EVALUATING THE POTENTIAL IMPACT OF CONDOMS AND VAGINAL MICROBICIDES TO REDUCE THE SPREAD OF HIV

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Declaration

No portion of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institution of learning.

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Dedication

To my special friend Chipo Chitewo.

Chapter 1

Introduction and Background

Since its emergence in the 1980s, the Human Immuno-deficiency Virus (HIV), the causative agent of Acquired Immune Deficiency Syndrome (AIDS) has claimed the lives of millions of people (20 million), and continues to exert significance socio-economic and public health burden, around the globe [1]. The current UN AIDS report estimates about 38.6 - 46 million people were living with HIV at the end of 2005, and 4.1 million new infections were recorded in that year. More than one-half of the 38.6 - 46 million people living with HIV/AIDS are women, with more than 90% of all adolescent and adult HIV infections resulting from heterosexual intercourse [2]. In Southern Africa the epidemic is exploding and non-levelling due to several factors; deteriorating health systems, poverty, traditional beliefs, increased substance abuse, sexual violence, high population mobility, stigma and discrimination and low risk-reduction education. Although the HIV/AIDS threat is great, there has been a lot of research on how to help people protect themselves from contracting the virus (primary prevention, for example condom use, vaginal microbicides, abstinence, etc) and how to prevent and minimize the health and psychological consequences of those living with the infection (secondary prevention). When the HIV pandemic first became visible in the early 1980s, global concern about the gravity of the virus began to fuel research on how to prevent transmission. Both HIV and efforts to respond to the disease surfaced early in Uganda. The prevention effort in Uganda, which has since spread to other countries in

Sub-Sahara Africa and beyond, was to be faithful, abstinence and use of condoms. While the idea of abstaining from sex had some success among young, unmarried people, the refusal of many married men to remain faithful to their often-monogamous wives made the use of condoms the only option feasible.

1.1 Condoms

Knowledge of condoms as a method of preventing pregnancy and HIV/AIDS is relatively good. However, there are many real and perceived barriers to condom use especially in stable sexual relationships. In stable long-term relationships, resistance to condom use is strongly related to its association with STDs (including HIV/AIDS). Men and women do not see the need for condom use in such relationships, maybe seen as a clear sign of infidelity. These attitudes represent major obstacle to the use of condoms as a method of protection. Equally difficult to measure is the proportion of individuals who use condoms consistently and correctly. While condoms may be readily available, the consistent and correct use also depends on individual's attitudes, beliefs and how informed they are on the risks associated with improper use of condoms. A study conducted among rural men and women in informal settlements in South Africa aimed at assessing the power of women to reduce the risk of HIV infection found that, about half of the women felt that they had no right to insist that their partner use condoms [11]. Condoms are more likely to be used in the beginning of a relationship or in relationship that trust has not been established. This is because of the uncertainty about the faithfulness of partners and the fear of acquiring an STD (including HIV) from a sexual partner, but some men are more likely to complain that condoms interrupt sexual activity, cause discomfort, and ruin the excitement of flesh to flesh contact. However, a major disadvantage of condoms is that it depends heavily on partner co-operation. Many of the male and female respondents reported negative attitudes on the part of their partners to the use of condoms [11]. But up-to-date, condom has remained the only available HIV prevention strategy. However condoms have always been available and currently are the only method of protection available for individuals who have vaginal sex,

and are highly effective at preventing HIV transmission with an estimated efficacy of 87% [20-22], but studies suggest that condom use is often low. Thus, there is an urgent need to provide an alternative mechanism of protection for women whose partners are unwilling to use condoms (e.g vaginal microbicides).

1.2 Vaginal microbicides

Vaginal microbicides are chemical compounds which can be applied topically to prevent or reduce the transmission of HIV, including neonatal transmission, and other sexually transmitted diseases [2]. Currently, there are around 60 candidate vaginal microbicides in development 18 of which have advanced to clinical testing. The funding stream and enthusiasm for microbicides is high, but microbicides are not expected to be on the market before 2013. Current efforts are aimed at developing intra-vaginal topical formulations to curb mucosal and perinatal HIV transmission by directly inactivating HIV or preventing HIV from attaching, entering or replicating in susceptible target cells as well as dissemination from target cells present in semen or the host cells that line the vaginal wall. Vaginal microbicides are believed to provide an alternative mechanism of protection for women whose partners are unwilling to use condoms, and could also be applied in addition to condoms [2]. In this section we investigate the effect of combined intervention strategy, a case when condoms and microbicides are used at the same time.

1.3 Transmission

Sexual contact is the main source of HIV infection. Transmission occurs when there is contact between sexual secretions of one partner with the rectal, genital or oral mucous membranes of another. Sexually Transmitted Diseases (STDs) increase the risk of infection by destroying the epithelial barrier through genital ulceration and also by accumulation of pools of HIV susceptible lymphocytes or HIV infected cells (macrophages) in semen and vaginal secretions.

The risk of HIV infection goes up four time in a person who has developed genital ulcers from syphilis or chancroid [28]. Use of a condom in a correct and consistent manner during heterosexual copulation reduces the risk of transmission by more than 80 percent (Cayley, 2004). Prevention can also be by way of abstinence especially in societies who shun and discourage condom use for example the Catholics and Muslims.

Recipients of blood products and people who share syringes contaminated with HIV are particularly at risk of contracting HIV. In North America where drug use is prevalent this form of transmission accounts for 50 percent of all new infections. In Zimbabwe hemophiliacs are not very common except in the homosexual and lesbian communities. However because of their own present higher risk of HIV transmission as opposed to heterosexual sex, it is difficult to measure the net effect of sharing syringes on HIV transmission rates among these groups.

1.4 Risk Factors for HIV Infection

Elements or activities that increase the likelihood of one acquiring HIV are as follows

- Unprotected Conjugation: During sex the vagina, penis, vulva, rectum all provide entry points for the virus.
- Having sexual relations with a person whose HIV status is unknown.
- Having sex with someone with many partners.
- Sharing needles and syringes.
- Sexually Transmitted Diseases retard the genital skins and provide entry points for the virus where those retarded points have come into contact with genital discharge and fluids in general from infected persons. Vaginal bacterias some of which are harmless in immuno active persons often cause infections that make the vaginal walls fragile and susceptible to retardation there by increasing chances for contraction of infections.

- Medical procedures such as blood transfusion and reception of blood products such as tissue membrane, artificial insemination also accentuate the risk of HIV infection. While in the majority of cases blood and blood products are tested for HIV, the risk exists because the current testing methods cannot detect HIV within the window period.

1.5 Parameters

Prediction and estimation of parameter values in HIV/AIDS transmission remains a problem especially in Africa. In trying to model the rate of transmission of HIV, we consider two important component parameters: c - the rate of acquisition of new sexual partners and β- the probability that a contact with an infected individual results in an infection.

c - the rate of acquisition of new sexual partners depends largely on social and environmental factors. Environmental factors are those that determine the living conditions, resources and social opportunities. Cultural and religious settings also have an influence on the number of new partners one can acquire. In Southern Africa, some cultural settings allow men to have as many partners as they wish and this has had a significant impact on the value of c. Mobility has increased, especially in Zimbabwe due to economic melt down, resulting in individuals working and staying far away from their homes, resulting in secret affairs, which contributed to an increase in the value of c. Many have indulged in risky sexual behaviours due to poor living conditions, the need for favours and financial support, a common scenario in Africa. Risk behavioural change can be measured by measuring the trends of the value c, a decline in the value of c indicating an increase in behavioral change. This calls for early child hood behavioural research with the aim of identifying psychological, social and environmental factors associated with risky sexual behaviour.

β - the average probability that an infected individual will infect a susceptible partner over the duration of their relationship. This parameter is equally difficult to determine and is largely related to attitude factors (negative attitude towards the use of condoms in particular), poor risk reduction (inability to use condoms correctly and consistently) and substance

abuse problems. An individual's risk of acquiring HIV is to a large extend determined by an individual's attitude and role during sexual intercourse.

1.6 Mathematical Modelling

Mathematical modelling is a process of representing a physical or biological phenomenon by means of equations or a function. A set of equations is used to describe the relationship between variables. The main thrust of developing and analysing mathematical models is therefore to have an understanding of the phenomenon under investigation. Modelling enforces clarity of thought, when assumption in the model are explicitly formulated and allows one to see implications and predictions. It also makes it easier to analyse physical and biological subsystems of interest and sometimes solves problems beyond laboratory instrument currently in use. Mathematical models can be divided into:

- Linear and nonlinear: In this case all the operators in the model present linearity otherwise the model is nonlinear.

- Deterministic and stochastic: In a deterministic model every set of variable is uniquely determined by parameters in the model and by sets of previous states of these variables. Thus deterministic models will give the same result for the same start. They are often appropriate for large population. In a stochastic model, randomness is present and variable states are described by probability distributions. They provide more information, for example means, covariances etc. Catters for all times: short and long term.

- Static or dynamic: Static models do not change with time whereas dynamic models are time dependent.

1.7 Objectives

The objectives of this thesis are:

- to develop a deterministic model for the theoretical assessment of HIV/AIDS intervention strategies; condoms and vaginal microbicides.
- analyse the mathematical properties of the model.
- incorporating more realistic features of HIV/AIDS pathogenesis and epidemiology such as
  - staged progression.
  - HIV/AIDS transmission by AIDS patients.
  - sex structures
- to determine the level of microbicide efficacy and use which is necessary to counterbalance a possible reduction in condom use.

1.8 Thesis Outline

The thesis is organised as follows: In chapter two we formulate the basic HIV/AIDS heterosexual model and analyse it. Chapter three is the thrust of the study of this thesis since it is in this chapter we introduce the two preventative strategies; condoms and vaginal microbicides. The equilibrium points and basic reproductive numbers are calculated and analysed to get an insight of the economic benefits. In chapter four, numerical simulations are carried out. Comparison with the analytic results are carried and conclusions drawn. Chapter five is a summary of results and the recommendations necessary for future research work.

Chapter 2

The Basic Model in a Heterosexual Setting

2.1 Introduction

Heterosexuality is considered to be the most common sexual orientation and a social norm in many societies. Heterosexuality usually implies an exclusive or predominant sexual orientation toward persons of the opposite gender. Thus, most STD models try to incorporate some kind of contact and mixing structure. With STDs, infective contacts are not made randomly as they are with the common cold and other easily communicable diseases, so it is worth noting that sexual contacts among humans occur most often within a pair of relationship of longer duration than a single contact [2].

2.2 Model Formulation

We are going to consider a model which divides the total sexually-active population $N(t)$ by gender. Let the total sexually-active male population, denoted by $N_m(t)$, be divided

into three mutually-exclusive sub-populations of susceptible $S_m(t)$, infected $I_m(t)$ and AIDS $A_m(t)$ individuals, so that $N_m(t) = S_m(t) + I_m(t) + A_m(t)$. Similarly, let the total sexually active female population denoted by $N_f(t)$ be divided into three mutually-exclusive sub-populations of susceptible $S_f(t)$, infected $I_f(t)$ and AIDS $A_f(t)$ individuals, so that $N_f(t) = S_f(t) + I_f(t) + A_f(t)$.

Thus, $N(t) = S_m(t) + I_m(t) + A_m(t) + S_f(t) + I_f(t) + A_f(t)$. We assume that HIV is transmitted via sexual intercourse so that the population under consideration is sexually active. Individuals are transferred from one class to the other as their status with respect to the disease change. At each time period, new recruits enter the heterosexually active population at a rate π. All new recruits are assumed susceptible with a proportion ρ of these individuals being males and the complementary proportion $(1 - \rho)$ are female susceptible. The fractions of infected females and males are $\frac{I_f(t)+A_f(t)}{N_f(t)}$ and $\frac{I_m(t)+A_m(t)}{N_m(t)}$, respectively. Let c_m be the rate of male acquisition of new sexual female partners and β_{fm} be the female infection probability. The force of infection is $\lambda_f = \frac{\beta_{fm}(I_f(t)+\eta A_f(t))}{N_f(t)}$, where $\eta \geq 1$ accounts for the relative infectiousness of individuals in the AIDS class in relation to infected female. It is assumed that owing to their high viral load, AIDS individuals are more infectious than infected female (in the $I_f(t)$ class). Thus, the product $c_m\lambda_f S_m(t)$ is the rate of formation of new male infections. Similarly, individuals in the $S_f(t)$ class acquire HIV infection at a rate $\lambda_m = \frac{\beta_{mf}(I_m(t)+\eta A_m(t))}{N_m(t)}$, with $c_f\lambda_m S_f(t)$ is the rate of formation of new female infections. The infected male and female individuals ($I_m(t)$ and $I_f(t)$) progress to AIDS at a rate σ. The losses from the system are due to natural death μ and those in AIDS stage have an additional disease-induced death d. The flowchart of the model is given in Figure 2.1.

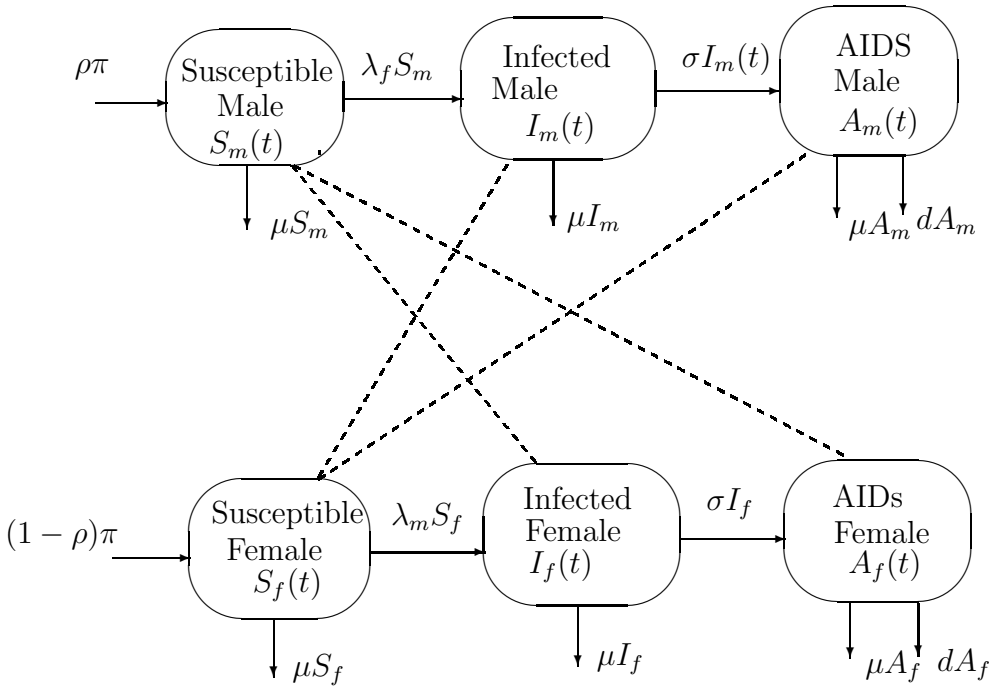

Figure 2.1: A compartmental diagram for the model system (2.1) – (2.6)

Thus, the model equations are given by

$$\frac{dS_m}{dt} = \rho\pi - c_m\lambda_f S_m(t) - \mu S_m(t) \tag{2.1}$$

$$\frac{dI_m}{dt} = c_m\lambda_f S_m(t) - (\mu+\sigma)I_m(t) \tag{2.2}$$

$$\frac{dA_m}{dt} = \sigma I_m(t) - (\mu+d)A_m(t) \tag{2.3}$$

$$\frac{dS_f}{dt} = (1-\rho)\pi - c_f\lambda_m S_f(t) - \mu S_f(t) \tag{2.4}$$

$$\frac{dI_f}{dt} = c_f\lambda_m S_f(t) - (\mu+\sigma)I_f(t) \tag{2.5}$$

$$\frac{dA_f}{dt} = \sigma I_f(t) - (\mu+d)A_f(t) \tag{2.6}$$

where

$$\lambda_m = \frac{\beta_{mf}(I_m(t)+\eta A_m(t))}{N_m(t)} \quad \text{and} \quad \lambda_f = \frac{\beta_{fm}(I_f(t)+\eta A_f(t))}{N_f(t)}$$

are the force of infection for males and females, respectively.

The total subpopulation of the sexually active male and female individuals changes according

to the following ordinary differential equations

$$\frac{dN_m}{dt} = \rho\pi - \mu N_m(t) - dA_m(t), \tag{2.7}$$

$$\frac{dN_f}{dt} = (1-\rho)\pi - \mu N_f(t) - dA_f(t) \tag{2.8}$$

Model system (2.1) - (2.6) has varying subpopulation sizes ($\frac{dN_m}{dt} \neq 0$ and $\frac{dN_f}{dt} \neq 0$) and therefore a trivial equilibrium is not feasible.

2.3 Positivity and Boundedness of Solutions

From system $(2.7) - (2.8)$, the time derivative of N along a solution path of the system gives

$$\begin{aligned}\frac{dN}{dt} &= \dot{N}_m(t) + \dot{N}_f(t) \\ &= \pi - \mu N(t) - d(A_m(t) + A_f(t)) \\ &\leq \pi - \mu N(t), \quad \text{since} \;\; d \geq 0\end{aligned}$$

Clearly,

$$0 \leq N(t) \leq N(0)e^{-\mu t} + \frac{\pi}{\mu}(1 - e^{-\mu t}).$$

where $N(0)$ represents the initial total sexual active population.

Thus as $t \to \infty$

$$0 \leq N \leq \frac{\pi}{\mu}$$

and we assume without loss of generality that the population size has reached its limiting value of $\frac{\pi}{\mu}$ (see Thieme 1992, 1993, 1994; Castillo-Chavez and Thieme, 1995). Thus the sexual active population dependent on the rate of recruitment of new sexually-active individuals and the natural death.

Therefore all feasible solutions of the system $(2.1) - (2.6)$ enter the region

$$\begin{aligned}\Omega = \Big\{&(S_m(t), S_f(t), I_m(t), I_f(t), A_m(t), A_f(t)) \in \mathbb{R}^6_+ | S_m(t), S_f(t), I_m(t), \\ &I_f(t), A_m(t), A_f(t) \geq 0; N(t) \leq \frac{\pi}{\mu}\Big\}\end{aligned}$$

Thus Ω is positively invariant and it is sufficient to consider solutions in Ω. Existence, uniqueness and continuation results for system $(2.1) - (2.6)$ hold in this region. It can be shown that all solutions of the system $(2.1) - (2.6)$ starting in Ω remain in Ω for all $t \geq 0$. All parameters and state variables for the model system are assumed to be non-negative for $t \geq 0$ since it monitors human population. Thus the model system $(2.1) - (2.6)$ is both well-posed and biologically meaningful.

2.4 Model Analysis

The system is characterised by two equilibrium points, the disease free equilibrium point, $\mathbf{x}^*$ and the endemic equilibrium point, $\mathbf{x}_e$. These equilibrium points are obtained when $\frac{dS_m}{dt} = \frac{dS_f}{dt} = \frac{dI_m}{dt} = \frac{dI_f}{dt} = \frac{dA_m}{dt} = \frac{dA_f}{dt} = 0$.

2.4.1 Disease-free Equilibrium Point

The first equilibrium state is the disease-free equilibrium point given by, $\mathbf{x}^*$. This is the state when all infected populations are equal to zero ($I_m(t) = I_f(t) = A_m(t) = A_f(t) = 0$), hence no disease.

Thus,

$$\mathbf{x}^* = \left(\frac{\rho\pi}{\mu}, \frac{(1-\rho)\pi}{\mu}, 0, 0, 0, 0 \right)$$

2.4.2 The Basic Reproductive Number ($\mathcal{R}_0$)

As in any model that endeavors to capture the transmission dynamics of a disease, the basic reproduction number of infection is central in determining the clearing or the persistence of an infection. It is defined to be the average number of secondary cases generated by one infectious individual introduced into a wholly susceptible population [8]. From this definition

it is immediately clear that when $\mathcal{R}_0 < 1$, each infected individual produces on average less than one new infected individual and we therefore predict that the infection will be cleared from the population. If $\mathcal{R}_0 > 1$, the infection is able to invade the susceptible population. This threshold behaviour is the most important and useful aspect of the $\mathcal{R}_0$ concept. In an endemic infection, we can determine which control measures and at what magnitude would be most effective in reducing $\mathcal{R}_0$ below one, providing important guidance for public health initiatives. The magnitude of $\mathcal{R}_0$ is also used to gauge the risk of an epidemic or pandemic in emerging infectious disease. For example, the estimation of $\mathcal{R}_0$ was of critical importance in understanding the outbreak and potential danger from Severe Acute Respiratory Syndrome (SARS) (Choi & Pak 2003; Lipsitch et al. 2003; Lloyd-Smith et al. 2003; Riley et al. 2003). $\mathcal{R}_0$ has been likewise used to characterise Bovine Spongiform Encephalitis (BSE) (Woolhouse & Anderson 1997; Ferguson et al. 1999; de Koeijer et al. 2004), Foot and Mouth Disease (FMD) (Ferguson et al. 2001; Matthews et al. 2003), novel strains of influenza (Mills et al. 2004; Stegman et al.2004) and West Nile virus (Wonham et al.2004) have been assessed using $\mathcal{R}_0$ in recent literature.

2.4.3 Computation of the Basic Reproductive Number

To find $\mathcal{R}_0$, we employ Van Den Driessche and James Watmough's technique. We sort out the compartments so that the first m compartments correspond to the infected compartments and the next $n - m$ to the uninfected compartments. We define $\mathbf{X}_s$ as

$$\mathbf{X}_s = \{x \geq 0 | x_i = 0, \quad i = 1, 2, \cdots, m\} \tag{2.9}$$

For the system

$$\dot{\mathbf{x}} = f(\mathbf{x}), \tag{2.10}$$

$$f(\mathbf{x}) = \mathcal{F}(\mathbf{x}) - \mathcal{V}(\mathbf{x}), \quad i = 1, 2, \cdots, n, \tag{2.11}$$

$$\mathcal{V}(\mathbf{x}) = \mathcal{V}^{-}(\mathbf{x}) - \mathcal{V}^{+}(\mathbf{x}), \tag{2.12}$$

where

$\mathcal{F}(\mathbf{x})$ - is the rate of appearance of the new infections in compartment i

$\mathcal{V}^-(\mathbf{x})$ - is the rate of transfer of individuals out of compartment i

$\mathcal{V}^+(\mathbf{x})$ - is the rate of transfer of individuals into compartment i

The above functions all represent transfer of individuals and therefore are non negative. Thus for $x_i \geq 0$, then $\mathcal{F} \geq 0$, $\mathcal{V}^- \geq 0$, $\mathcal{V}^+ \geq 0$ for $i = 1, 2, \cdots, n$. If a compartment is empty then there can be no transfer of individuals from that compartment either by death or by infection. Therefore if $x_i = 0$ then $\mathcal{V}^- = 0$. If a compartment is empty then there can not be any incidence of infection and therefore $\mathcal{F} = 0$ if $i > m$. If a population is free of infection then we assume it will remain so and that there will be no immigration of infectives i.e if $x \in \mathbf{X}_s$ then $\mathcal{F}(\mathbf{x}) = 0$ and $\mathcal{V}^+ = 0$ for $i = 1, 2, \cdots, m$. If $\mathcal{F} = 0$ then all eigenvalues of $Df(\mathbf{x}^*)$ have negative real parts.

The infected compartments are I_m, I_f, A_m and A_f, and giving $m = 4$.

The above conditions allow us to partition the matrix $Df(\mathbf{x}^*)$ as follows:

$$\mathcal{F}(\mathbf{x}) = \begin{pmatrix} c_m \lambda_f S_m(t) \\ c_f \lambda_m S_f(t) \\ 0 \\ 0 \end{pmatrix},$$

$$\mathcal{V}^-(\mathbf{x}) = \begin{pmatrix} (\mu + \sigma) I_m(t) \\ (\mu + \sigma) I_f(t) \\ (\mu + d) A_m(t) \\ (\mu + d) A_m(t) \end{pmatrix}$$

and

$$\mathcal{V}^+(\mathbf{x}) = \begin{pmatrix} 0 \\ 0 \\ \sigma I_m(t) \\ \sigma I_f(t) \end{pmatrix}$$

Therefore,

$$\mathcal{V}(\mathbf{x}) = \begin{pmatrix} (\mu+\sigma)I_m(t) \\ (\mu+\sigma)I_f(t) \\ -\sigma I_m(t) + (\mu+d)A_m(t) \\ -\sigma I_f(t) + (\mu+d)A_m(t) \end{pmatrix}$$

The associated non-negative matrix, F, at $\mathbf{x}^*$ for the new infective terms, and the non-singular M-matrix, V, for the remaining transfer terms, are respectively given by

$$F = \begin{pmatrix} 0 & \frac{\beta_{fm}c_m S_m^*(t)}{N_f^*(t)} & 0 & \frac{\beta_{fm}c_m\eta S_m^*(t)}{N_f^*(t)} \\ \frac{\beta_{mf}c_f S_f^*(t)}{N_m^*(t)} & 0 & \frac{\beta_{mf}c_f\eta S_f^*(t)}{N_m^*(t)} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

$$= \begin{pmatrix} 0 & \beta_{fm}c_m\frac{\rho}{1-\rho} & 0 & \beta_{fm}c_m\eta\frac{\rho}{1-\rho} \\ \beta_{mf}c_f\frac{1-\rho}{\rho} & 0 & \beta_{mf}c_f\eta\frac{1-\rho}{\rho} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \mu+\sigma & 0 & 0 & 0 \\ 0 & \mu+\sigma & 0 & 0 \\ -\sigma & 0 & \mu+d & 0 \\ 0 & -\sigma & 0 & \mu+d \end{pmatrix},$$

where, $F = \frac{\partial \mathcal{F}(\mathbf{x})}{\partial \mathbf{x}}$, $V = \frac{\partial \mathcal{V}(\mathbf{x})}{\partial \mathbf{x}}$, and $\mathbf{x} = (I_m, I_m, A_m, A_f)^T$.

V is non-singular, thus,

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

The next generation operator FV^{-1} is given by

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\beta_{fm}c_m(\mu+d+\eta\sigma)}{(\mu+d)(\mu+\sigma)}\frac{\rho}{1-\rho} & 0 & \frac{\beta_{fm}c_m\eta}{(\mu+d)}\frac{\rho}{1-\rho} \\ \frac{\beta_{mf}c_f(\mu+d+\eta\sigma)}{(\mu+d)(\mu+\sigma)}\frac{1-\rho}{\rho} & 0 & \frac{\beta_{mf}c_f\eta}{(\mu+d)}\frac{1-\rho}{\rho} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

The next generation operator, FV^{-1} has only one nonzero eigenvalue corresponding to the spectral radius $\rho(FV^{-1})$ of the operator FV^{-1}.

Thus the basic reproduction number $\mathcal{R}_0$ can be written as

$$\mathcal{R}_0 = \sqrt{\left(\frac{(\mu+d+\eta\sigma)c_f\beta_{mf}}{(\mu+d)(\mu+\sigma)}\right)\left(\frac{(\mu+d+\eta\sigma)c_m\beta_{fm}}{(\mu+d)(\mu+\sigma)}\right)} \tag{2.13}$$

The reproduction number can be represented as

$$\mathcal{R}_0 = \sqrt{\mathcal{R}_{0m}\mathcal{R}_{0f}}$$

where $\mathcal{R}_{0f}$ and $\mathcal{R}_{0m}$ are partial reproductive numbers give by

$$\mathcal{R}_{0f} = \frac{(\mu+d+\eta\sigma)c_f\beta_{mf}\rho}{(\mu+d)(\mu+\sigma)(1-\rho)}$$

which is the expected number of secondary female infections generated by a typically infected male individual over his infectious lifetime in a totally susceptible population.

$$\mathcal{R}_{0m} = \frac{(\mu+d+\eta\sigma)c_m\beta_{fm}(1-\rho)}{(\mu+d)(\mu+\sigma)\rho}$$

which is the expected number of secondary male infections generated by a typically infected female individual over her infectious lifetime in a totally susceptible population.

2.4.4 Discussion of $\mathcal{R}_0$

We now try to give a full explanation of the terms in (2.13),

1. $\frac{1}{\mu+\sigma}$ is the average time a male or female individual spend in compartment $I_m(t)$ or $I_f(t)$.

2. $\frac{\sigma}{\mu+\sigma}$ is the proportion of individuals who are infected that progress to the AIDS compartment from the infected compartment.

3. $\frac{1}{\mu+d}$ is the death adjusted infective period of individuals with AIDS.

4. $\frac{(\mu+d+\eta\sigma)c_f\beta_{mf}}{(\mu+d)(\mu+\sigma)}$ is the expected number of secondary female infections generated by a typical infected male individual over his infectious lifetime in a totally susceptible population.

5. $\frac{(\mu+d+\eta\sigma)c_m\beta_{fm}}{(\mu+d)(\mu+\sigma)}$ is the expected number of secondary male infections generated by a typically infected female individual over her infectious lifetime in a totally susceptible population.

So we observe that the model basic reproductive number is the geometric mean of the male and female reproductive numbers.

2.4.5 Local Stability of the Disease-free Equilibrium

Equilibria analysis in the absence of infection gives conditions under which a disease will establish itself or be eradicated in the population. Using theorem 2 in [8] the following result is established.

Theorem 2.1 *The model system* $(2.1) - (2.6)$ *has a disease-free equilibrium point* $\left(\frac{\rho\pi}{\mu}, \frac{(1-\rho)\pi}{\mu}, 0, 0, 0, 0\right)$. *If* $\mathcal{R}_0 < 1$ *the disease-free equilibrium point is locally asymptotically stable. If* $\mathcal{R}_0 > 1$ *the disease-free equilibrium point is unstable.*

Proof:

The above theorem can also be proved using the asymptotic dynamics of the disease-free equilibrium which are governed by the following Jacobian matrix for the system $(2.1)-(2.6)$ evaluated at the disease-free equilibrium point

$$\mathbf{J}_{\mathbf{x}^*} = \begin{pmatrix} -\mu & 0 & 0 & \beta_{fm}c_m\frac{\rho}{1-\rho} & 0 & \beta_{fm}c_m\eta\frac{\rho}{1-\rho} \\ 0 & -\mu & \beta_{mf}c_f\frac{1-\rho}{\rho} & 0 & \beta_{mf}c_f\frac{1-\rho}{\rho} & 0 \\ 0 & 0 & -(\mu+\sigma) & \beta_{fm}c_m\frac{\rho}{1-\rho} & 0 & \beta_{fm}c_m\eta\frac{\rho}{1-\rho} \\ 0 & 0 & \beta_{mf}c_f\frac{1-\rho}{\rho} & -(\mu+\sigma) & \beta_{mf}c_f\eta\frac{1-\rho}{\rho} & 0 \\ 0 & 0 & \sigma & 0 & -(\mu+d) & 0 \\ 0 & 0 & 0 & \sigma & 0 & -(\mu+d) \end{pmatrix},$$

If λ_i are the eigenvalues of $\mathbf{J}_{\mathbf{x}^*}$, then

$$(\lambda+\mu)^2 det\begin{pmatrix} -(\mu+\sigma) & \beta_{fm}c_m\frac{\rho}{1-\rho} & 0 & \beta_{fm}c_m\eta\frac{\rho}{1-\rho} \\ \beta_{mf}c_f\frac{1-\rho}{\rho} & -(\mu+\sigma) & \beta_{mf}c_f\eta\frac{1-\rho}{\rho} & 0 \\ \sigma & 0 & -(\mu+d) & 0 \\ 0 & \sigma & 0 & -(\mu+d) \end{pmatrix} = 0$$

Let

$$\mathbf{B} = \begin{pmatrix} -(\mu+\sigma) & \beta_{fm}c_m\frac{\rho}{1-\rho} & 0 & \beta_{fm}c_m\eta\frac{\rho}{1-\rho} \\ \beta_{mf}c_f\frac{1-\rho}{\rho} & -(\mu+\sigma) & \beta_{mf}c_f\eta\frac{1-\rho}{\rho} & 0 \\ \sigma & 0 & -(\mu+d) & 0 \\ 0 & \sigma & 0 & -(\mu+d) \end{pmatrix}.$$

Then, from the matrix $\mathbf{B}$ we have

$\det(\mathbf{B}) = \beta_{mf}\beta_{fm}c_mc_f(\mu+d+\eta\sigma)^2\frac{1-\mathcal{R}_0^2}{\mathcal{R}_0^2}$ and $\text{Trace}(\mathbf{B}) = -2(\mu+(\mu+\sigma)+(\mu+d))$.

Clearly, $\text{Trace}(\mathbf{B}) < 0$ since all parameters μ, σ and d are positive. $\beta_{mf}\beta_{fm}c_mc_f > 0$ since β_{mf}, β_{fm}, c_m, c_f are positive. The determinant of $\mathbf{B}$ to be > 0, we should have $\mathcal{R}_0 < 1$. By the Routh Hurwirtz criterion it follows that all the eigenvalues have negative real parts if $\mathcal{R}_0 < 1$ and the disease-free equilibrium is asymptotically stable.

If $\mathcal{R}_0$ is greater than 1 then at least one eigenvalue has a positive real part and the DFE

point will be unstable. An introduction of an infective will result in a persistent infection called the endemic infection.

The epidemiological implication of theorem 2.1 is that HIV can be eliminated when $\mathcal{R}_0 < 1$, i.e, if the initial sizes of the sub-populations of the model are in the basin of attraction of $\mathbf{x}^*$. We carry out numerical simulations to find the relationship between $\mathcal{R}_{0m}$, $\mathcal{R}_0$ and $\mathcal{R}_{0f}$ as we vary the number of sexual partners using parameter values in Table 4.1.

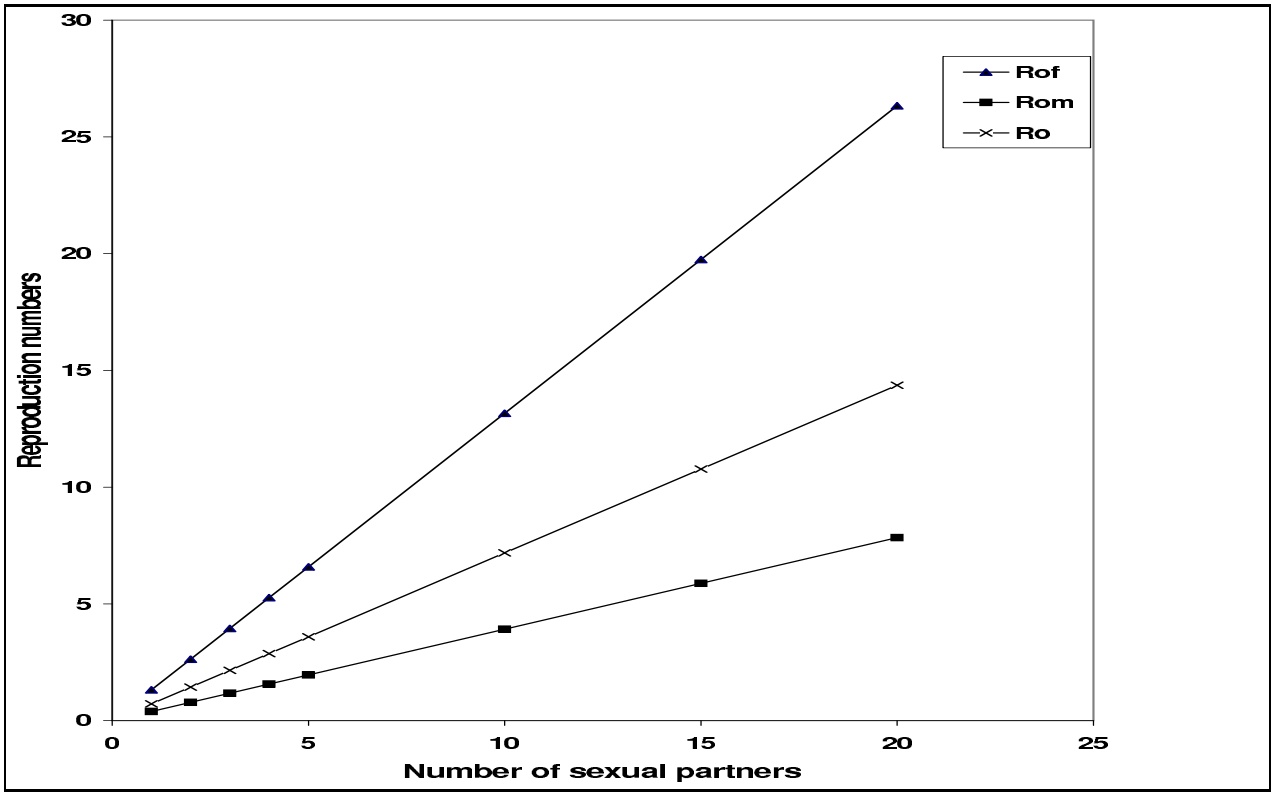

Figure 2.2: Graph of Reproduction numbers for varying sexual partners. R_{0m}, R_{0f} and R_0 represent the male reproductive number, female reproduction number and the model reproduction number respectively for model system (2.1) – (2.6).

Figure 2.2 presents the behaviour of the reproduction numbers as we vary the number of sexual partners of males and females. For the parameters in Table 4.1 the trend is showing that $\mathcal{R}_{0m} < \mathcal{R}_0 < \mathcal{R}_{0f}$, that is the expected number of secondary male infections generated by a typical infected female over her infectious lifetime is less than the average number of secondary cases infected by a typical infected individual and is also less than the expected number of female infections generated by a typical infected male over his infectious lifetime. This shows that for the same number of sexual partners, females are at much greater risk of

infection as compared to males. Thus there is a great need of female controlled protection mechanisms such as female condoms, vaginal microbicides etc.

2.4.6 Global Stability of the Disease-free Equilibrium

We present two conditions to be met to guarantee the global asymptotic stability of the disease free state following the method by Diekmann et al [24]. We write system $(2.1)-(2.6)$ as

$$\dot{\mathbf{X}} = F(\mathbf{X}, \mathbf{Z}), \tag{2.14}$$

$$\dot{\mathbf{Z}} = G(\mathbf{X}, \mathbf{Z}), \quad G(\mathbf{X}, 0) = 0 \tag{2.15}$$

where $\mathbf{X} = (S_m, S_f)$ and $\mathbf{Z} = (I_m, I_f, A_m, A_f)$ with $\mathbf{X} \in \mathbb{R}^2$ representing the number of uninfected individuals and $\mathbf{Z} \in \mathbb{R}^4$ representing the number of infected individuals. The disease free equilibrium can now be written as

$$U_0 = (\mathbf{X}^*, 0) = \left(\frac{\rho\pi}{\mu}, \frac{(1-\rho)\pi}{\mu}, 0, 0, 0, 0\right).$$

The conditions $(H1)$ and $(H2)$ below must be met to guarantee global asymptotic stability.

$$\begin{aligned} (H1) \quad & \text{For } \frac{d\mathbf{X}}{dt} = F(\mathbf{X}, \mathbf{0}), \quad \mathbf{X}^* \quad \text{is locally asymptotically stable,} \\ (H2) \quad & G(\mathbf{X}, \mathbf{Z}) = A\mathbf{Z} - \hat{G}(\mathbf{X}, \mathbf{Z}), \quad \hat{G}(\mathbf{X}, \mathbf{Z}) \geq 0 \quad \text{for} \quad (\mathbf{X}, \mathbf{Z}) \in \Omega \end{aligned}$$

where $A = D_{\mathbf{Z}} G(\mathbf{X}^*, \mathbf{0})$ is an M-matrix (the off diagonal elements of A are non-negative) and Ω is the region where the model makes biological sense. In this case

$$F(\mathbf{X}, 0) = \begin{bmatrix} \rho\pi - \mu S_m \\ (1-\rho)\pi - \mu S_f \end{bmatrix},$$

$$A = \begin{bmatrix} -(\mu+\sigma) & \beta_{fm} c_m \frac{\rho}{1-\rho} & 0 & \beta_{fm} c_m \eta \frac{\rho}{1-\rho} \\ \beta_{mf} c_f \frac{1-\rho}{\rho} & -(\mu+\sigma) & \beta_{mf} c_f \eta \frac{1-\rho}{\rho} & 0 \\ \sigma & 0 & -(\mu+d) & 0 \\ 0 & \sigma & 0 & -(\mu+d) \end{bmatrix}$$

and

$$\hat{G}(\mathbf{X},\mathbf{Z}) = \begin{bmatrix} \hat{G}_1(\mathbf{X},\mathbf{Z}) \\ \hat{G}_2(\mathbf{X},\mathbf{Z}) \\ \hat{G}_3(\mathbf{X},\mathbf{Z}) \\ \hat{G}_4(\mathbf{X},\mathbf{Z}) \end{bmatrix} = \begin{bmatrix} c_m\beta_{fm}(I_f + \eta A_f)(1 - \frac{S_m}{N_f}) \\ c_f\beta_{mf}(I_m + \eta A_m)(1 - \frac{S_f}{N_m}) \\ 0 \\ 0 \end{bmatrix}$$

Since $0 \leq S_m \leq N_f$ and $0 \leq S_f \leq N_m$, it is clear that $\hat{G}(\mathbf{X},\mathbf{Z}) \geq 0$ for all $(\mathbf{X},\mathbf{Z}) \in \Omega$. We also note that matrix A is an M-matrix since its off diagonal elements are non-negative. Theorem 2.2 summarises the result.

Theorem 2.2 *The disease free equilibrium point* $U_0 = (\mathbf{X}^*, 0) = \left(\frac{\rho\pi}{\mu}, \frac{(1-\rho)\pi}{\mu}, 0, 0, 0, 0\right)$ *is globally asymptotically stable equilibrium point of the system* $(2.1) - (2.6)$ *provided* $\mathcal{R}_0 < 1$ *and assumptions in* $(2.16) - (2.17)$ *are satisfied.*

2.4.7 Endemic Equilibrium Point

The second equilibrium state is the endemic equilibrium point given by $\mathbf{x}_e$. This is the state when the disease persists. To conduct the analytic analysis of the local stability of the endemic equilibrium point we assume that the sub-population sizes $N_m(t)$ and $N_f(t)$ have reached their limiting values.
i.e $N_m(t) \equiv \frac{\rho\pi}{\mu}$, and $N_f(t) \equiv \frac{(1-\rho)\pi}{\mu}$
Substitute,

$$S_m(t) = N_m(t) - I_m(t) - A_m(t)$$

and

$$S_f(t) = N_f(t) - I_f(t) - A_f(t)$$

into (2.1) – (2.6) we get,

$$\begin{aligned}
\frac{dI_m}{dt} &= c_m\lambda_f(N_m(t) - I_m(t) - A_m(t)) - (\mu+\sigma)I_m(t) && (2.16)\\
\frac{dI_f}{dt} &= c_f\lambda_m(N_f(t) - I_f(t) - A_f(t)) - (\mu+\sigma)I_f(t) && (2.17)\\
\frac{dA_m}{dt} &= \sigma I_m(t) - (\mu+d)A_m(t) && (2.18)\\
\frac{dA_f}{dt} &= \sigma I_f(t) - (\mu+d)A_f(t) && (2.19)\\
\frac{dN_m}{dt} &= \rho\pi - \mu N_m(t) - dA_m(t) && (2.20)\\
\frac{dN_f}{dt} &= (1-\rho)\pi - \mu N_f(t) - dA_f(t) && (2.21)
\end{aligned}$$

If we set $i_m = \frac{I_m}{N_m}$, $i_f = \frac{I_f}{N_f}$, $a_m = \frac{A_m}{N_m}$, $a_f = \frac{A_f}{N_f}$ and decoupling equations in model system (2.16) – (2.21), then our model system with dimensionless variables becomes

$$\begin{aligned}
i'_m &= c_m\lambda^*_f(1 - i_m - a_m) - (\mu+\sigma)i_m, && (2.22)\\
i'_f &= c_f\lambda^*_m(1 - i_f - a_f) - (\mu+\sigma)i_f, && (2.23)\\
a'_m &= \sigma i_m - (\mu+d)a_m, && (2.24)\\
a'_f &= \sigma i_f - (\mu+d)a_f, && (2.25)
\end{aligned}$$

where $\lambda^*_f = \beta_{fm}(i_f + \eta a_f)$ and $\lambda^*_m = \beta_{mf}(i_m + \eta a_m)$, $0 \le i_m + a_m \le 1$ and $0 \le i_f + a_f \le 1$.

Stationary solutions satisfy

$$\begin{aligned}
c_m\lambda^*_f(1 - i_m - a_m) - (\mu+\sigma)i_m &= 0 && (2.26)\\
c_f\lambda^*_m(1 - i_f - a_f) - (\mu+\sigma)i_f &= 0 && (2.27)\\
\sigma i_m - (\mu+d)a_m &= 0 && (2.28)\\
\sigma i_f - (\mu+d)a_f &= 0 && (2.29)
\end{aligned}$$

To find the endemic equilibrium point $\mathbf{x}_e$, we introduce the following notation,

$$\mathcal{R}_{0f} = \frac{\beta_{mf}c_f(\mu+d+\eta\sigma)}{(\mu+d)(\mu+\sigma)}, \qquad \mathcal{R}_{0m} = \frac{\beta_{fm}c_m(\mu+d+\eta\sigma)}{(\mu+d)(\mu+\sigma)} \qquad \text{and} \qquad \theta = \frac{\sigma}{\mu+d}.$$

Equations (2.28) and (2.29) gives

$$a_m = \theta i_m \tag{2.30}$$

$$a_f = \theta i_f \tag{2.31}$$

From equations (2.26) and (2.27) using (2.30) and (2.31) we have

$$i_m^e = \frac{\mathcal{R}_0^2 - 1}{(1+\theta)(\mathcal{R}_0^2 + \mathcal{R}_{0f})}$$

$$i_f^e = \frac{\mathcal{R}_0^2 - 1}{(1+\theta)(\mathcal{R}_0^2 + \mathcal{R}_{0m})}$$

From (2.30) and (2.31) we have

$$a_m^e = \frac{\mathcal{R}_0^2 - 1}{(1+\theta)(\mathcal{R}_0^2 + \mathcal{R}_{0f})}$$

$$a_f^e = \frac{\mathcal{R}_0^2 - 1}{(1+\theta)(\mathcal{R}_0^2 + \mathcal{R}_{0m})}$$

The values of S_m^e, I_m^e, A_m^e, S_f^e, I_f^e and A_f^e are given by
$S_m^e = (1 - i_m^e - a_m^e)N_m$, $I_m^e = i_m^e N_m$, $A_m^e = a_m^e N_m$, $S_f^e = (1 - i_f^e - a_f^e)N_f$, $I_f^e = i_f^e N_f$, $A_f^e = a_f^e N_f$.
The endemic equilibria exists when $I_m^e, I_f^e, A_m^e, A_f^e > 0$, for $\mathcal{R}_0^2 > 1$, and thus $\mathcal{R}_0 > 1$.
Thus the endemic equilibria exists when $\mathcal{R}_0 > 1$ and we summarise the results in lemma 2.1.

Lemma 2.1 *The endemic equilibria exists when* $\mathcal{R}_0 > 1$.

2.4.8 Local Stability Analysis of the Endemic Equilibrium

The standard technique of determining the local stability of the endemic equilibrium is by finding the Jacobian matrix evaluated at the endemic equilibrium from which one can infer the stability of the equilibrium point.

Theorem 2.3 *If $R_0 > 1$, then the endemic equilibrium point is locally asymptotically stable..*

Proof: To establish the stability of $\mathbf{x}_e$, we use the fact that at the endemic equilibrium point,

$a_m = \theta i_m \qquad$ and $\qquad a_f = \theta i_f$.

System $(2.26) - (2.29)$ reduces to

$$i'_m = \beta_{fm} c_m (1+\eta\theta)(1-(1+\theta)i_m)i_f - (\mu+\sigma)i_m \tag{2.32}$$

$$i'_f = \beta_{mf} c_f (1+\eta\theta)(1-(1+\theta)i_f)i_m - (\mu+\sigma)i_f \tag{2.33}$$

Linearizing the system $(2.32) - (2.33)$ at $\mathbf{x}_e$ gives

$$\mathbf{J_{x_e}} = \begin{pmatrix} -(\mu+\sigma)\left(\frac{\mathcal{R}_0^2+\mathcal{R}_{0f}}{\mathcal{R}_{0f}+1}\right) & (\mu+\sigma)\left(\frac{\mathcal{R}_0^2+\mathcal{R}_{0m}}{\mathcal{R}_0^2+\mathcal{R}_{0f}}\right) \\ (\mu+\sigma)\left(\frac{\mathcal{R}_0^2+\mathcal{R}_{0f}}{\mathcal{R}_0^2+\mathcal{R}_{0m}}\right) & -(\mu+\sigma)\left(\frac{\mathcal{R}_0^2+\mathcal{R}_{0m}}{\mathcal{R}_{0m}+1}\right) \end{pmatrix}$$

with $\text{Trace}(\mathbf{J_{x_e}})$ and $\text{Det}(\mathbf{J_{x_e}})$ given by

$$\text{Trace}(\mathbf{J_{x_e}}) = -(\mu+\sigma)\left(\frac{\mathcal{R}_0^2+\mathcal{R}_{0f}}{\mathcal{R}_{0f}+1} + \frac{\mathcal{R}_0^2+\mathcal{R}_{0m}}{\mathcal{R}_{0m}+1}\right) < 0$$

and

$$\det(\mathbf{J_{x_e}}) = (\mu+\sigma)^2(\mathcal{R}_0^2-1) > 0 \qquad \text{for} \quad \mathcal{R}_0 > 1.$$

Thus the matrix $\mathbf{J_{x_e}}$ has negative eigenvalues when $R_0^2 - 1 > 0$, which implies $R_0 > 1$ and thus the endemic equilibrium point is locally asymptotically stable when $R_0 > 1$.

2.4.9 Conclusion

In this chapter we looked at a basic HIV/AIDS heterosexual model without intervention. We showed that the solutions to our model $(2.1) - (2.6)$ exist and are positively invariant in Ω and are unique thus are mathematically and epidemiologically well-posed. Equilibrium points and their stability were analysed. It was found that the disease-free equilibrium point is asymptotically stable if $\mathcal{R}_0 < 1$ and when $\mathcal{R}_0 > 1$ the disease persists.

Chapter 3

Effects of Preventative Measures on HIV Prevalence

3.1 Condom Use in Heterosexual Setting

We extend the model system $(2.1) - (2.6)$ by incorporating the use of condoms as a preventative strategy for heterosexual transmission of HIV in a sexually-active population.

3.2 Model Formulation

Suppose that condoms have an efficacy ϵ_1 and compliance α_1 with $0 \leq \epsilon_1, \alpha_1 \leq 1$, so that the product $p_1 = \epsilon_1\alpha_1$ measures the level of protection against HIV by the use of condoms. p_1 is defined as the condom induced preventability of HIV transmission per year [10]. This implies that the HIV transmission rate will decrease by p_1, or equivalently, the transmission rates in both directions (from males to females and from females to males) will be reduced so that $\beta_j^{new} = (1 - p_1)\beta_j^{old}$, where $j = mf$ or fm. $(1 - p_1)$, measures the condom induced preventability failure. Thus, per exposure risk of infection for male and female individuals

changes to

$\lambda_m = \frac{\beta_{mf}(1-p_1)(I_m(t)+\eta A_m(t))}{N_m(t)}$ and $\lambda_f = \frac{\beta_{fm}(1-p_1)(I_f(t)+\eta A_f(t))}{N_f(t)}$.

Thus, the nonlinear system of differential equations that describes the rate of change in population sizes of various classes is:

$$\begin{aligned}
\frac{dS_m}{dt} &= \rho\pi - \frac{\beta_{fm}c_m(1-p_1)(I_f(t)+\eta A_f(t))}{N_f(t)}S_m(t) - \mu S_m(t) && (3.1)\\
\frac{dI_m}{dt} &= \frac{\beta_{fm}c_m(1-p_1)(I_f(t)+\eta A_f(t))}{N_f(t)}S_m(t) - (\mu+\sigma)I_m(t) && (3.2)\\
\frac{dA_m}{dt} &= \sigma I_m(t) - (\mu+d)A_m(t) && (3.3)\\
\frac{dS_f}{dt} &= (1-\rho)\pi - \frac{\beta_{mf}c_f(1-p_1)(I_m(t)+\eta A_m(t))}{N_m(t)}S_f(t) - \mu S_f(t) && (3.4)\\
\frac{dI_f}{dt} &= \frac{\beta_{mf}c_f(1-p_1)(I_m(t)+\eta A_m(t))}{N_m(t)}S_f(t) - (\mu+\sigma)I_f(t) && (3.5)\\
\frac{dA_f}{dt} &= \sigma I_f(t) - (\mu+d)A_f(t) && (3.6)
\end{aligned}$$

3.3 Positivity and Boundedness of Solutions

Similarly to section 2.3 we consider solutions of $(3.1)-(3.6)$ in the following positively invariant subset of $\mathbb{R}^6_+$:

$$\begin{aligned}
\Omega = \Big\{ &(S_m(t), S_f(t), I_m(t), I_f(t), A_m(t), A_f(t)) \in \mathbb{R}^6_+ | S_m(t), S_f(t), I_m(t), I_f(t),\\
&A_m(t), A_f(t) \geq 0; N(t) \leq \frac{\pi}{\mu} \Big\}
\end{aligned}$$

Again, we assume without loss of generality that in the absence of the disease the population size has reached its limiting value of $\frac{\pi}{\mu}$.

3.4 Model Analysis

The system is characterised by two equilibrium points, the disease-free equilibrium and the endemic equilibrium point.

3.4.1 Disease-free Equilibrium and Endemic Equilibrium Points

The disease-free equilibrium point $\mathbf{x}^*$, is similar to the one is section 2.4.1, and is given by

$$\mathbf{x}^* = (S_m^*, S_f^*, I_m^*, I_f^*, A_m^*, A_f^*) = \left(\frac{\rho\pi}{\mu}, \frac{(1-\rho)\pi}{\mu}, 0, 0, 0, 0\right)$$

The endemic equilibrium point is given by $E^e = (i_m^e, i_f^e, a_m^e, a_f^e)$,
where

$$i_m^e = \frac{(1-p_1)^2\mathcal{R}_0^2 - 1}{(1+\theta)(1-p_1)\big((1-p_1)\mathcal{R}_0^2 + \mathcal{R}_{0f}\big)}$$

$$i_f^e = \frac{(1-p_1)^2\mathcal{R}_0^2 - 1}{(1+\theta)(1-p_1)\big((1-p_1)\mathcal{R}_0^2 + \mathcal{R}_{0m}\big)}$$

$$a_m^e = \frac{\theta(1-p_1)^2\mathcal{R}_0^2 - 1}{(1+\theta)(1-p_1)\big((1-p_1)\mathcal{R}_0^2 + \mathcal{R}_{0f}\big)}$$

$$a_f^e = \frac{\theta(1-p_1)^2\mathcal{R}_0^2 - 1}{(1+\theta)(1-p_1)\big((1-p_1)\mathcal{R}_0^2 + \mathcal{R}_{0m}\big)}$$

The values of S_m^e, I_m^e, A_m^e, S_f^e, I_f^e and A_f^e are given by
$S_m^e = (1 - i_m^e - a_m^e)N_m$, $I_m^e = i_m^e N_m$, $A_m = a_m^e N_m$, $S_f^e = (1 - i_f^e - a_f^e)N_f$, $I_f^e = i_f^e N_f$, $A_f = a_f^e N_f$.

3.4.2 Computation of the Condom-induced Reproductive Number ($\mathcal{R}_c$)

Re-arrange the compartments with the first m compartments corresponding to the infected individuals.

$$\frac{dI_m}{dt} = \frac{\beta_{fm}c_m(1-p_1)(I_f(t)+\eta A_f(t))}{N_f(t)}S_m(t) - (\mu+\sigma)I_m(t) \tag{3.7}$$

$$\frac{dI_f}{dt} = \frac{\beta_{mf}c_f(1-p_1)(I_m(t)+\eta A_m(t))}{N_m(t)}S_f(t) - (\mu+\sigma)I_f(t) \tag{3.8}$$

$$\frac{dA_m}{dt} = \sigma I_m(t) - (\mu+d)A_m(t) \tag{3.9}$$

$$\frac{dA_f}{dt} = \sigma I_f(t) - (\mu+d)A_f(t) \tag{3.10}$$

$$\frac{dS_m}{dt} = \rho\pi - \frac{\beta_{fm}c_m(1-p_1)(I_f(t)+\eta A_f(t))}{N_f(t)}S_m(t) - \mu S_m(t) \tag{3.11}$$

$$\frac{dS_f}{dt} = (1-\rho)\pi - \frac{\beta_{mf}c_f(1-p_1)(I_m(t)+\eta A_m(t))}{N_m(t)}S_f(t) - \mu S_f(t) \tag{3.12}$$

The infected compartments are I_m, I_f, A_m and A_f, and giving $m = 4$. Writing the model system $(3.7) - (3.12)$ in the form:

$$\dot{\mathbf{x}} = \mathcal{F}(\mathbf{x}) - \mathcal{V}(\mathbf{x}), \tag{3.13}$$

where,

$$\mathcal{F}(\mathbf{x}) = \begin{pmatrix} c_m(1-p_1)\lambda_f S_m(t) \\ c_f(1-p_1)\lambda_m S_f(t) \\ 0 \\ 0 \end{pmatrix},$$

and

$$\mathcal{V}_i(\mathbf{x}) = \begin{pmatrix} (\mu+\sigma)I_m(t) \\ (\mu+\sigma)I_f(t) \\ -\sigma I_m(t) + (\mu+d)A_m(t) \\ -\sigma I_f(t) + (\mu+d)A_m(t) \end{pmatrix}$$

The associated non-negative matrix F, for the new infective terms, and the non-singular

M-matrix V, for the remaining transfer terms, are respectively given by

$$F = \begin{pmatrix} 0 & \frac{\beta_{fm}c_m(1-p_1)\rho}{(1-\rho)} & 0 & \frac{\beta_{fm}c_m(1-p_1)\eta\rho}{(1-\rho)} \\ \frac{\beta_{mf}c_f(1-p_1)(1-\rho)}{\rho} & 0 & \frac{\beta_{mf}c_f(1-p_1)\eta(1-\rho)}{\rho} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$V = \begin{pmatrix} \mu+\sigma & 0 & 0 & 0 \\ 0 & \mu+\sigma & 0 & 0 \\ -\sigma & 0 & \mu+d & 0 \\ 0 & -\sigma & 0 & \mu+d \end{pmatrix},$$

The next generation operator FV^{-1} is given by

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\beta_{fm}c_m k_1(\mu+d+\eta\sigma)\rho}{(\mu+d)(\mu+\sigma)(1-\rho)} & 0 & \frac{\beta_{fm}c_m k_1\eta\rho}{(\mu+d)(1-\rho)} \\ \frac{\beta_{mf}c_f k_1(\mu+d+\eta\sigma)(1-\rho)}{(\mu+d)(\mu+\sigma)\rho} & 0 & \frac{\beta_{mf}c_f k_1\eta(1-\rho)}{(\mu+d)\rho} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

where $k_1 = 1 - p_1$. The next generation operator, FV^{-1} has only one nonzero eigenvalue corresponding to the spectral radius $\rho(FV^{-1})$ of the operator FV^{-1}. Thus, the condom-induced reproductive ratio $\mathcal{R}_c$ can be written as

$$\begin{aligned} \mathcal{R}_c = \mathcal{R}(p_1) &= (1-p_1)\sqrt{\left(\frac{(\mu+d+\eta\sigma)c_f\beta_{mf}}{(\mu+d)(\mu+\sigma)}\right)\left(\frac{(\mu+d+\eta\sigma)c_m\beta_{fm}}{(\mu+d)(\mu+\sigma)}\right)} \\ &= (1-p_1)\mathcal{R}_0 \\ &= (1-\epsilon_1\alpha_1)\mathcal{R}_0. \end{aligned}$$

We also have the following result for model system (3.1) – (3.6)

Theorem 3.1 *Consider the system* (3.1) – (3.6)*,*

(i) the disease free equilibrium point $\mathbf{x}^*$ *is locally asymptotically stable if* $\mathcal{R}_c < 1$ *and unstable if* $\mathcal{R}_c > 1$*.*

(ii) the endemic equilibrium point is locally asymptotically stable if $\mathcal{R}_c > 1$.

3.4.3 Discussion on $\mathcal{R}_c$

We write $\mathcal{R}_c = \mathcal{R}(p_1 = \alpha_1\epsilon_1)$ to emphasize the role of condom use as a preventative strategy for heterosexual transmission of HIV. If there is no condom use, i.e $\alpha_1 = 0$, then $\mathcal{R}(0) = \mathcal{R}_0$. Thus,

$$\begin{cases} \mathcal{R}_c < \mathcal{R}_0 & \text{if } \alpha_1 > 0 \\ \mathcal{R}_c = \mathcal{R}_0 & \text{if } \alpha_1 = 0 \end{cases}$$

This suggests that consistent and correct use of condoms as a single prevention strategy can help reduce the spread of HIV.

Setting the condom-induced basic reproductive number to one i.e $\mathcal{R}_c = 1$ and solving for p_1 gives the threshold preventability value for HIV/AIDS in the population

$$p_1^c = 1 - \frac{1}{\mathcal{R}_0}. \tag{3.14}$$

This suggests that HIV/AIDS can be controlled in a population with condom use if the condom-induced preventability $p_1 = \alpha_1\epsilon_1 > p_1^c - \epsilon_1^c\alpha_1^c$. But, as obtained by Moghadas et al. [10], that p_1^c increases with increasing average number of HIV/AIDS-infected partners of susceptible individuals and for such populations where the average number of HIV-infected partners is large, the associated preventability threshold is high and perhaps unattainable, suggesting that for such populations, HIV may not be controlled using condoms alone.

3.5 Condoms and Vaginal Microbicides Use

Again let us extend the model system $(3.1) - (3.6)$ to inclide vaginal microbicide. Assume that the microbicides have efficacy ϵ_2 and compliance α_2, with $0 \leq \epsilon_2, \alpha_2 \leq 1$, so that the product $p_2 = \epsilon_2\alpha_2$ measures the level of protection against HIV by the use of microbicides. p_2 is defined as the microbicides-induced preventability of HIV transmission per year. Thus, $(1 - p_2)$ measures the microbicides-induced preventability failure which we will assume the

same for transmission in both directions. The parameter $(1-p_1)(1-p_2)$ models the condom and microbicides use. The per exposure risk of infection becomes $\beta_j = \beta_j(1-p_1)(1-p_2)$, where $j = mf$ or fm. Thus, the model system $(3.1) - (3.6)$ becomes

$$\begin{aligned}
\frac{dS_m}{dt} &= \rho\pi - c_m(1-p_1)(1-p_2)\lambda_f S_m(t) - \mu S_m(t) && (3.15)\\
\frac{dI_m}{dt} &= \beta_{fm}c_m(1-p_1)(1-p_2)\lambda_f S_m(t) - (\mu+\sigma)I_m(t) && (3.16)\\
\frac{dA_m}{dt} &= \sigma I_m(t) - (\mu+d)A_m(t) && (3.17)\\
\frac{dS_f}{dt} &= (1-\rho)\pi - \beta_{mf}c_f(1-p_1)(1-p_2)\lambda_m S_f(t) - \mu S_f(t) && (3.18)\\
\frac{dI_f}{dt} &= \beta_{mf}c_f(1-p_1)(1-p_2)\lambda_m S_f(t) - (\mu+\sigma)I_f(t) && (3.19)\\
\frac{dA_f}{dt} &= \sigma I_f(t) - (\mu+d)A_f(t) && (3.20)
\end{aligned}$$

The mathematical properties of the above model system are similar to the mathematical properties of model system $(3.1) - (3.6)$, thus we do not include some of the mathematical analysis for model system above to avoid repetition. The model system above has an infection free equilibrium point given by

$$\mathbf{x}^* = (S_m^*, S_f^*, I_m^*, I_f^*, A_m^*, A_f^*) = \left(\frac{\rho\pi}{\mu}, \frac{(1-\rho)\pi}{\mu}, 0, 0, 0, 0\right) \tag{3.21}$$

3.5.1 Condom-Microbicide Induced Reproductive Number ($\mathcal{R}_{cm}$)

The condom-microbicide induced reproductive number is given by

$$\begin{aligned}
\mathcal{R}_{cm} &= \mathcal{R}(p_1, p_2)\\
&= (1-p_1)(1-p_2)\sqrt{\left(\frac{(\mu+d+\eta\sigma)c_f\beta_{mf}}{(\mu+d)(\mu+\sigma)}\right)\left(\frac{(\mu+d+\eta\sigma)c_m\beta_{fm}}{(\mu+d)(\mu+\sigma)}\right)}\\
&= (1-p_1)(1-p_2)\mathcal{R}_0
\end{aligned}$$

which defines the number of secondary infections in the presence of condoms ($p_1 = \alpha_1\epsilon_1$) and vaginal microbicides ($p_2 = \alpha_2\epsilon_2$).

3.5.2 Discussion on $\mathcal{R}_{cm}$

We write $\mathcal{R}_{cm} = \mathcal{R}(p_1, p_2)$ to emphasize the role of condom use (p_1) and microbicides use (p_2) as control strategies for heterosexual transmission of HIV. When there is no condom use, $\alpha_1 = 0$, we have for this case,

$$\mathcal{R}_{cm} = \mathcal{R}(0, p_2) = \mathcal{R}_m = \mathcal{R}(p_2) = (1 - p_2)\mathcal{R}_0,$$

where $\mathcal{R}_m$ is the microbicides-induced basic reproductive number and $\mathcal{R}_0$ is the basic reproductive number when there are no HIV intervention strategies in a community.
From previous studies condom efficacy is greater than the microbicides efficacy and microbicides usage depends heavily on the present levels of condom usage, it is likely that $\mathcal{R}_c < \mathcal{R}_m$. Thus, if there is no microbicides use i.e $\alpha_2 = 0$, $\mathcal{R}(p_1, 0) = \mathcal{R}(p_1)$ and if there is no condom or microbicides use, i.e $\alpha_1 = 0$ and $\alpha_2 = 0$, $\mathcal{R}(0, 0) = \mathcal{R}_0$. This with the above argument suggest that $\mathcal{R}_{cm} < \mathcal{R}_m < \mathcal{R}_c < \mathcal{R}_0$ for all $0 < p_1, p_2 < 1$. This suggests that consistent and correct use of both condoms and vaginal microbicides would help in eradicating HIV.
Thus we conclude the chapter with the following theorem.

Theorem 3.2 *For the system* (3.15) − (3.20)

(i) The disease free equilibrium point $\mathbf{x}^*$ *is locally asymptotically stable if* $\mathcal{R}_{cm} < 1$ *and unstable if* $\mathcal{R}_{cm} > 1$.

(ii) The endemic equilibrium point is locally asymptotically stable if $\mathcal{R}_{cm} > 1$.

3.5.3 Conclusion

In this chapter we looked at the effects of condoms and vaginal microbicides on the transmission of HIV/AIDS. We saw that $R_0 < (1 - p_1)R_0$ for all $0 < p_1 < 1$ implying condoms have a great impact at reducing the spread of HIV. Again we shall see that since condom

efficacy is already known and is estimated at 87% the consistence and correct use are the major contributing factors in reducing the spread of HIV. Again we see that the inclussion of microbicides further reduce the spread of HIV provided they are high effective and used correctly and consistently.

Chapter 4

Numerical Simulations

4.1 Introduction

We are supposed to make sure that the analysis and observation make sense. Therefore, we are going to explore the numerical solutions of the equations $(2.1) - (2.6)$, $(3.1) - (3.6)$ and $(3.15) - (3.20)$ in order to investigate the effects of condoms and vaginal microbicides on the transmission of HIV/AIDS. This is going to be enabled through the use of fourth order Runge-Kutta coded in Matlab code. We also intend to simulate different model reproductive numbers against number of sexual partners, condom-induced reproductive number against condom compliance and lastly condom microbicide induced reproductive number against compliance. The parameter values used are in table 4.1. Some of these parameter estimates are obtained from published data.

4.2 Numerical Solutions

Using initial population of sexually-active people (between the ages of (15 - 49) of 25 million [9], so that $N(0) = 25$ million, with the following initial conditions $S_m(0) = 1000000$, $S_f(0) = 12000000$, $I_m(0) = 50000$, $I_f(0) = 50000$, $A_m(0) = 50$, $A_f(0) = 50$ we get the graph below.

Description	Symbol	Values	Source
Natural death rate	μ	0.02	[CSZ]
AIDS induced death rate	d	0.09 - 0.102	[CSZ]
Male transmission probability	β_{mf}	$0.011 - 095$	[14]
Female transmission probability	β_{fm}	$0.011 - 095$	[14]
Rate of progression to AIDS	σ	0.2	[4]
Modification parameter	η	1.2	Estimate
Rate of partner formation by male	c_m	$1 - 20$	Estimate
Rate of partner formation by females	c_f	$1 - 20$	Estimate
Condom efficacy	ϵ_1	0.87	[2]
Condom compliance	α_1	0.3	Estimate
Microbicides efficacy	ϵ_2	0.3	Estimate
Microbicides compliance	α_2	0.3	Estimate

Table 4.1: Parameter values for the HIV/AIDS model

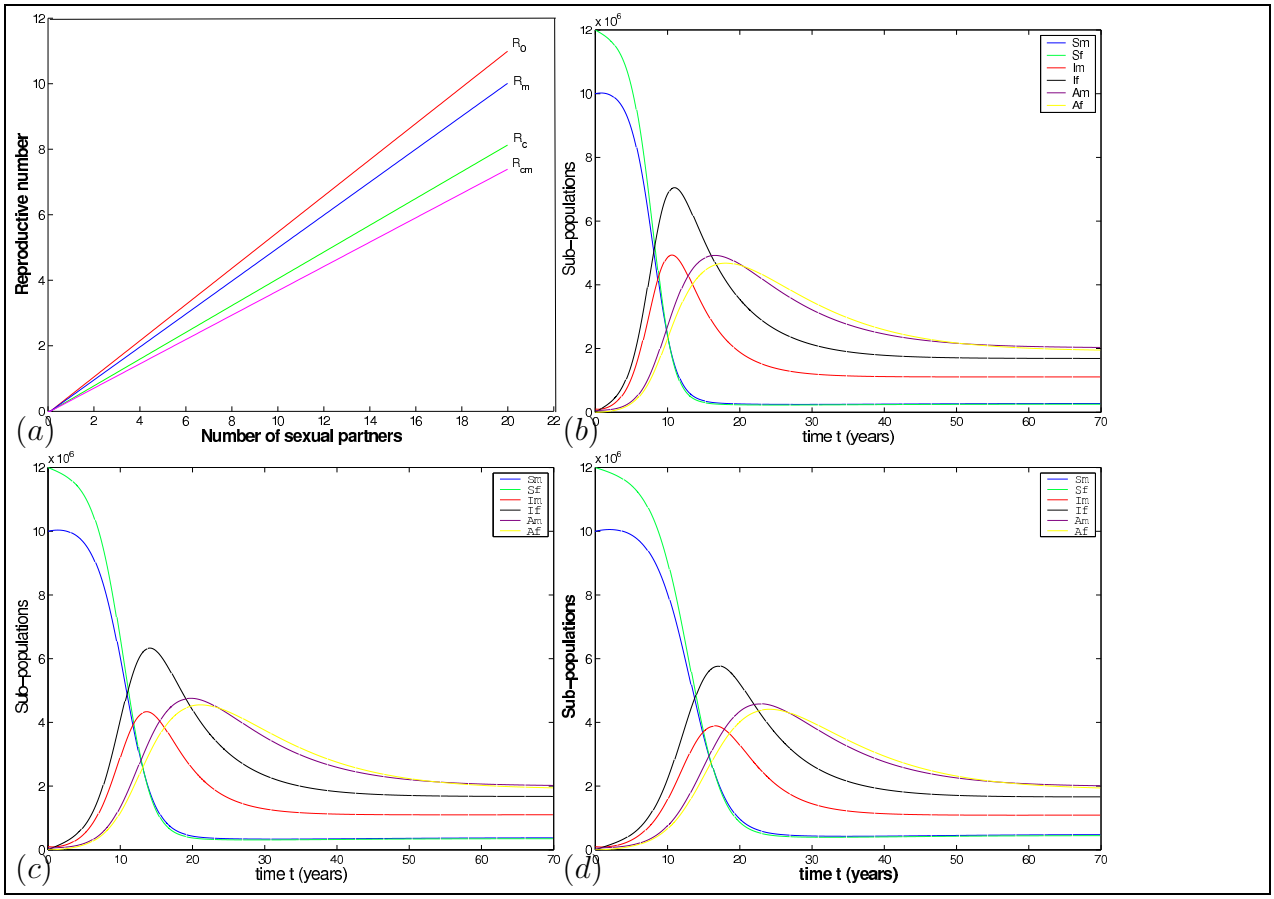

Figure 4.1: Simulation results showing (a) Trend $\mathcal{R}_0$, $\mathcal{R}_c$, $\mathcal{R}_m$, $\mathcal{R}_{cm}$ of the basic reproductive numbers for varying number of sexual partners per unit time. Sexual partners $c_m = c_f$ are varied from 0 to 20 per unit time and other model parameters are in table 4.1, (b) Profiles for subpopulations S_m, S_f, I_m, I_f A_m and A_f for model without prevention with $c_m = c_f = 2$, (c) Profiles for subpopulations S_m, S_f, I_m, I_f A_m and A_f for model with condom use with $c_m = c_f = 2$, (e) Profiles for subpopulations S_m, S_f, I_m, I_f A_m and A_f for model with condom and vaginal microbicide with $c_m = c_f = 2$.

Figure 4.1(a) illustrates the relationship and behaviour of $\mathcal{R}_0$, $\mathcal{R}_c$, $\mathcal{R}_m$ and $\mathcal{R}_{cm}$ for increasing number of sexual partners per unit time, using parameter values in Table 4.1. The illustration confirms the analytic result that a combination of condom use and microbicides use will effectively help reduce the spread of HIV/AIDS. Figure 4.1(a) shows that $\mathcal{R}_{cm} < \mathcal{R}_c < \mathcal{R}_m < \mathcal{R}_0$ for the given parameter values. It should be noted that the relationship between $\mathcal{R}_m$ and $\mathcal{R}_c$ depends on condom compliance and microbicides efficacy. From figure 4.1(a), $\mathcal{R}_c < \mathcal{R}_m$ implying that directly replacing condom use with microbicide use will have high negative impact as this will even worsen the situation. From the simulation data on the reproduction numbers we see that the level of microbicide efficacy and usage necessary to counterbalance a possible reduction in condom use is

88% usage for a 30% efficacy product and 52% for a 50% efficacy product. So in a nut shell, if low or moderate efficacy microbicides product become available then it will be critical to ensure that individuals who are currently using condoms fairly frequently do not choose to replace condoms with microbicides. Figure 4.1(b) shows the trend of susceptible, infected and AIDS male and female for the model without any intervention strategy. Both graphs of the susceptible males and females are falling sharply and levelling off after 15 years. The infected and AIDS population for both groups are increasing and reaching their maximum after 12 years and 18 years respectively, and begin to decrease to some limiting values. Thus the system settles at an endemic steady state $(S_m^*, S_f^*, I_m^*, I_f^*, A_m^*, A_f^*) = (250000, 250000, 1000000, 2000000, 2500000, 2500000)$, with reproduction number $\mathcal{R}_0 = 1.0542$. This confirms the local stability of the endemic equilibrium point whenever the reproduction number $\mathcal{R}_0$ is above unity.

In figure 4.1(c), using the same parameter values and initial conditions as in figure 4.1(b), but introducing condoms, we see that susceptibles decrease and levels off after 20 years as compared to 15 years in figure 4.1(b).

Figure 4.1(d) shows that implementing both condoms and vaginal microbicides as preventative strategies have positive effects as evident by the graphs of susceptible males and females which are levelling off after 25 years.

4.3 Incorporating gender differences in HIV transmission

We now incorporate the differences that gender contributes to the dynamics of HIV. The incubation of AIDS is long and variable depending on patient's age and sex and generally males progress to AIDS faster than females [28,29]. Male and female life expectancies differ and in Zimbabwe male and female life expectancies are 37 and 34 years respectively [30]. We now introduce parameters that model gender differences in HIV transmission with the view of understanding the core role of gender in relation to the epidemic. The natural death rate for males and females are μ_m and μ_f, respectively, infected males and females progress to AIDS at the rates σ_m and σ_f respectively and AIDS induced death rate for males and females are d_m and d_f respectively. The model equations

of the new model system becomes

$$\begin{aligned}
\frac{dS_m}{dt} &= \rho\pi - c_m\lambda_f S_m(t) - \mu_m S_m(t), && (4.1)\\
\frac{dI_m}{dt} &= c_m\lambda_f S_m(t) - (\mu_m + \sigma_m)I_m(t), && (4.2)\\
\frac{dA_m}{dt} &= \sigma_m I_m(t) - (\mu_m + d_m)A_m(t), && (4.3)\\
\frac{dS_f}{dt} &= (1-\rho)\pi - c_f\lambda_m S_f(t) - \mu_f S_f(t), && (4.4)\\
\frac{dI_f}{dt} &= c_f\lambda_m S_f(t) - (\mu_f + \sigma_f)I_f(t), && (4.5)\\
\frac{dA_f}{dt} &= \sigma_f I_m(t) - (\mu_f + d_f)A_f(t), && (4.6)
\end{aligned}$$

where

$$\lambda_m = \frac{\beta_{mf}(I_m(t)+\eta A_m(t))}{N_m(t)} \qquad \text{and} \qquad \lambda_f = \frac{\beta_{fm}(I_f(t)+\eta A_f(t))}{N_f(t)}$$

are the force of infection for males and females, respectively.

The mathematical analysis for model system (4.1) - (4.6) is similar to the analysis of model system (3.15) - (3.20) so using a similar approach [8,24] the reproduction number is given as

$$R_h = \sqrt{R_{hf}R_{hm}}$$

which is the average number of secondary cases infected by a typical infected individual in a population that is fully susceptible during the entire period of infectiousness.

$$R_{hf} = \frac{(\mu_f + d_f + \eta\sigma_f)c_f\beta_{mf}\rho}{(\mu_f + d_f)(\mu_f + \sigma_f)(1-\rho)},$$

is the expected number of secondary female infections generated by a typical infected male over his infectious lifetime in an otherwise totally susceptible population and

$$R_{hm} = \frac{(\mu_m + d_m + \eta\sigma_m)c_m\beta_{fm}(1-\rho)}{(\mu_m + d_m)(\mu_m + \sigma_m)\rho},$$

is the expected number of secondary male infections generated by a typical infected female over her infectious lifetime in an otherwise totally susceptible population. We have shown most of the calculations in the model without parameter heterogeneity and we are now interested in the numerical simulations when we incorporate parameter heterogeneity in order to tell its effects. The parameter values used are listed in Table 4.2.

Description	Symbol	Values	Source
Recruitment rate	π	10000	Estimate
Proportion of male new recruits	ρ	0.4	CSO
Female progression rate to AIDS	σ_f	2	[Estimate]
Male progression rate to pre-AIDS	σ_m	2.6	[31]
Female natural death rate	μ_f	0.0294	[30]
Male natural death rate	μ_m	0.027	[30]
Female disease induced death rate	d_f	0.333	[30]
Male disease induced death rate	d_m	0.3	Estimate
Rate of partner formation by males	c_m	3	Estismate
Rate of partner formation by females	c_f	2	Estimate
Male probability of infection	β_{mf}	0.0497	[30]
Female probability of infection	β_{fm}	0.167	[30]
Modification parameter for AIDS infectiousness	η	3	Estimate

Table 4.2: Parameter values for the HIV/AIDS model

We plot the graphs of the corresponding reproduction numbers for varying number of sexual partners for both males and females presented in Figure 4.2. Figure 4.2 shows the plot of generated reproduction numbers as we vary the number of sexual partners for the models (system (2.1) - (2.6) and system (4.1) - (4.6). We observe that the incorporation of gender related parameters in our system has the effect of increasing the expected number of secondary female infections generated by a typical infected male and decreasing the expected number of secondary male infections generated by a typical infected female over the infective's infectious lifetime in an otherwise totally susceptible population. Overally this has reduced the model reproduction number.

We computed and compared the basic reproductive numbers of the models (3.15) - (3.20) and (4.1) - (4.6) to assess the role of gender in relation to the transmission of HIV/AIDS.

The obtained results show that $R_{0m} < R_0 < R_{0f}$ and $R_{hm} < R_h < R_{hf}$, that is the female reproduction number is greater than the model reproduction number which is also greater than the male reproduction number for both model system (3.15) - (3.20) and model system (4.1) - (4.6). The results indicate that females are at higher risk of infection as compared to their counterparts. After introducing the different parameter values for the transmission, progression to AIDS induced death of females and males we observe a decrease in the male reproduction number R_{hm}, an increase in the female reproduction number R_{hf} and overally a decrease in the model reproduction number.

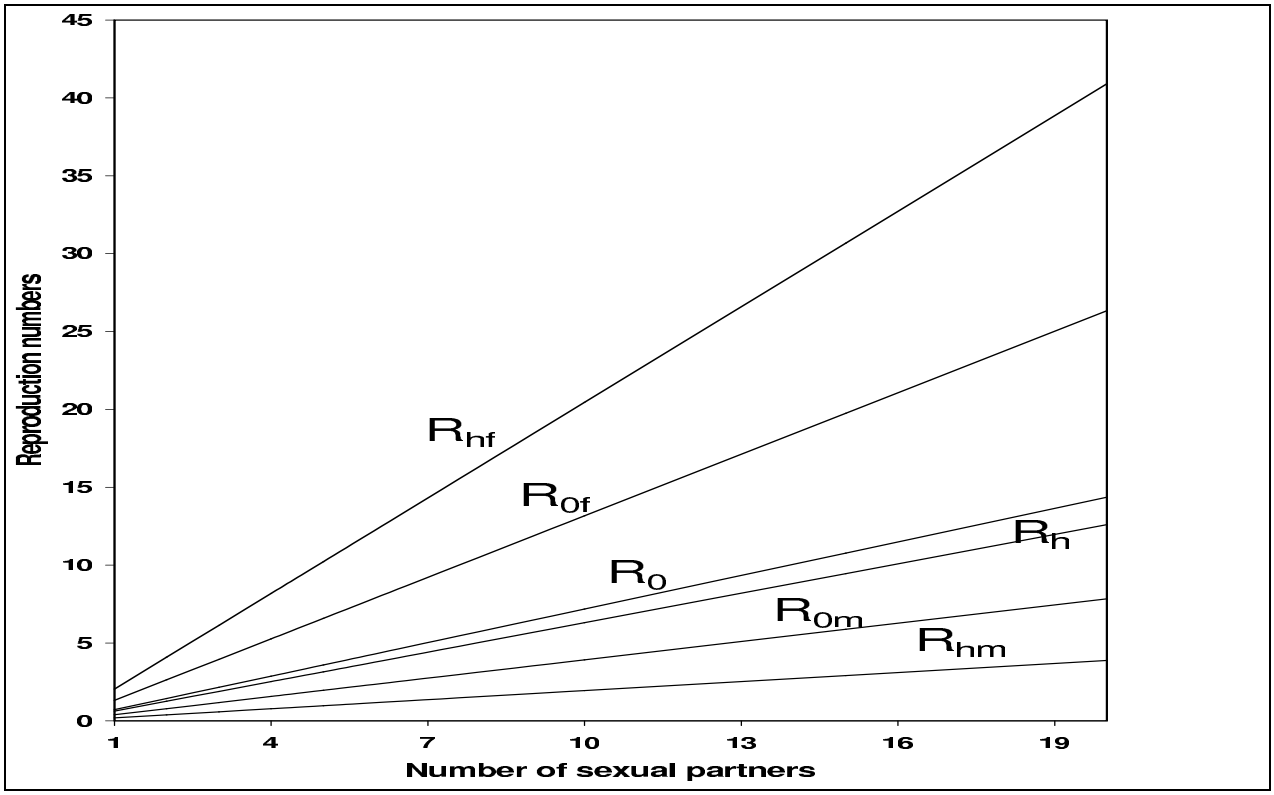

Figure 4.2: Graph of Reproduction numbers for varying sexual partners. R_{0f}, R_{0m} and R_0 represent the female reproductive number, male reproduction number and the model reproduction number respectively for model system $(3.15) - (3.20)$ and R_{hf}, R_{hm} and R_h represent the female reproductive number, male reproductive number and the model reproductive number respectively for model system $(4.1) - (4.6)$.

Chapter 5

Conclusion

This study provides insights into the benefits that condoms and vaginal microbicides prevention strategies provide in slowing HIV/AIDS transmission. Vaginal microbicides prevention strategy studied in this thesis is not currently available until 2013 [2], but condoms are readily available. In this thesis, we begin by formulating and analysing a basic heterosexual model that we extended to incorporate condom use based on efficacy and compliance. Further, we extended the basic heterosexual model with condom use by incorporating vaginal microbicides again based on efficacy and compliance. We saw from figure 4.1 that both susceptible population decrease instantly to a certain limiting value within 12 years and when condoms and microbicide were introduced the time frame almost doubled to 24 years implying that condoms and microbicide can effectively help prevent the rapid spread of HIV/AIDS if used consistently and correctly.

The basic reproductive number for the model were computed,analysed and simulated to assess the benefits of using condoms and microbicides. It is clear in the study that success is achieved when the reproductive number in the presence of intervention is reduced below the threshold of unity and this is achieved by using condoms and microbicide consistently and correctly and keeping partner formation very small and in this study we encourage one sexual partner. Thus, in a nut shell, the analysis of the models illustrate that proper condom use and microbicides use can effectively slow the spread of HIV/AIDS.

However, in case of 'condom replacement', using the reproduction numbers we determined the microbicide usage required, but is largely dependent upon both the expected microbicide efficacy and

current condom usage. If microbicide efficacy is substantially lower than condom efficacy (which appears likely, since its estimated to be 30%) then directly replacing condom usage with microbicide usage will have negative impact since the microbicide-induced reproductive number is greater than the condom-induced reproductive number ($\mathcal{R}_m > \mathcal{R}_c$). For individuals who continue to use condoms at the same rate after the introduction of microbicides, then maximising microbicide usage than efficacy is important.

Moreover, for individuals who abandon condoms, if microbicide efficacy is 30% we need 88% microbicide usage in order not to increase the risk of acquiring HIV, which is not just too high but unattainable, and for a 50% microbicide efficacy we need 52% microbicide usage. Thus, as condoms have proved beyond doubt to be very effective in preventing HIV/AIDS transmission we encourage a dual protective strategy (both condom and microbicide use). We extended the model to incorporate gender parameter heterogeneity in model system (4.1) -(4.6). We computed and compared the basic reproductive numbers of the models to assess the role of gender in relation to the transmission and containment of HIV/AIDS. The obtained results show that $R_{0m} < R_0 < R_{0f}$ and $R_{hm} < R_h < R_{hf}$, that is the female reproduction number is greater than the model reproduction number which is also greater than the male reproduction number for both model system (3.15) - (3.20) and model system (4.1) - (4.6). The results indicate that females are at higher risk of infection as compared to their counterparts. After introducing the different parameter values for the transmission, progression to AIDS induced death of females and males we observe a decrease in the male reproduction number R_{hm}, an increase in the female reproduction number R_{hf} and overally a decrease in the model reproduction number R_h

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