1} = = 500$, $N_{W2} = = 500$, *and* $N_{M2} = 500$.

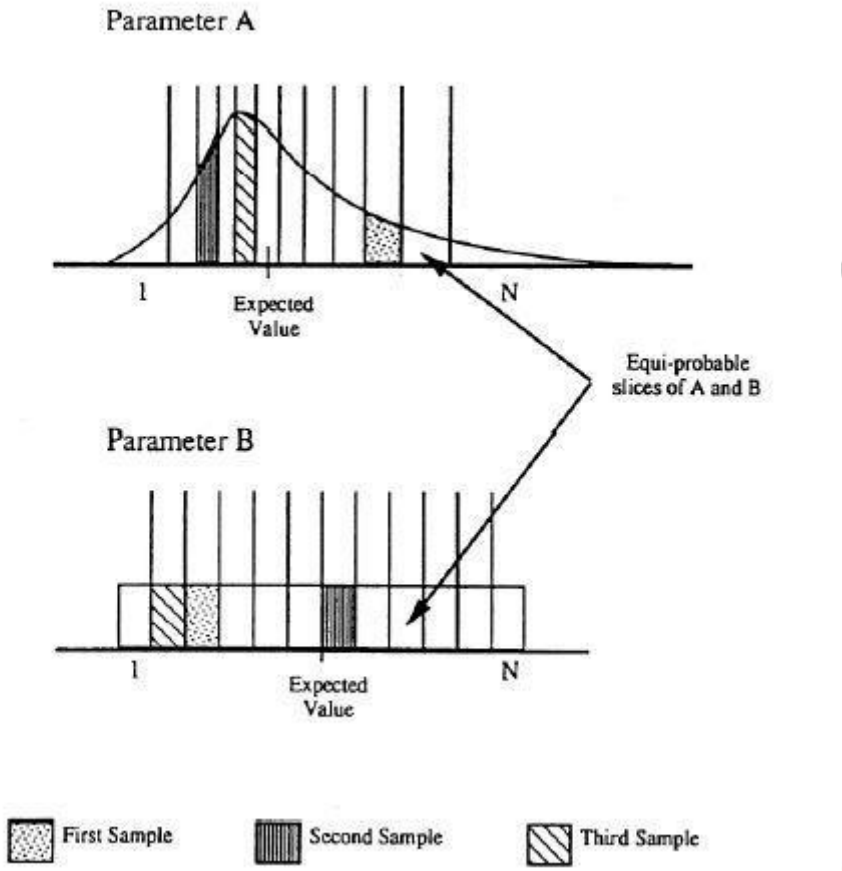


Figure 4.2: *A pictorial description of the LHS method.*

Two parameters defined by particular probability-distribution functions are split into equal intervals and sampled without replacement. These parameter values are then run through the model, and the resulting output variables are analyzed using PRCC (taken from Blower et al (1994)) effect. LHS analysis confirms that effect, but also suggests that the rate at which individual's progress to AIDS has a large effect on the results.

One observation we have made regarding LHS is the importance of defining reasonable probability distribution functions for the parameters. Inputting too wide of a range of parameter values ultimately biases the results. It is therefore important to base our

probability distributions on reliable surveys and literature. In addition, more work should be done to identify the patterns in sensitivity for other model outcomes

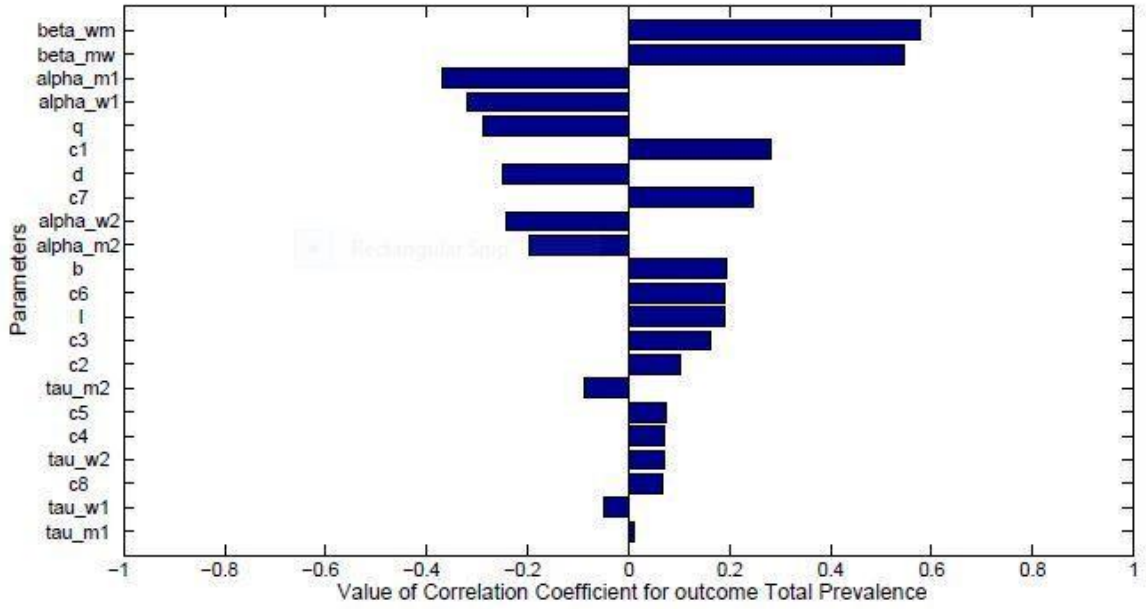


Figure 4.3: *Preliminary LHS analysis results. This tornado plot shows the relative importance of each of the parameter choices compared to changes in the total prevalence. We see from this plot that the two infection forces* β_{MW} *and* β_{WM} *both have a large effect. We also see that parameters such as* C_{1-8} *or the* α *parameters do not have a clear pattern.*

4.4 Basic Reproductive Number

The basic reproductive number (R_0) of an epidemiological model is a parameter that helps determine whether a disease will become endemic in a population or die out based on the specific parameter combinations. Understanding the parameter values that yield endemic population values is essential to understanding the behavior of the model. This section describes how the basic reproductive number was characterized for our model.

4.4.1 Theory

The epidemiological definition of $R_0$is the number of susceptible people an infected person could infect during one time period. We can imagine that if the infected person infects more than one person, and every subsequent infected person does the same, the disease will spread.

We can also imagine that if the infected person does not infect any susceptible individuals the disease will die out. R_0 serves, therefore, as a threshold parameter that determines whether or not a disease will be endemic (R_0 greater than 1) or whether the disease will die out (R_0 less than 1).

In mathematical terms, the basic reproductive number is the spectral radius of the "next generation matrix" (Diekmann, 1990). The analysis of the basic reproductive number allows us to determine which parameters are most important in disease outbreak and, subsequently, which parameters we may be interested in altering to see the disease die out over time.

Calculating the basic reproductive number for simple epidemiological models is relatively straightforward, as it is often represented by the transmission rate divided by the death rate in the population (Lloyd, 1996). Because the dynamics of our model are dependent on both sex and population characteristics, we have to resort to analytical techniques to determine the basic reproductive number. By reading the literature and observing the methods used to determine the basic reproductive number for other twosex epidemic models (Doyle, 1998).

In order to explained how to calculate the basic reproductive number for a generic compartment model, van den Driessche (2002) outline a precise definition for the basic reproduction number for compartment models producing systems of ordinary

differential equations, which is summarized nicely by Hefiernan , (2005).

Let us assume that a model has n compartments, m of which is compartments containing individuals that are infected. Let us also define x_i to be the number of individuals in the i^{th}compartment. If we define $F_i(x_i)$ to be the rate of appearance of new infections in an infected compartment i and $V_i(x_i)$ define to be the rate of transfer into and out of an infected compartment i by all other means, the two matrices can be defined as:

$$F = \left[\frac{\delta F_i(x_0)}{\delta X j}\right]$$

$$V = \left[\frac{\delta V_i(x_0)}{\delta X j}\right]$$

Where i, j = 1, ..., m and x_O represents the disease-free equilibrium. The next generation matrix is then defined by FV^{-1} give the rate at which infected individuals in x_J produce new infections in x_i , multiplied by the average time each individual spends in compartment j. The basic reproductive number is then defined as

$$R_0 = \sigma(F * V^{-1})$$

where σ is the spectral radius of the matrix product (van den Driessche and Watmough, 2002).

4.4.2 Results

We can define F and V for our models as follows:

$$0 \qquad \frac{\beta_{MWC1}}{2}$$

$$F = \begin{bmatrix} \text{——} & 0 & 0 & \text{——} & 0 \\ 0 & \frac{\beta_{MWC5}}{2} & \text{——} & & 0 \\ \text{——} & 0 & & \text{——} & 0 \\ & & \text{——} & & \end{bmatrix}$$

$$V = \begin{bmatrix} q+ d +\tau_{W1} +\alpha & 0 & 0 & 0 \\ 0 & q+ d +\tau_{M1} +\alpha & 0 & 0 \\ 0 & 0 & q+ d +\tau_{W2} +\alpha & 0 \\ 0 & 0 & 0 & q+ d +\tau_{M2} +\alpha \end{bmatrix}$$

The basic reproductive number for the preliminary model, without the AIDS class and without treatment, can be found explicitly

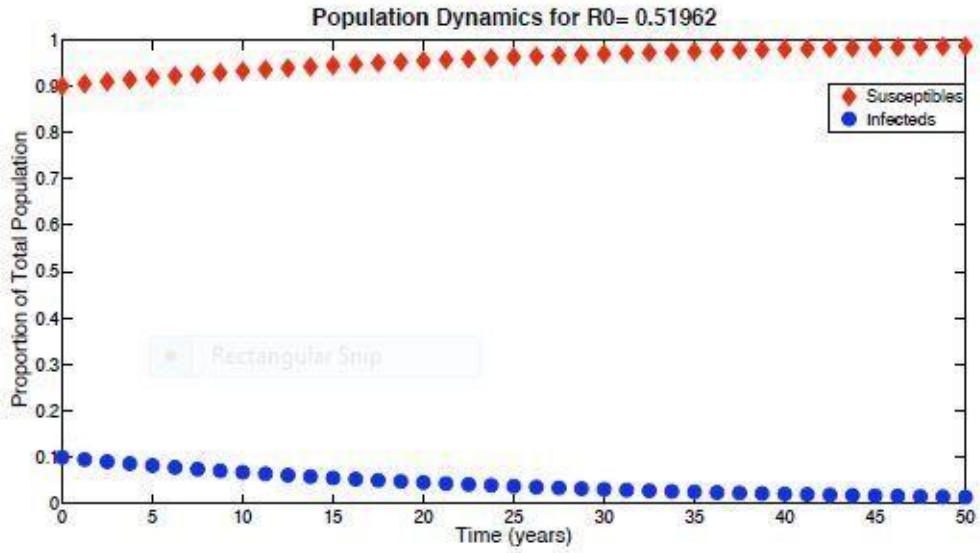
$$R^0 = \frac{1}{4d}\left(2\beta_{MW}\beta_{WMc_3c_1} + 2\beta_{MW}\beta_{WMc_4c_5} + 2\beta_{MW}\beta_{WMc_8c_6} + 2\beta_{MW}\beta_{WMc_2c_7} + 2\beta_{MW}\beta_{WM}(c_3^2c_1^2 + 2c_3c_1c_4c_5 - 2c_8c_6c_3c_1 + 2c_3c_1c_2c_7 + c_4^2c_5^2 + 2c_4c_5c_8c_6 - 2c_4c_5c_2c_7 + c_2^2c_7^2 + 2c_8c_8c_2c_7 + 4c_3c_5c_8c_2 + 4c_7c_6c_4c_1)^{\frac{1}{2}})^{\frac{1}{2}}$$

4.4.3 Simulations

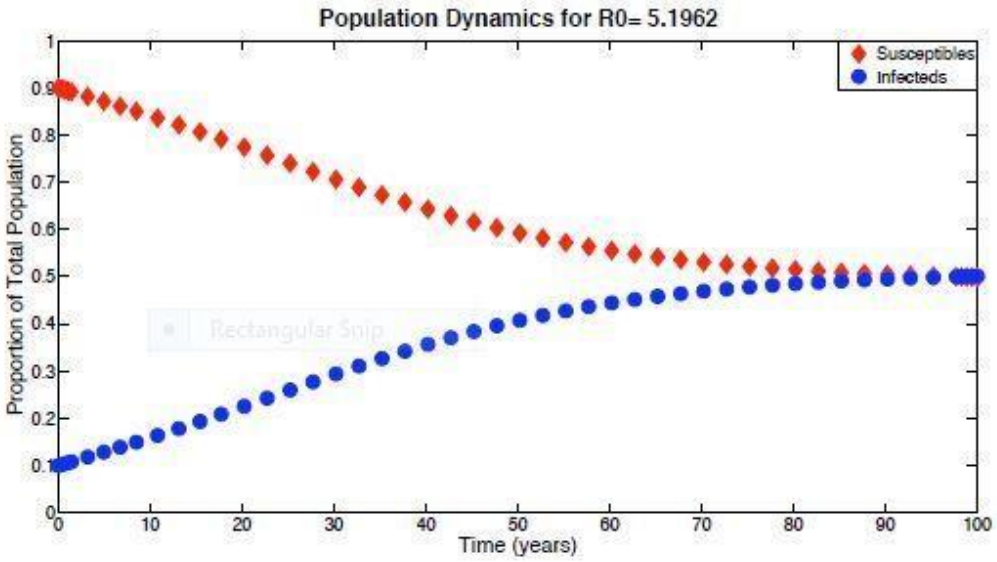
The basic reproductive number allows us to understand the parameter values at which one would expect to observe the presence of an endemic equilibrium. After running a number of simulations focusing on varying the probability of transmission, β, we have observed that low transmission probabilities do not favour the presence of endemic equilibria (Figure 4.6). The basic reproductive number could therefore be used to predict stability of equilibria from certain parameter spaces.

4.5 Equilibria and Stability Analysis

In order to understand the dynamics of the model in full, we seek to define as thoroughly and precisely as possible the endemic equilibria. We also would like to have conditions under which we would expect these endemic equilibria to exist.

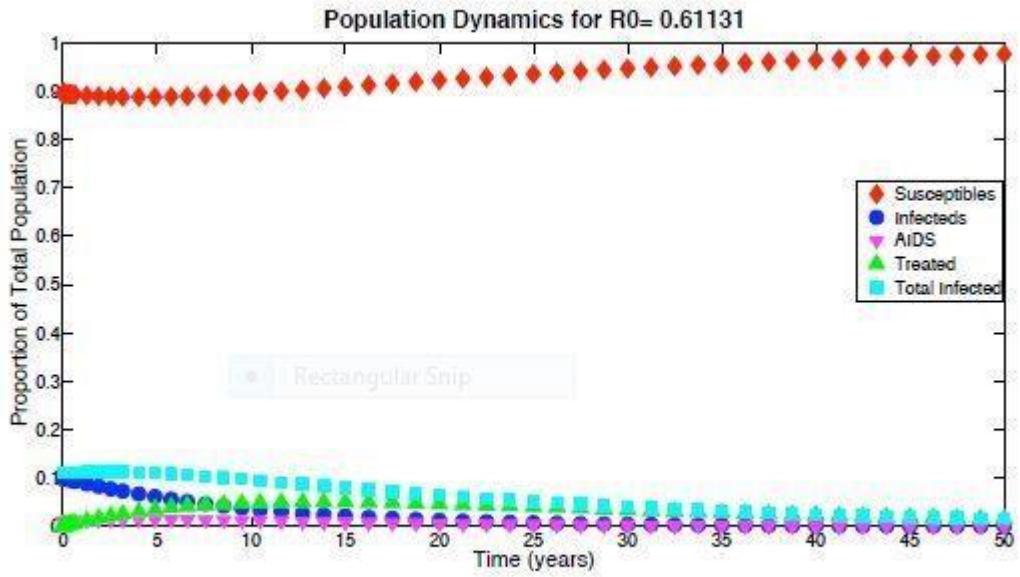


(a) $R_0 < 1$.



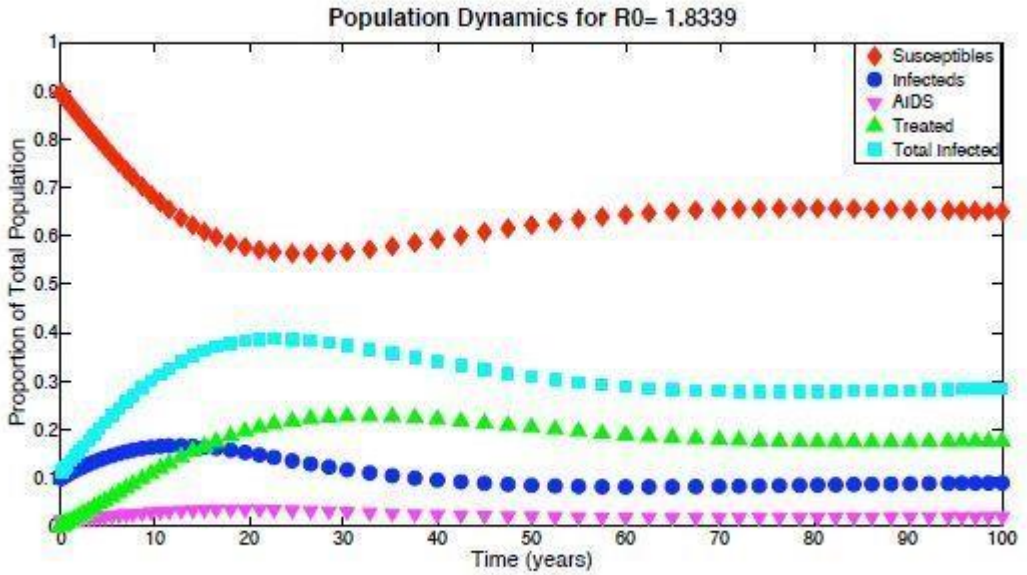
(b) $R_0 > 1$.

Figure 4.4: *R_0 and preliminary model simulation agreement. Parameters were defined as follows for both plots: c_{1-8} = 60, b = 0.02, and d = 0.05.The first plot was produced with β_{MW} = 0:0003 and β_{WM} = 0:0001. The second plot was produced with β_{MW} = 0:003 and β_{WM} = 0:001. Initial conditions for both plots were 10 percent with HIV in both populations, NW_1 = 500, NM_1 = 500, NW_2 = 500, and NM_2 = 500.*



(a) $R_0 < 1$.

(a) $R_0 < 1$.



(b) $R_0 > 1$.

Figure 4.5*: R_0 and advanced model simulation agreement. Parameters were defined as follows for both plots: b = 0.05, d = 0.02, q = 0.01, l = 0.03, c_{1-8} = 60, t = 0.1, and a = 0.04. Parameters used for plot 1 were $\beta MW = 0.003$ and $\beta WM = 0.001$. Parameters used for plot 2 were $\beta MW = 0.009$ and $\beta WM = 0.003$. Initial conditions for both plots were 10 percent with HIV in both populations; 1 percent with HIV in both populations; 1 percent on treatment in both populations: NW1 = 500, NM1 = 500, NW2 = 500, and*

NM2 = 500.

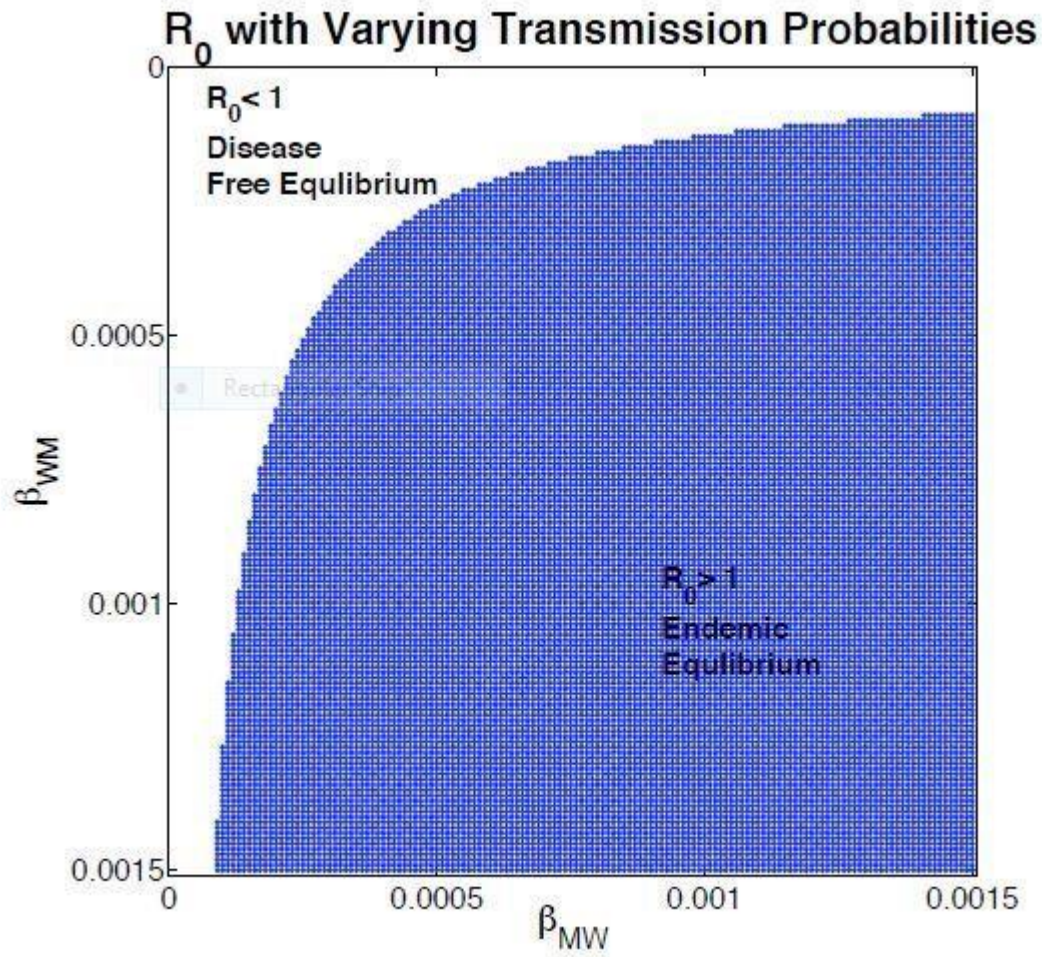


Figure 4.6: *Stability of endemic equilibria over varying probability of transmission values.*

Because the model with treatment and AIDS is complex and contains a great number of parameters, we often need to refer to our simpler model for analysis and then extend these results to the larger model.

4.5.1 Definition of Endemic Equilibria

The interest is in observing the effects of treatment on the future spread of HIV in all populations. We are therefore interested in instances where infected individuals are present. This motivates the understanding of the conditions under which endemic equilibria occur.

Theory

As described in detail in Lloyd, (1996), the equilibria of the model can be solved for analytically by setting each of the differential equations in our model to zero and solving for the respective state variables. This process is more complicated in models with internal structure and coupling. Often large sets of nonlinear algebraic equations need to be solved in order to analytically determine the values of the equilibria. Starting from the analysis with the preliminary model without treatment and AIDS classes and proceeded to complete the analysis for the model with treatment and AIDS classes. In the following discussion, all state variables with a star ($*$) superscript will be assumed to be equilibrium values.

4.5.2 Preliminary Model

Due to our desire to define endemic equilibria as explicitly as possible, it was often necessary to begin the analysis on small pieces of the model. With this requirement, the model was broken down by both sex and population. In each case we define a quantity (Λ^*) that acts as the main transmission term and a recovering term in all equilibrium states.

PRELIMINARY MODEL

Population 1: Women

Following the analysis presented by Lajmanovich , (1976), let us define

$$\Lambda_1^* = \frac{\beta_{MW}(c_1 IM_1^* + c_{2I} M_2^*)}{NM_1 + NM_2}$$

Then the explicit equilibria equations for women in the first population are as follows:

$$SW_1^* = \frac{bNW_1}{(d + \Lambda_1^*)'}$$

$$IW_1^* = \frac{bNW_1 \Lambda_1^*}{(d + \Lambda_1^*)d}$$

Population 1: Men

Similarly, let us define the quantity

$$\Lambda_2^* = \frac{\beta_{WM}(c_3 IW_1^* + c_4 IW_2^*)}{NW_1 + NW_2}$$

Then the explicit equilibria equations for men in the first population are

$$SM_1^* = \frac{bNM_1}{(d + \Lambda_2^*)'}$$

$$IM_1^* = \frac{bNM_1 \Lambda_2^*}{(d + \Lambda_2^*)d}$$

Population 2: Women

Additionally, let us define the quantity

$$\Lambda_3^* = \frac{\beta_{MW}(c_5 IM_1^* + c_6 IM_2^*)}{NM_1 + NM_2}$$

Then the explicit equilibria equations for women in the second population are

$$SW_2^* = \frac{bNW_2}{(d + \Lambda_3^*)'}$$

$$IW_2^* = \frac{bNW_2\Lambda_3^*}{(d + \Lambda_3^*)d}$$

Population 1: Men

Finally, let us define the quantity

$$\Lambda_4^* = \frac{\beta_{WM}(c_7 IW_1^* + c_8 IW_2^*)}{NW_1 + NW_2}$$

Then the explicit equilibria equations for men in the second population are

$$SM_2^* = \frac{bNM_2}{(d + \Lambda_4^*)'}$$

$$IM_2^* = \frac{bNM_2\Lambda_4^*}{(d + \Lambda_4^*)d}$$

The equilibria equations would then form a nonlinear system of equations from which the Λ^* can be solved and explicit equations for the equilibria states can be found.

Model with AIDS and Treatment

Following the same strategy elicited above, the endemic equilibria for the larger model with AIDS and treatment can be found. We will be adding two additional equilibrium states to each subpopulation here by expanding the complexity of the system.

Population 1: Women

For women in the first population, let us define the quantity

$$\Lambda_1^* = \frac{\beta_{MW}(c_1 IM_1^* + c_{2I} M_2^*)}{NM_1 + NM_2}$$

Then the equations describing the equilibrium values for women in the first population are

$$SW_1^* = \frac{bNW_1}{(d + \Lambda_1^*)'}$$

$$IW_1^* = \frac{bNW_1 \quad \Lambda_1^*}{(d + \Lambda_1^*)(d + q + \tau w_1 + \alpha)'}$$

$$AW_1^* = \frac{bNW_1 \quad \Lambda_1^* \quad \alpha}{(d + \Lambda_1^*)(d + q + \tau w_1 + \alpha)(\tau W_1 + l + d)'}$$

$$TW_1^* = \frac{\tau w_1}{d}\left(\frac{bNW_1 \quad \Lambda_1^*}{(d+\Lambda_1^*)(d+q+\tau w_1+\alpha)} + \frac{bNW_1 \quad \Lambda_1^* \quad \alpha}{(d+\Lambda_1^*)(d+q+\tau w_1+\alpha)(\tau w_1+l+d)}\right)$$

Population 1: Men

Let us define the quantity

$$\Lambda_2^* = \frac{\beta_{WM}(c_3 IW_1^* + c_4 IW_2^*)}{NW_1 + NW_2}$$

Then the equations describing the equilibrium values for men in the first population are

$$SM_1^* = \frac{bNM_1}{(d + \Lambda_1^*)'}$$

$$IM_1^* = \frac{bNM_1 \quad \Lambda_2^*}{(d + \Lambda_2^*)(d + q + \tau w_1 + \alpha)'}$$

$$AM_1^* = \frac{bNM_1 \quad \Lambda_2^* \quad \alpha}{(d + \Lambda_2^*)(d + q + \tau w_1 + \alpha)(\tau w_1 + l + d)'}$$

$$TM_1^* = \frac{\tau M_1}{d}\left(\frac{bNM_1 \quad \Lambda_2^*}{(d+\Lambda_2^*)(d+q+\tau w_1+\alpha)} + \frac{bNW_1 \quad \Lambda_2^* \quad \alpha}{(d+\Lambda_2^*)(d+q+\tau w_1+\alpha)(\tau w_1+l+d)}\right)$$

Population 2: Women

For women in the second population, let us define the quantity

$$\Lambda_3^* = \frac{\beta_{MW}(c_5 IM_1^* + c_6 IM_2^*)}{NM_1 + NM_2}$$

Then the equations describing the equilibrium values for women in the Second population are

$$SW_2^* = \frac{bNW_2}{(d + \Lambda_3^*)'}$$

$$IW_2^* = \frac{bNW_2 \quad \Lambda_3^*}{(d + \Lambda_3^*)(d + q + \tau w_2 + \alpha)'}$$

$$AW_2^* = \frac{bNW_2 \quad \Lambda_3^* \quad \alpha}{(d + \Lambda_3^*)(d + q + \tau w_2 + \alpha)(\tau w_2 + l + d)'}$$

$$TW_2^* = \frac{\tau w_2}{d}\left(\frac{bNW_2 \quad \Lambda_3^*}{(d+\Lambda_3^*)(d+q+\tau w_2+\alpha)} + \frac{bNW_2 \quad \Lambda_3^* \quad \alpha}{(d+\Lambda_3^*)(d+q+\tau w_2+\alpha)(\tau w_2+l+d)}\right)$$

Population 2: Men

Finally, let us define the quantity

$$\Lambda_4^* = \frac{\beta_{WM}(c_7 IW_1^* + c_8 IW_2^*)}{NW_1 + NW_2}$$

Then the equations describing the equilibrium values for men in the second population are

$$SM_2^* = \frac{bNM_2}{(d + \Lambda_2^*)'}$$

$$IM_2^* = \frac{bNM_2 \quad \Lambda_4^*}{(d + \Lambda_4^*)(d + q + \tau M_2 + \alpha)'}$$

$$AM_2^* = \frac{bNM_2 \quad \Lambda_4^* \quad \alpha}{(d + \Lambda_4^*)(d + q + \tau M_2 + \alpha)(\tau M_2 + l + d)'}$$

$$TM_2^* = \frac{\tau M_2}{d}\left(\frac{bNM_2 \quad \Lambda_4^*}{(d+\Lambda_4^*)(d+q+\tau M_2+\alpha)} + \frac{bNM_2 \quad \Lambda_4^* \quad \alpha}{(d+\Lambda_4^*)(d+q+\tau M_2+\alpha)(\tau M_2+l+d)}\right)$$

It will be possible to solve for each of these equilibrium values once we solve the following nonlinear set of equations for each of the Λ^* values:

$$\Lambda_1^* = \frac{\beta_{MW}}{(NM_1+NM_2)}\left(\frac{C_1 bNM_1}{(d+\Lambda_2^*)(d+q+\tau M_1+\alpha)} + \frac{C_2 bNM_2}{(d+\Lambda_4^*)(d+q+\tau M_2+\alpha)}\right)$$

$$\Lambda_2^* = \frac{\beta_{WM}}{(NW_1+NW_2)}\left(\frac{C_3 bNW_1}{(d+\Lambda_1^*)(d+q+\tau W_1+\alpha)} + \frac{C_4 bNW_2}{(d+\Lambda_3^*)(d+q+\tau W_2+\alpha)}\right)$$

$$\Lambda_3^* = \frac{\beta_{MW}}{(NM_1+NM_2)}\left(\frac{C_5 bNM_1}{(d+\Lambda_2^*)(d+q+\tau M_1+\alpha)} + \frac{C_6 bNM_2}{(d+\Lambda_4^*)(d+q+\tau M_2+\alpha)}\right)$$

$$\Lambda_4^* = \frac{\beta_{WM}}{(NW_1+NW_2)}\left(\frac{C_7 bNW_1}{(d+\Lambda_1^*)(d+q+\tau W_1+\alpha)} + \frac{C_8 bNW_2}{(d+\Lambda_3^*)(d+q+\tau W_2+\alpha)}\right)$$

4.5.3 Stability of Endemic Equilibria

Besides attempting to describe the endemic equilibria in analytical terms, we would also like to better understand the conditions under which we would expect to observe endemic equilibria. To do so, we made a thorough search of the literature to better understand the methods through which we could predict the presence of endemic equilibria. We also sought to compare these conditions to the results from our definition of the basic reproduction number. If we could get agreement on both conditions under which we would expect endemic equilibria and also where the basic reproduction number is greater than one, we could be confident that the analyses on both fronts is accurate and thorough. Throughout the literature there are papers that describe conditions and analyses through which one can better understand the presence of endemic equilibria in various models.

The paper that has been most useful was Lajmanovich, (1976). In this paper, the authors prove a theorem that we have used to produce a condition on our preliminary model for which we would expect endemic equilibria to occur. The analysis presented in Lajmanovich, (1976) does not allow us to include treatment and AIDS classes. After doing a thorough search of the literature we were able to find a number of papers that dealt with models with additional classes in addition to infected and susceptible classes. Hethcote (1978) describes his analysis of a model with additional removal classes like our own. We have yet to do a thorough analysis such as that presented in the paper, in part because of our unfamiliarity with the methods used. Lloyd, (2004) also provide an analysis of a Meta population model with removal rates, and their analysis focuses on the simplification of more complex models to those that represent basic susceptible- infected-recovered (SIR) models. The rest of this chapter will focus on our own analysis that follows the analysis provided in Lajmanovich and Yorke (1976).

4.5.4 Theory

Lajmanovich, (1976) assume for their analysis that the model in question has a constant disease-free solution characterized by only susceptible individuals. Their analysis and proof seek to show that either the disease-free equilibrium is globally asymptotically stable or that there is another constant solution (i.e., endemic equilibria) that is asymptotically stable. In order to prove this assertion, the authors proceed to partition the equations of the model into smaller parts. They define the matrix A, which constitutes the bulk of their analysis, as follows:

Let us assume that A = (a_{ij}), where i , j are indices distinguishing populations or sexes. They define the elements of A based on the values of i and j If $i \neq j$ then $a_{ij} = \beta_{ij} c_{ij} N_i$ where β_{ij} is the probability of transmission from i to j; c_{ij} is the number of encounters per year between i and j; and N_i is the population size. The quantity a_{ij} basically represents

the infection rate in the population. If, however, $i = j$ then the elements $a_{ij=-r}$ simply the recovery rate (the rate at which infected individuals are reintroduced as susceptibles) in the model. The authors proceed to prove that if none of the eigenvalues of the matrix A is greater than zero, then the disease free equilibrium is globally asymptotically stable. If, on the other hand at least one of the eigenvalues of A is greater than zero, then there exists an endemic equilibrium that is globally asymptotically stable.

Preliminary Model

After attempting the analysis described in Lajmanovich , (1976) on our own preliminary model, we were able to obtain the matrix A, which is represented as follows:

$$A = \begin{bmatrix} 0 & \frac{\beta MWC_1 NW_1}{NM_1 + NM_2} & 0 & \frac{\beta MWC_2 NW_1}{NM_1 + NM_2} \\ \frac{\beta WMC_3 NM_1}{NW_1 + NW_2} & 0 & \frac{\beta WMC_4 NM_1}{NW_1 + NW_2} & 0 \\ 0 & \frac{\beta MWC_5 NW_2}{NM_1 + NM_2} & 0 & \frac{\beta MWC_6 NW_2}{NM_1 + NM_2} \\ \frac{\beta WMC_7 NM_2}{NW_1 + NW_2} & 0 & \frac{\beta WMC_8 NM_2}{NW_1 + NW_2} & 0 \end{bmatrix}$$

Using Mathematics, we are able to find the eigenvalues explicitly for this matrix; because of their length and their complexity, they will not be replicated.

The sign and relative magnitude of these eigenvalues depend on the values of the parameters chosen for each simulation of the model. It can therefore been seen, that in order to make any conclusions about the stability or existence of endemic equilibria, it is necessary to do a numerical simulation, evaluate the values of the eigenvalues of A, and determine whether those eigenvalues are greater than, less than, or equal to zero to determine the stability of the system with regard to that specific parameter set (as described in theory 4.5.4).

4.6 Treatment Simulations

In order to determine whether or not preferential treatment strategies will be effective at combating the future spread of HIV/AIDS in rural and urban communities, it will be important to test the effect of varying treatment strategies on this spread. In this section we will describe the progress we have made in determining which treatment strategy will deter the largest number of future HIV/AIDS-related deaths and also the largest number of future infections.

4.6.1 Exploratory Simulations

In order to begin our analysis, we chose to run a number of basic simulations with varying treatment strategies to see what would happen to the infected proportions of both male and female populations and rural and urban populations over time. We did so by changing the treatment rate while keeping all other variables constant in our simulations. The parameter values chosen for each simulation are those found to be the most robust and in closest agreement with the literature (see appendix A). In the following simulations, population one is assumed to be urban (i.e., large population sizes and higher frequency of interactions) and population two is assumed to be rural

(i.e., small population sizes and smaller frequencies of interactions).

Treating Only Women

There have been many studies in the literature that have pointed towards the use of preferential treatment for women as a way to prevent the future spread of HIV/AIDS in both rural and urban communities. This strategy is also advertised and suggested by the WHO, because it considers women to be a disadvantaged group in many developing countries (UNAIDS, 2005). Based on this theory, simulations were performed in which we only treated women and did not treat men, to see the effects this approach would have

on the infected populations over an extended period of time (100 years). The results can be visualized in Figure 4.7. It was observe that, treating both urban and rural women at the same rate, which in this case means treating 10 percent of the infected women over an extended period of time (100 years), the potential spread of HIV/AIDS in these populations can controlled. (As described by the model assumptions in Section 3.3.1) that the AIDS class and infected classes are not interacting, and thus if these interactions were taken into account we might expect to observe very different dynamics.

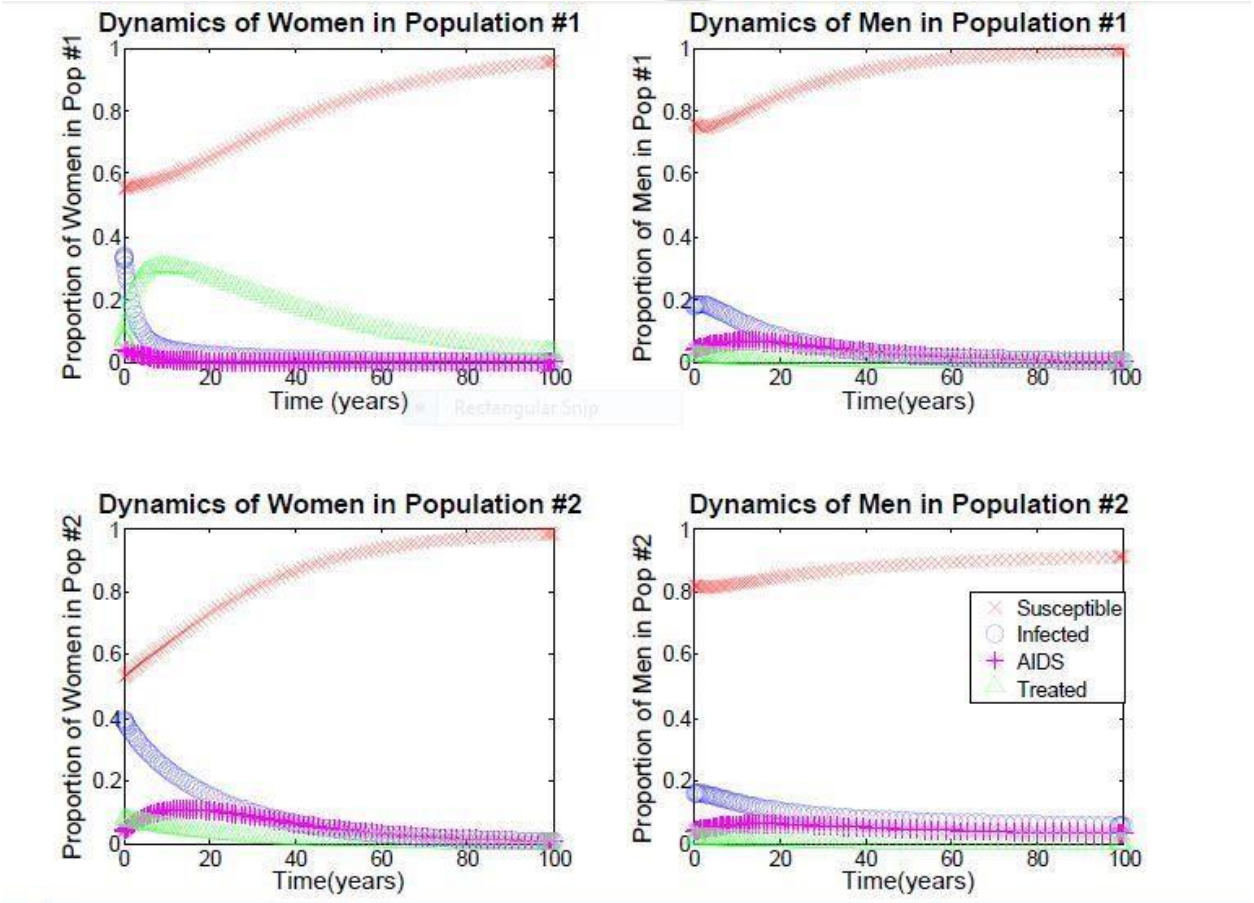


Figure 4.7*: Simulation results for preferential treatment of rural and urban women. These plots show that focusing treatment efforts on women may have a positive effect on the future spread of HIV in both urban and rural communities. The parameter values unique to this plot are:* $\beta_{MW} = 0{:}0032$; $\beta_{WM} = 0{:}001$; $\tau_{W1} = \tau_{W2} = 0{:}1$; $\tau_{M1} = \tau_{M2} = 0{:}$

Treating Only Urban Women

Accessibility to drugs and health centers is often an issue for individuals living in rural areas, and so many health organizations and non-profit organizations have focused their prevention efforts on individuals within urban areas that are within reach (UNAIDS, 2005). It is also often the case that those individuals living in urban areas are better educated than those who live in rural areas. There may, therefore, be advantages to focusing treatment and prevention programs on women living in urban areas. Putting large amounts of resources and effort into treating women living in urban areas is thus a relevant and interesting treatment scheme to explore. When explored treating women living in urban areas exclusively in the simulations (Figure 4.8), it was successful at controlling the future spread of HIV/AIDS in both rural and urban communities. This result is not surprising for two main reasons. First, the number of women and people in the urban areas is very large and therefore treating 30 percent of the infected female population is treating a large number of women.

Second, one of the implicit assumptions in the model structure is that women in urban areas will have more encounters with men than women living in rural areas, simply because of the density of people and the difference in the amount of social interaction expected for these two groups.

Treating Only Rural Women

In addition to the large number of programs and health organizations that focus their efforts on urban populations, there are a large number of private organizations and local organizations that attempt to provide medication to those individuals living in rural areas (UNAIDS, 2005). These organizations focus the majority of their energy and resources in treating people that are far away from city centers and major health facilities. The

effects of dedicating a large number of resources to treating individuals with lower amounts of promiscuous sexual encounters and dealings with urban areas is an interesting simulation to consider.

As can be seen from the simulation results (Figure 4.9), treating rural women has a large effect on reducing the number of infected women in the rural population, but does little to reduce the amount of infection in the urban populations. A steady decrease in infection is seen in all populations, but nothing significant enough to be able to conclude that solely treating rural women would be a sufficient and adequate strategy to fight future HIV infection in rural and urban communities.

Treating Only Men

In contrast to the studies cited above, some studies support focusing prevention and treatment programs on men's reproductive health (Crepaz, 2006). It is often seen, and assumed in the simulations, that men have

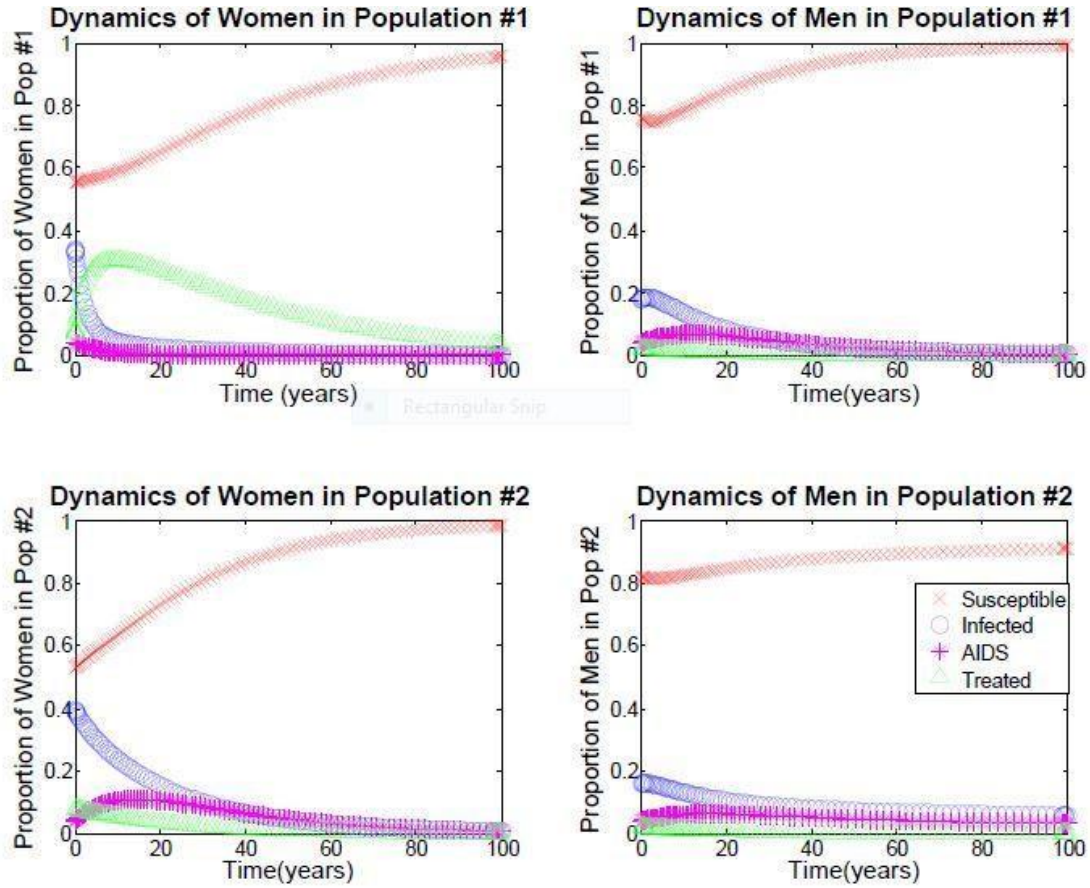


Figure 4.8: *Simulation results for preferential treatment of urban women. These plots show that treating urban women thoroughly has a positive effect on the future spread of HIV in all population subgroups. The parameter values unique to this plot are:* $\beta_{MW} = 0.0032$; $\beta_{WM} = 0.001$; $\tau_{W_1} = 0.3$, $\tau_{W_2} = \tau_{M_1} = \tau_{M_2} = 0$:

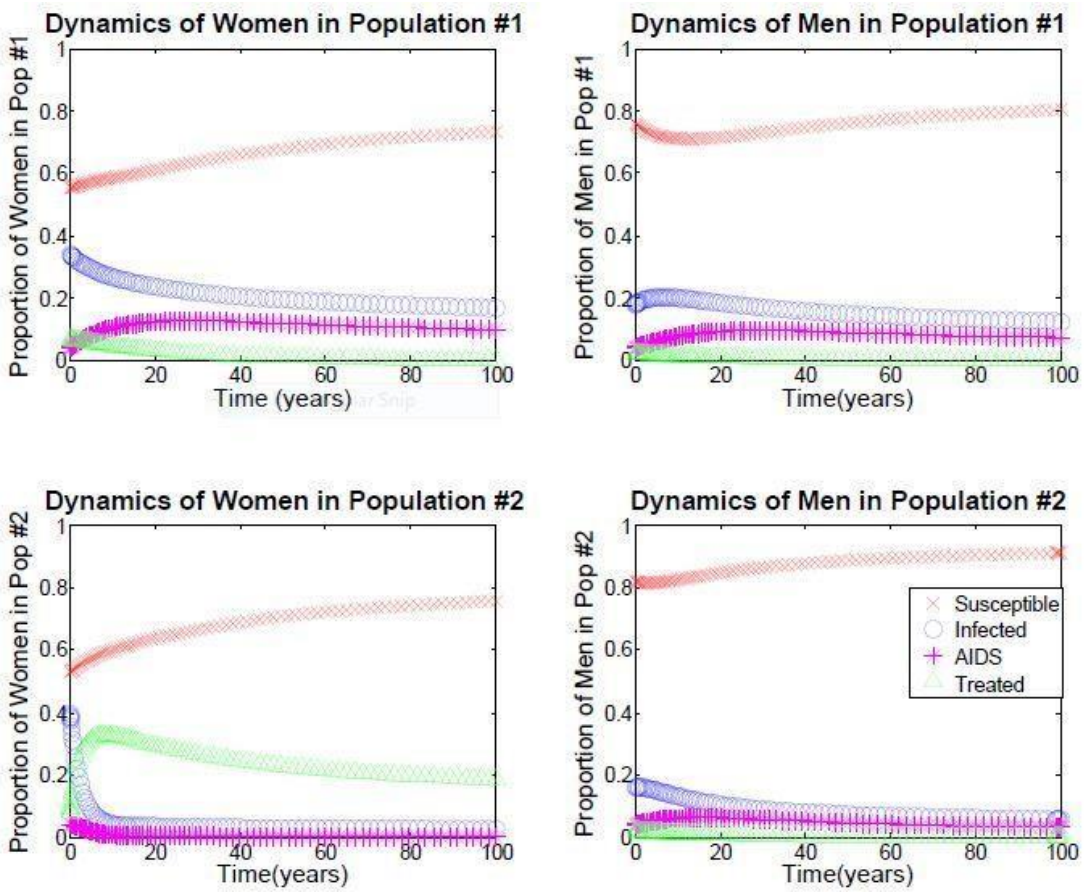


Figure 4.9: *Simulation results for preferential treatment of rural women. This plot shows that treating rural women is not an effective strategy for reducing the spread of HIV in both urban and rural populations. The parameter values unique to this plot are:* $\beta_{MW} = 0.0032$; $\beta_{WM} = 0.001$; $\tau_{W2} = 0.3$, $\tau_{W1} = \tau_{M1} = \tau_{M2} = 0$.

Many more sexual encounters then women per year, and a large proportion of these sexual encounters are promiscuous. It is also the case that the probability of transmission from males to females is much higher than the transmission rate of females to males. Thus, it may be the case that focusing prevention and treatment strategies on males may actually be a decent strategy to prevent the future spread of HIV infection in both female and male populations in both rural and urban areas. When we run simulations in which treatment is limited to men (Figure 4.10), we see a similar result to that observed for solely treating women.

The prevalence rates in all populations slowly decreases, until after 100 years we actually observe very little infection present in any of the populations studied. It is seen that there is symmetry present in the model that allows this to happen, but based on studies and other published material, we wouldn't expect this symmetry to be present. That is, we might expect there to be an advantage to treating men over women or women over men but not both. Thus Section 5.2 is dedicated to exploring how changes to the infection parameters affect the prevention of infection in these populations, as it is assume that changing parameter values may disrupt this symmetry.

Treating Urban Areas

The proximity of urban populations to health centers and ART distribution centers puts urban residents at a distinct advantage over those living in rural areas. Resourceconstrained countries would have to put little to no energy into treating those living in urban areas and this makes the strategy very appealing. In addition, most resourceconstrained countries, like Ghana, would not have to improve infrastructure in order to treat a significant portion of the population. When simulations are run in which treatment is limited to men and women in urban areas (Figure 4.11) it is seen that this strategy has an extremely positive effect on the future spread of HIV in all populations. These results confirm and agree with those described in chapter 2 by Wilson, (2006).

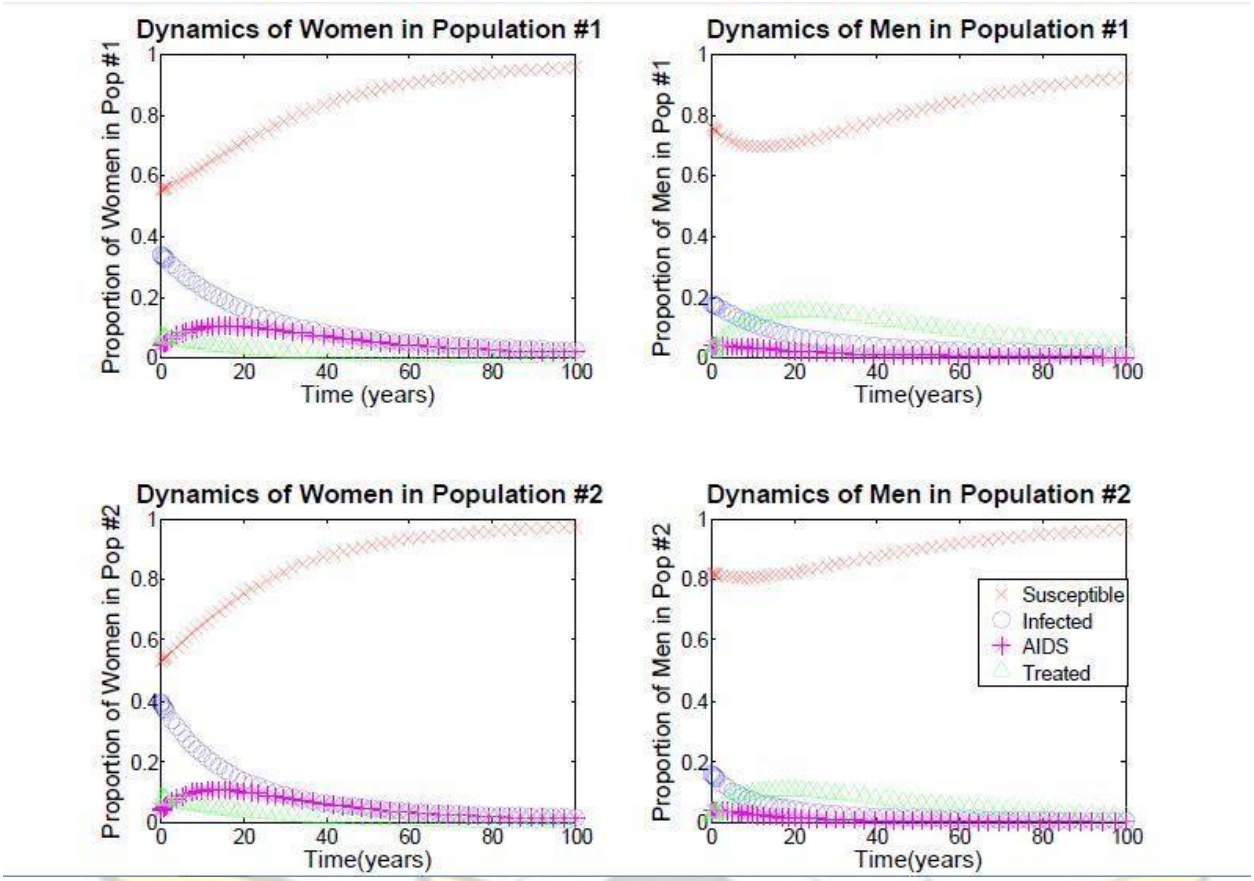


Figure 4.10*: Simulation results for preferential treatment of rural and urban men. This plot shows that the treatment of men has very similar repercussions to the treatment of women, and motivates investigation into this symmetry. The parameter values unique to this plot are:* $\beta MW = 0.0032$; $\beta WM = 0.001$; $\tau M_1 = \tau M_2 = 0.1$; $\tau W_1 = \tau W_2 = 0$:

Treating Rural Areas

In contrast to the supply of drugs in urban areas, the distribution of drugs in rural areas is stunted by distance from health-care centers and the lack of infrastructure in rural areas of resource-constrained countries. We examine the distribution of drugs to rural areas in order to explore the WHO document's recommendation of focusing treatment to disadvantaged populations. It is seen that in the simulations (Figure 4.12) preferential treatment to rural areas alone does not have a positive effect on the future spread of HIV.

In fact, this strategy does not reduce the infected population load nearly as much as any other treatment rationing strategy.

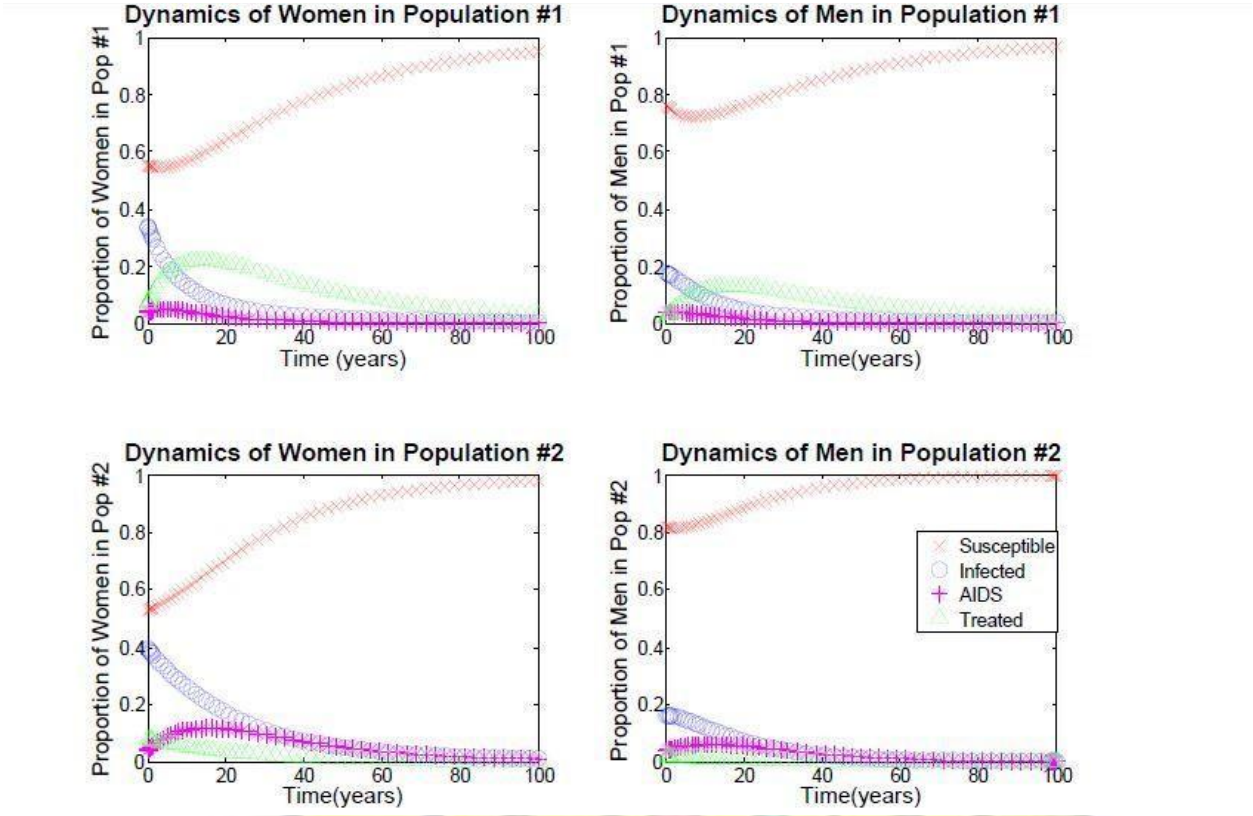


Figure 4.11: *Simulation results for preferential treatment of urban areas. We see that treating urban populations has a large positive effect on both urban and rural areas, suggesting this is the best preferential treatment strategy. The parameter values unique to this plot are:* $\beta_{MW} = 0{:}0032$; $\beta_{WM} = 0{:}001$; $\tau_{M_1} = \tau_{M_2} = 0{:}1$; $\tau_{W_1} = \tau_{W_1} = 0$:

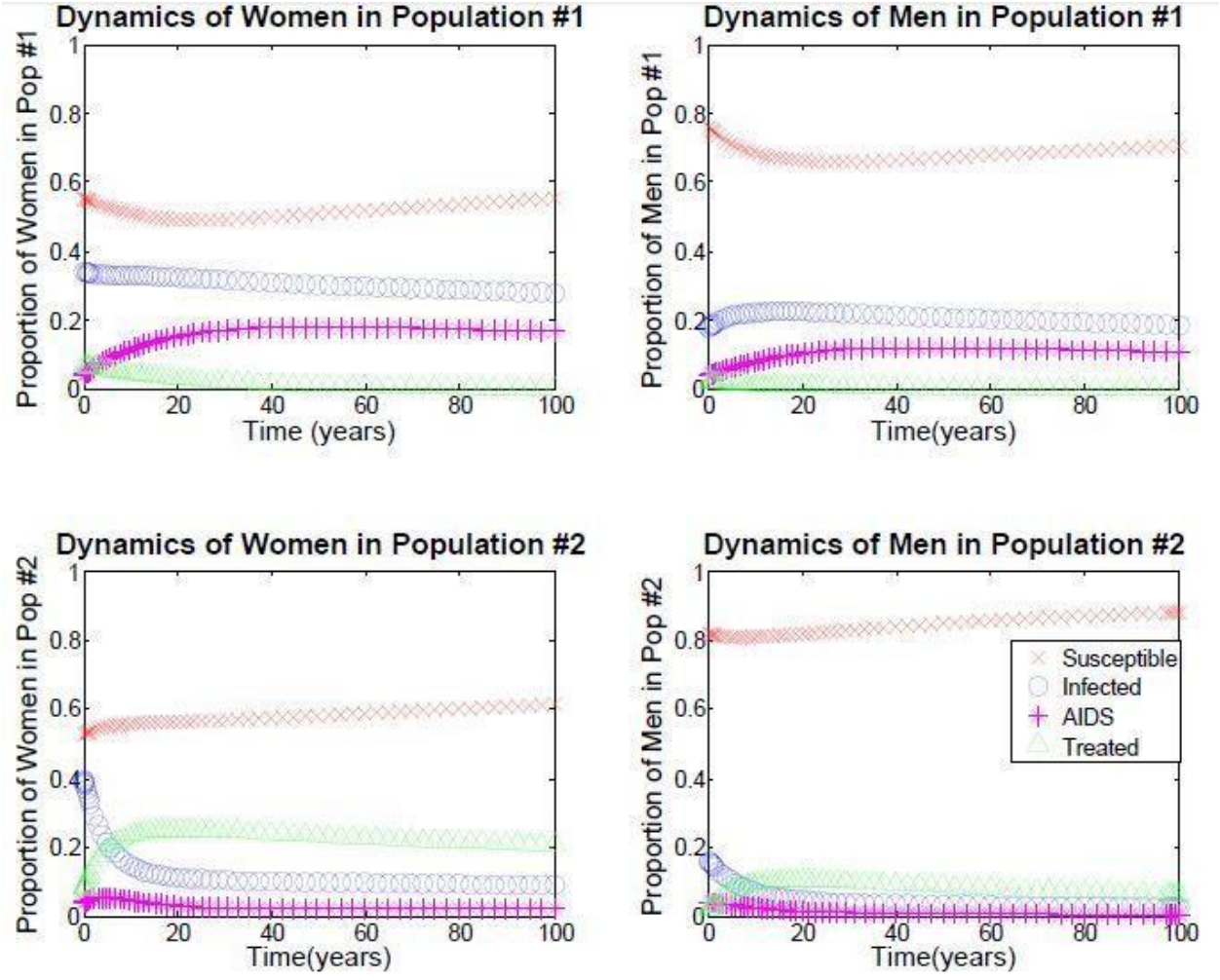


Figure 4.12*: Simulation results for preferential treatment of rural areas. These simulation results suggest that preferential treatment in rural areas is not a reasonable strategy to fight future HIV infections. The parameter values unique to this plot are:* $\beta_{MW} = 0{:}0032$; $\beta_{WM} = 0{:}001$; $\tau W_2 = \tau M_2 = 0{:}1$; $\tau W_1 = \tau M_1 = 0$:

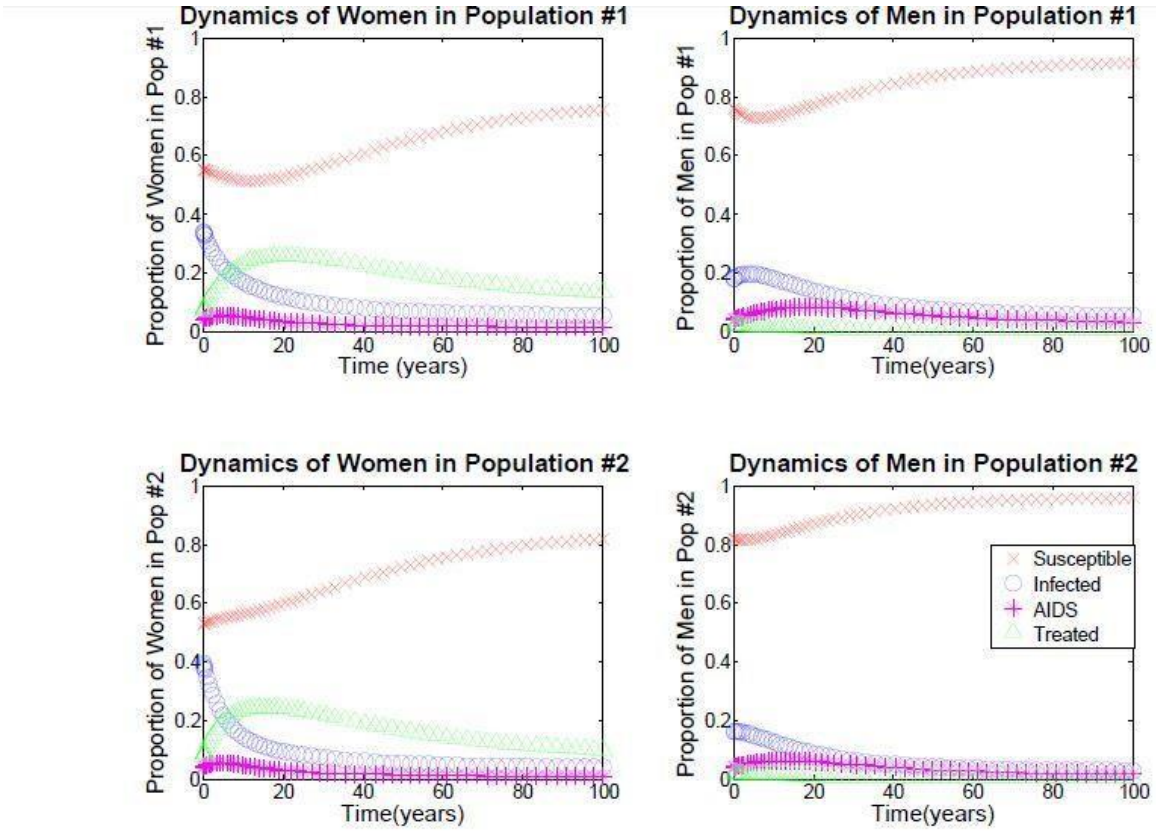


Figure 4.13: *Simulation results for preferential treatment of women with increased* β_{MW}. *This plot shows that with stronger male-to-female transmission probabilities, treating women does not have as strong an effect on the future spread of HIV as seen in the scenario depicted in Figure 6.1. The parameter values unique to this plot are:* $\beta_{MW} = 0:005$; $\beta_{WM} = 0:001$; $\tau W_1 = \tau W_2 = 0:1$; $\tau M_1 = \tau M_2 = 0$:

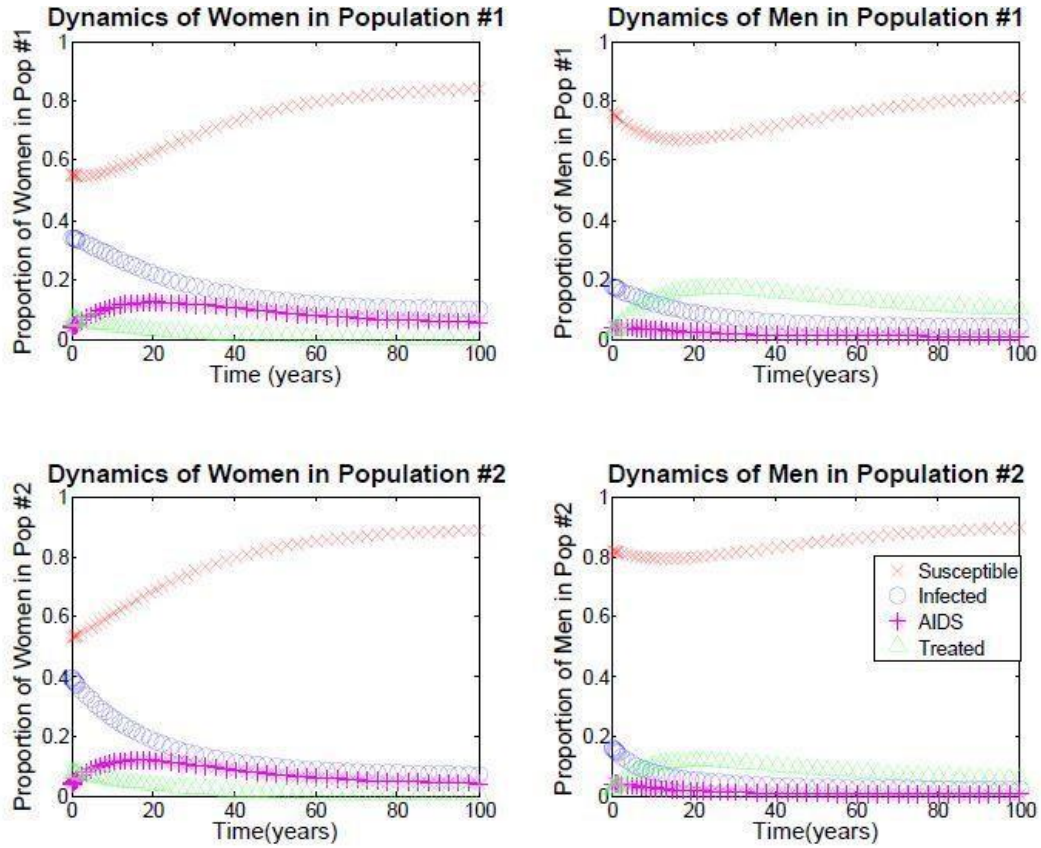


Figure 4.14: *Simulation results for preferential treatment of men with increased* βMW. *This plot shows that when the probability of transmission from men to women is increased, the effect of treating only men is not as strong in preventing infection in women as in the scenario are depicted in Figure 6.4. The parameter values unique to this plot are:* $\beta MW = 0{:}005$; $\beta WM = 0{:}001$; $\tau M_1 = \tau M_2 = 0{:}1$; $\tau W_1 = \tau W_2 = 0{:}$

4.7 Summary

In this chapter, tools such as Latin Hypercube Sensitivity analysis, Basic Reproductive Number, Equilibria and Stability analysis were implored to analyze the infections and the spread of

HIV/AIDS base on the model. Simulation diagrams were also used to analyze the preferential treatment that determines which treatment strategy affect the future spread of HIV/AIDS. The next chapter presents the summary, conclusion and recommendation of the study.

CHAPTER FIVE

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter presents the summary, conclusions drawn from the study and a recommendation to help Ghana Aids Commission to streamline strategy to reduce the transmission rate and increase the treatment of AIDS.

5.2 Summary of Results

Following the results of our sensitivity analysis (Chapter 3), in which we concluded that the parameter that would have the largest effect on the simulation and model analysis was the probability of transmission (β), we decided to run simulations to determine whether changing these parameters had an effect on the future spread of infection. In the following simulations, we wanted to observe the effect of increasing the probability of transmission from male to female βMW while keeping the female to male probability of transmission βWM constant to see what effect variation in β would have on the differences in outcomes of treating men and women. It is expected that as the probability of transmission is increased from males to females, a larger positive effect from the treatment of males than from treating females would be seen.

What is seen in the simulation results for both treatment of only women and treatment of only men (Figures 4.13 and 4.14, respectively), is that when the probability of transmission is high, it is harder to prevent the future spread of HIV, even with treatment. It seen that when you treat only women, we would be able to reduce the amount of HIV prevalence in both rural and urban women and men, respectively, but we are unable to get the larger population's prevalence rates as low as we can by lowering transmission rates.

It can also be seen that in the case of treating only men that although there is an initial decrease in the prevalence of HIV among women, we do not see a drastic reduction in prevalence over time as we see in the case with a lower probability of transmission. These simulations confirm the results of the sensitivity analysis; changes in the probability of transmission have an effect on the future spread of HIV/AIDS.

5.3 Conclusion

Of all the treatment strategies explored in the simulations, it can be concluded that the preferential treatment of urban populations may be the most effective at reducing the number of future infections in all populations. It can be seen that by focusing prevention and treatment strategies on women in urban areas, resource-constrained countries may be able to reduce the disease characteristics of urban and rural areas as a whole. Because we assume that urban women have more sexual encounters then rural women, and further that urban men have more interactions then rural men, we see that the treatment of women has a drastic effect on the spread of the disease in all populations.

Treating both urban women and rural women has a similar effect on the reduction of future HIV infection, but does not reduce infection in all populations as quickly has the sole treatment of urban women or the treatment of men and women in urban populations. The results differ slightly, therefore, than the recommendations by the WHO. Focusing treatment distribution in rural areas, we have found, reduces the infection prevalence in those areas but does very little to affect the prevalence rates in urban areas. On the other hand, focusing attention to the more populated urban areas has a positive effect on both the urban and rural areas.

The results do confirm though that the preferential treatment of women, considered here a disadvantaged population, in urban areas is a legitimate and positive step towards decreasing the rate of infection in all regions.

5.4 Recommendation

We hope that further research into dynamical systems analysis methods for the determination of the existence and stability of endemic equilibria will make clear the reasons for the discrepancy in the predictions of the basic reproductive number and the analysis presented in Lajmanovic, (1976).

In addition, looking more closely into the analysis presented by Hethcote, (1978) and attempting to apply it to our own model may be a fruitful endeavor.

We hope that by finding agreement between these two predictors of stability we will further understand the stability of the model and the presence of endemic equilibria.

Future work should also seek to relax the assumptions described in the previous section. Relaxation needs to begin with a better understanding of the consensus in the literature on many of the issues. Two assumptions that need to be addressed, in particular, are those regarding treated individuals having only protected sex and the estimate of intermediate probability for the infection parameter.

Two assumptions that we seek to eliminate from the model to make it more realistic are those that assume heterosexual transmission is the only form of infection and that of individuals being completely compliant with medication.

In many cases, the assumptions may not be relaxed, but all attempts should be made to make the model as realistic as possible in order to understand the true dynamics of HIV prevalence in Ghana. The relaxation of assumptions should be approached cautiously, attempting to minimize the number of new parameters introduced in the process. At a certain point, the relaxation of assumptions must be limited in order to limit the number of parameters that need to be estimated and analyzed.

Further, we seek to incorporate long distance population dynamics, using the method described by Keeling and Rohani (2002). Incorporating these dynamics will allow us to

make conclusions about the dynamics between faraway villages in Ghana and thus understand HIV transmission in rural areas. Incorporating these long distance dynamics will also allow us to develop, potentially, a spatial map that tracks HIV prevalence over time according to certain population levels and transmission rates across the country.

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APPENDIX A

Results from PRCC are presented in Table A. There are a number of parameters that have significant correlations with changes in total prevalence .The two parameters with the lowest p-value are those of the infection rates β_{MW} and β_{WM}, as expected.

parameter	PRCC	p-value	Significant?
β_{MW}	0.545	$2.02x10^{-7}$	**
β_{WM}		0.578	$2.45x10^{-8}$ **
c_1		0.280	0.012 **
c_2	0.102	0.369	
c_3	0.162	0.153	
c_4	0.071	0.531	
c_5	0.073	0.523	
c_6	0.191	0.091	
c_7	0.245	0.029	**
c_8	0.067	0.555	
τ_{w1}	-0.048	0.672	
τ_{M1}	0.011	0.920	
τw_2	0.071	0.534	
τ_{M2}	-0.089	0.435	
b	0.195	0.085	**
d	-0.250	0.026	**
q	-0.288	0.010	
l	0.190	0.093	**
αW_1	-0.312	0.004 **	αM_1 -0.37 0.001 **
αW_2	-0.244	0.030	
αM_2	-0.196	0.083	

Table A: *LHS partial rank correlation coefficients. Parameters with significant correlations at the* $\alpha = 0.5$ *level are demarcated by two stars. The infection force* β *seems to have the largest effect on total prevalence*