Using Mathematical and Economic Epidemiology tools for modelling HIV infection in Serodiscordant Couples.

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Abstract

We investigate the appropriate strategies that reduce the HIV transmission rate amongst the serodiscordant married couples. In particular, we formulate two discrete sub-models, the formation of married serodiscordant couples through marriage of single individuals and the formation of married serodiscordant couples through infection of HIV concordant negative married couples. We incorporate a constant treatment rate and solve these sub-models analytically. Our results showed that the formation of married serodiscordant couples through marriage of single individuals sub-model has no disease free equilibrium point because the serodiscordant couples are always present in the population. We computed the invasion reproductive number and showed that the endemic equilibrium point is stable when the invasion reproduction number is greater than one. In the formation of serodiscordant couples through infection of HIV concordant negative married couples, our results revealed that there exist a disease free equilibrium point and the endemic equilibrium point. We use the fixed point theory to determine the existence of the endemic equilibrium. We showed that when the basic reproduction number is less than unity, then it will be possible to control the HIV epidemic in serodiscordant couples otherwise the infection will persist. Sensitivity analysis revealed that for the disease to be controllable, intervention strategies must target to increase the treatment rate to reduce the HIV transmission rate. We then formulated the main model combining the dynamics of the two sub-models and incorporate treatment rate as the price-dependent demand function. We use the main model to explore the effects of treatment under eight different intervention strategic scenarios. Our results showed that out of the eight strategies only six were capable of reducing the HIV transmission rate amongst the serodiscordant married couples. The most effective intervention strategy was to treat directly the serodiscordant married couples. This strategy is expected to be cost efficient and could be implemented in poor resource setting.

Declaration

I declare that this dissertation presents my original work and effort. It was carried out under the supervision of Dr. F. Chirove in the School of Mathematics, Statistics and Computer Sciences, University of KwaZulu-Natal, Pietermaritzburg Campus.

It has not been submitted in any form to any university or institution of higher learning for any degree or qualification. Where use has been made of the work of others it is duly acknowledged.

Student: _____ _____

Mtshali M. Siphiwo Date

Supervisor: _____ _____

Dr. F. Chirove Date

Dedication

To my parents Mr Nimrod. K. Mtshali and Mrs Thandi. E. Mtshali, my late son Siyanda Ndumiso Mtshali and my whole family and friends.

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Chapter 1

Introduction

1.1 Background

An Infectious disease is an illness or disorder that is caused by a particular biological infectious agent or even its toxic product resulting from an infected individual or animal to a disease free host, this can happen directly or indirectly through plant intermediary, vector, animal host and inanimate environment [6]. The infectious diseases agents are metazoa, protozoa, fungi, bacteria, rickettsia, viruses and prions, and each group has its own characteristics. The causes and examples of infectious diseases are: Metazoa are mostly parasites and there are multicellular animals. Metazoa cause diseases such as trichinosis, hookworm and schistosomiasis. Protozoa sometimes called human parasites directly affect human and they are single-cellular organisms with a clear and structured nucleus. Protozoa cause diseases such as malaria, giardiasis, toxoplasmosis and pneumocystis *carinii* pneumonia. Fungi are organisms that are nonmotile and filamentous and can cause diseases that can be very difficult to cure or treat, such as histoplasmosis and candidiasis. Bacteria are organisms without a nucleus and there are single-celled. Most human diseases such as tuberculosis, staphylococcal disease, gonorrhea and chlymidia, meningitis, tetanus and diphtheria, pertusis, haemophilus influenza and pneumococcal disease are caused by bacteria. Rickettsia are infectious agents that are usually found in lice, ticks, fleas and mites and they are genus of bacteria but there are smaller than most bacteria and share some characteristics of viruses. Examples of infectious diseases caused by rickettsia are rocky mountain spotted fever and typhus. Prions are organisms with no genes and they have protein with an aberrant structure which replicates in animal or human tissue. Viruses are organisms that consists

of an RNA or DNA core and an outer coat of protein and they are very small. Examples of diseases which are transmitted by viral agents and confer immunity against infection are measles, chicken pox, German measles and influenza. HIV is also transmitted by viral agent by does not confer immunity against infection [7, 8].

Infectious diseases are responsible for a high mortality rate in low -and-middle-income countries and also responsible for a quarter of all annual deaths worldwide. Infectious diseases have a negative effect on the worlds economic growth and reduces the lifespan of the human population. Everyday scientists attempt to formulate new models to capture the changing conditions of the real world and also try to match infectious diseases with specific optimal intervention strategies. Mathematical models have been used for a very long time to capture the issue of epidemic infectious diseases affecting the human population. Economists are interested in formulating economic models which capture and seek solutions to the issue of infectious diseases [9, 7]. The concepts of mathematical and economical epidemiology have been successful in explaining the theory of infectious diseases and intervention strategies separately. It is however important to combine the two concepts to produce improved models and better results [10].

The human population has been concerned about the Human Immunodeficiency Virus (HIV) which is the cause of the Acquired Immunodeficiency Syndrome (AIDS) for more than three decades. This infectious disease is one of the most vicious diseases that mankind has ever faced. The world leading cause of death is the HIV/AIDS. Approximately 30 million people have died of AIDS-related causes since the first case was reported in 1981. There is an estimated number of 35.3 million people living with HIV, including 3.3 million children worldwide. The estimated number of new infections is 2.3 million per year. Despite treatment improvements and preventions, there is still no cure for HIV. The most affected region in the world is the sub-Saharan African region with an estimated number of 25 million HIV infected people. The largest number of people living with HIV in the sub-Saharan African region is women with approximately 58%. An estimated 1.5 million new infections and 1.1 million people died of AIDS related causes in 2013 [11, 12]. The sub-Saharan region has a large number of youth population that start having unprotected sex at very young age and contract the HIV. Having multiple sexual partners is a norm in this region, even when people are married [13]. In recent years, the spread of the HIV disease has been mostly amongst the serodiscordant married

couples in the sub-Saharan African region [14]. In most sub-Saharan countries, an estimated 60% to 94% of new infections resulted from the serodiscordant couples [15].

1.1.1 Mathematical Epidemiology

Mathematical epidemiology is the field that uses mathematical models to capture the mechanism that influences the spread of diseases and seek better ways to control the spread of diseases [16]. Infectious diseases mathematical models have been used by scientists to improve public policies since the eighteenth century. In 1766, Bernoulli did not understand the mechanism of infectious diseases and how the diseases lead to the death of people but he projected smallpox mortality to contend for increased inoculation [17]. In 1854, John Snow identified that a source of a cholera outbreak was a single water pump and his finding contributed largely in epidemiology developments [7]. In 1882 Koch designed a formal structure to illustrate how specific microbes cause specific diseases and so the process of how infectious agents spread was understood [18]. In the twentieth century, Hamer and Ross formed models for measles in 1906 and malaria in 1910, respectively, and the mathematical theory of epidemics was formed in 1927 by Kermack and Mckendrick. In 1950s mathematical models were successful in finding infectious diseases stochastic aspects, the eradication of measles in particular, and a vital factor to sustain an epidemic [7]. In the second half of the twentieth century further improvements were made on mathematical models to incorporate the incursion and persistence of human pathogens. Consequently, the process of how epidemics spread and a proper way to allocate measures to control the diseases in host populations, environment and to a wide range of pathogens was established. Mathematical epidemiology models are formulated as MSEIR models in which the epidemiological status of a person in the host population is illustrated as one of the following states: M represents newly born babies who preserve some protective maternal antibodies, S represents a class of susceptible individuals, E represents the exposed class of individuals which are infected but not infectious, I represents infectious class, and R represents the removed class of individuals who are dead or recovered. The quantitative influence on epidemiological parameters usually transmission rates, infectious and latent periods are used to model control treatments [7].

1.1.2 Economic Epidemiology

Economic epidemiology is the field that focuses on relating economics, human behavior, and ecology of diseases and largely relies on the mathematical formulations [10]. The main aim of the field is to find efficient policies and strategies to provide clear explanation about the issue of the spread of infectious agents and to find optimal control measures. Many mathematical models have been formed in recent years to test for the effectiveness and efficiency of public health intervention strategies. However, mathematical models commonly do not take into account the changing individuals responses to the outbreak of diseases and the models barely consider the social and economic perspective in which public health policies are implemented and also individual response to those policies [10]. Economic epidemiology is motivated by the economic impact of infectious diseases and the need to understand individuals behavior and response to the infection and to find optimal ways to design and allocate required resources to the communities through public health intervention programs [7]. The main priority of epidemiological research in the context of economics during the twentieth century was to focus on specific effects of income, nutrition, social class, occupation exposures and behaviors, disease risks and mortality. Recently, the focus on epidemiological research expanded to include the importance of macroeconomic influences on health to assist on understanding other environmental factors which could contribute to the spread of infectious disease [9].

1.2 Problem statement

Infectious diseases contribute largely on the worlds mortality and there are responsible for about a quarter of all deaths worldwide. The current literature on infectious diseases continue to exhibit the challenges brought about by infectious diseases which affect human lives and the environment that they live in as well as the global economy. Mathematical epidemiology has proven to be the powerful field in identifying and capturing problems regarding infectious diseases and their spreading mechanisms, and it is also playing a massive role in finding solutions to the infectious diseases problems. The economic epidemiology is a field that is relatively new, combines economics, human behavior and environment. Existing economic epidemiology research contributed positively in modeling and resolving infectious diseases problems by incorporating additional factors from economics such as costs and social welfare to improve the public health intervention strategies. Although mathematical and economical epidemiology have shown excellency in modeling, solving and analysis of infectious

diseases as separate fields, the two fields complement each other in formulation and implementation of intervention strategies. The problem is that there has not been a balance of focus on these two fields combined to evaluate the benefits and improvements which could be obtained from economic epidemiology mathematical models. In this study we want to formulate a discrete mathematical HIV model and incorporate economic aspects in the treatment rate. We want to investigate best intervention strategy to prevent an increase in the rate of HIV transmission for HIV serodiscordant couples.

1.3 Aim and Objectives

1.3.1 Aim:

The main aim of the study is to formulate a discrete mathematical model which incorporates economics aspects in the treatment rate of HIV that can be used to enhance the understanding of the impacts brought about by the intervention strategies for HIV epidemic factoring in the benefits weighted against the costs of implementing the strategies.

1.3.2 Objectives:

In this study we seek to address the following:

1. Develop and analyze two discrete sub-models of HIV with a constant treatment rate, presenting the formation of the serodiscordant married couples. Then combine the dynamics of the two sub-models to formulate the main discrete mathematical model. In the main model incorporate HIV treatment rate as the prevalence and price dependent demand function,
2. Analyze the main model numerically to obtain the best intervention strategies in terms of reducing HIV transmission amongst serodiscordant married couples and by other infected individuals in resource-poor settings.

1.4 Significance

Infectious diseases epidemics have devastating effects on public policies and responses to various intervention strategies especially in resource-poor settings. Therefore, this study may contribute significantly since economic and mathematical epidemiology provides an interface to enable health officials to come up with policies that are informed by the processes and patterns emanating from interaction on individuals with different infection capabilities as well as the trade-off based on decisions made by such individuals.

1.5 Plan of the study

The study has five chapters with sections and subsections in each chapter. Chapter 1 gives introduction, background information, problem statement and motivation, aims and objectives and significance of the study. Chapter 2 will give the literature review and preliminaries. Chapter 3 will give the formulation of HIV sub-models and solve them analytically, and the formulation of the main HIV model and incorporate the aspects. Chapter 4 will provide the numerical simulations based on the main model to investigate effective intervention strategies of reducing the rate of HIV transmission. Chapter 5 will provide discussion and recommendations and also the limitation of the study.

1.6 Summary

This chapter gave an introduction to the problem under study, where it stated the effects of infectious diseases in human lives and gave some examples of infectious diseases and also briefly stated the importance of mathematical and economic epidemiology. It also looked at the background information of mathematical and economic epidemiology, where detailed history of mathematical epidemiology was stated and also indicated that economic epidemiology is relatively a new field which has proved to be very useful in studying the infection diseases epidemics. The aim and objectives of the study were stated in detail. The significance of the study was also stated, where it was indicated that the importance and contribution the study could make on improving the public health intervention strategies and policies. Finally, the chapter gave the structure of the study. In the next chapter, we

review in detail some selected studies that give a deeper background of mathematical and economical epidemiology to get an understanding of what has been done in these two fields and also highlight some of the techniques used in the current study.

Chapter 2

Literature Review And Preliminaries

In this chapter, we are going to review studies on mathematical and economic epidemiology of infectious diseases. We will use these studies as building blocks to the problem under study. The chapter will have a section on the review of studies in mathematical epidemiology and on economic epidemiology. The chapter will also look at the preliminary concepts to be used in the study, where we will look at some mathematical models and tools to solve these models.

2.1 Mathematical Epidemiology Review

Kar and Jana [19] investigated a theoretical study on mathematical modeling of an infectious disease with application of optimal control. The aim of the study was to propose and analyze an epidemic problem which could be controlled by vaccination as well as treatment. The study investigated dynamical system with fixed control for both treatment and vaccination. The system with fixed control was modified to incorporate a control strategy which reduced the number of infected individuals and the related costs. The results showed that vaccination as a strategy could be a powerful method in controlling the disease but not perfect to eradicate the infection. Vaccination has been proven to be too slow in reacting to prevent a large unexpected epidemic outbreak. This could be because of adverse side effects posed by some vaccines. Therefore, in most cases, alternative control measures like treatment are highly useful and recommended. The simulation results from the study were not based on any real world data and sensitivity analysis was only based on selected parameters. Consequently drawing conclusion on general level is not possible.

Pienaar [20] studied a model on tuberculosis (TB) transmission and intervention strategies in an urban residential area. The aim of the study was to use a mathematical model of TB transmission to explore the dynamics of the spread of TB in an informal settlement and determine suitable intervention strategies. The dynamics of the model distinguished between the three different social patterns: interaction of random diurnal, commuters during travel and familiar exposure at night. The general SLIR model was used, where the population was divided into susceptible (S), latently infected (L), infectious (I) and recovered individuals. The risk of exposure for TB was based on the duration, proximity and frequency of encounters with infectious persons. Strategies such as vaccination, latent infectious prophylactic treatment, mask wear during the commune and treatment were investigated by applying the SLIR model to a hypothetical population. Intervention parameters were varied in order to determine the impact of different intervention strategies on the disease outcome over a number of years. Results from the study revealed that smaller families were less responsible for transmission of the disease than bigger families, regular users of the public transport contributed significantly towards disease transmission, improved treatments and diagnosis contributed significantly in reducing the spread of the disease when properly implemented and that it was important to put a detection mechanism as soon as an outbreak was suspected.

Bowong and Alaoui [21] used the concept of optimal control to investigate the optimal intervention strategy for TB. The aim of the study was to examine the optimal control of a deterministic model of tuberculosis and interventions. A model on tuberculosis without control which incorporated the critical biological and epidemiological disease features was analyzed. The results exhibited the existence of a backward bifurcation, where one or multiple stable endemic equilibria and a stable disease free equilibrium co-exists when the related basic reproduction number is less than unity. It was shown that the re-infectious of latently infected individuals caused the backward bifurcation. The tuberculosis control was formulated and solved as an optimal control problem based on the continuous model. The model revealed how control terms on the chemoprophylaxis and detection should have been introduced in the population to minimise the number of individuals with active tuberculosis. Through simulations it was shown that the infection level decreased but was never eliminated. However, it was also established that the level of infection could increase again at the end of the chemoprophylaxis and detection. It was suggested that TB could be successfully controlled by a cost-effective balance of detection and chemoprophylaxis.

Heffernan and Dunningham [22] simplified mathematical modelling to test intervention strategies

for Chlymidia. The purpose of the study was to develop a simple mathematical model to study the results of interventions in lowering rates of Chlymidia in a high-risk population of ages between 16 and 24. The model could be easily updated as data change frequently. They were three preventative strategies which were to be tested by this model, namely, screening, partner notification and condom use. The population averaging model was used to show the impact of using a condom when every other parameter is fixed. The model showed that infection rates decreased substantially when condoms were used. A major decrease was observed in the occurrence of Chlymidia for 25 percent increase in the per-act rate of condom use. Results from the model also revealed that there was a remarkable decrease when check-ups were done after every 12 to 15 months and a significant decrease when check-ups were done every 9 months on average. Contact tracing was shown to be least successful in decreasing the incidence of Chlymidia as a single strategy.

Granich *et al.* [23] studied a universal voluntary HIV testing with immediate antiretroviral therapy (ART), the aim of the study was to investigate a theoretical strategy of universal voluntary HIV testing and immediate treatment with ART and examine the conditions under which the HIV epidemic could be steered towards elimination. The deterministic transmission model was used to test their test-case sample community aged 15 years and older, every 12 months people were given ART immediately after they got diagnosed HIV positive. The strategy of antiretroviral therapy greatly accelerated the transition from present endemic phase, in which most adults living with HIV were not receiving ART. It was projected that ART strategy could reduce HIV incidence and mortality to less than one case per 1000 people per year by 2016 or within 10 years of full implementation of the strategy as well reduce the prevalence of HIV to less than 1 percent within 50 years. It was estimated that in 2032, the yearly cost of the antiretroviral therapy and the theoretical strategy would be 1.7 billion US dollars. Beyond 2032 it was estimated that the cost of the ART would continue to increase whereas that of the theoretical strategy would decrease. The study could be improved by using current data. The study only considered a preliminary costing exercise. A full economic analysis of the strategy that is proposed may be required to improve the understanding of the economic implications of the theoretical strategy.

We have gathered that mathematical models are very useful in explaining the dynamics of infectious diseases and also helps in the formulation and implementation of different intervention strategies as mentioned in [19, 20, 21, 22, 23]. However, in the real world the mathematical epidemiological models on their own live gaps especially when we look at the implementation of intervention strategies, as

it requires a detailed economic analysis.

2.2 Economic Epidemiology Review

Greeff *et al.* [24] studied the economic analysis of pertusis illness in the Dutch population investigating the implications for current and future vaccination strategies. The study described the age-specific health care utilization and costs associated with pertusis in the Netherlands taking into account unregistered patients costs in the notification system. The study also evaluated the cost-utility of the preschool booster vaccination introduced in the Netherlands in the beginning of 2002. Patients registries from continuous registration and mandatory notification system were used to estimate the number of patients with pertusis. The results showed that even though infants represented 5 percent of cases but they accounted for 50% of the total costs while the other 50% was distributed amongst the other age groups. The study suggested that costs per infant case largely determined the economic burden of pertusis . Results also indicated that the preschool booster was not considered cost-effective, even though there was a huge reduction in the number of cases.

Jit and Brisson [25] modelled the epidemiology of infectious diseases for decision analysis. The aim of the study was to model infectious diseases and take into account infectious diseases features that are unique and can affect intervention estimated value. The study indicated that vaccination, screening, social distancing, culling and post-exposure were interventions that could be modelled and implemented at low costs if research is done. However, the study did not provide an equilibrium point where interventions match the decisions of public health authorities and society.

Aadland, Finnoff and Haung [26] examined the dynamic properties of rational expectation models of economic epidemiology. The study mainly investigated the stability properties of the relationship between the public health intervention policy and models of economic epidemiology. Also key in the study was investigating whether or not a well-structured public policy has potential to contribute to aggregate public volatility and instability. In addition, the study investigated how susceptible individuals incentives and choices may have caused the system to move towards a socially-optimal transition path when multiple equilibrium paths existed. The results revealed that the economic SIRS system was able to produce an unstable eradication steady state and two endemic steady states on average. The SIRS system was recommended in general to handle cases of diseases with permanent immunity

such as chicken pox, disease with permanent infection such as HIV/AIDS, and diseases with recovery but no immunity such as common cold. The study showed that the marginal costs of additional exposure was low and there was no endemic steady state exposure at low levels of the health gap. The health gap was increased further and the marginal benefit and marginal costs curves reached a unique endemic steady state exposure. The health gap was further increased and the marginal benefit and marginal cost curves intersected and formed two endemic steady states, namely, low exposure steady state where individuals were less exposed to HIV/AIDS and the high exposure steady state where individuals were highly exposed to HIV/AIDS because of lack of information about HIV/AIDS and lack of prevention methods . It was also indicated that the aggregate welfare was always higher along the transition path to the low-exposure endemic steady state. The susceptible individuals optimized value function is bigger along the transition path to the high-exposure endemic steady state in the case of observed host immunity. The aggregate welfare was shown to be decreased by reducing the health gap through drug treatment or new therapies. The marginal costs of exposure was shown to have declined as health gap is decreased. In addition, it was revealed that the system can be moved from a unique stable equilibrium to the high exposure steady state that showed indeterminacy and aggregate instability, the cause of this is the reduction of the health gap. However this study does not provide specific policy recommendations by looking at and examining policy costs. Also the study could give more and detailed explanation to check if the methods outlined in the paper were applied to specific diseases.

Economic epidemiology models play a vital role mostly in the analysis of the economic state of the society in which interventions are to be implemented and also in the analysis of cost efficiency. However, economic models do not capture the conditions and environment in broader scope as mathematical models do.

Mathematical and economic epidemiology are two separate fields which have contributed largely in the modeling of infectious diseases, even though economic epidemiology is relatively a new field. However, these two fields combined have not been given much attention in modelling of infectious diseases. Formulating models based on the combination of mathematical and economic epidemiology models could improve the strategic choices taken by public health officers.

2.3 Preliminary Concepts

Mathematical models give a clear structure within which to improve and communicate an understanding of the dynamics of infectious disease transmission and incorporates the dynamics of intervention strategies [27]. We state and define some mathematical models and tools to solve population dynamics models.

2.3.1 Deterministic models

Deterministic models are mathematical models that describe basic fundamental relationships between variables of a problem. In most cases deterministic models are constructed on macro-level states or group aggregate. Where the number of infectious individuals is very small the deterministic models are not appropriate for modeling the beginning and the end of an epidemic [28]. Deterministic models are classified into continuous and discrete models.

Discrete models

Discrete models use difference equations to show the change in the population model over the entire time step used. The discrete models present a discrete data which ensures that the formulated model matches the data directly. Lags are easily incorporated in discrete time systems. Lags include, time spent exposed to disease, time spent infected, length of time lived before death after infection, etc. Stochastic processes can be in incorporated easily, probabilities instead of proportions. Implementation of intervention processes are more realistically incorporated in discrete systems since interventions are often discrete. Discrete systems improve computational efficiencies, therefore providing accurate numerical integration. Discrete time models require an appropriate discretization of parameters of event under study into a finite number of temporally-regular time steps of which for complex system its tedious. Careful consideration of the specific time step length in discrete time analysis is important because if the time step is not chosen to match the scale of the system, errors could be experienced. Discrete models can be more computationally demanding than continuous models [27].

Continuous models

In continuous models, modelling events happen at some point in time. The presentation of those models is in differential equations. Models of discrete systems are often an approximation to the models of continuous system, and simplifying assumptions may be needed. In general, a discrete model results tend to be closer to those of the continuous time model when the time interval is shorter. In continuous models it is easy to establish a comparison baseline[1].

2.4 Tools to solve mathematical models

2.4.1 Basic epidemiology terminology [1, 2]

1. The prevalence is a percentage of a specific observed population that is infected with a particular disease. Usually the introduction of a disease into a population leads to an increase in the prevalence rate.

2. The incidence of a disease is the rate at which new infections occur. Let$R$ be the size of the population, i, be the infected individuals at the start of a specific year and p be the new infections occurring in that year. Then the prevalence rate is $\frac{i}{R}$ and the incidence rate is $\frac{p}{R-i}$ per year .

3. Serodiscordant couple is a couple where one partner is infected with a disease and the other partner does not have that disease. The infected partner is referred to as seropositive partner and the uninfected partner is referred to as seronegative partner.

4. Concordant negative couple is a couple where both partners do not have a disease in their systems.

5. Concordant positive couple is a couple where both partners are infected with a disease.

2.4.2 Invariance principle

Definition 1. *A set N is an invariant set with respect to a system of ordinary differential equations*

$\dot{y} = f(y)$ *if* $y(0) \in N \qquad y(t) \in N$, *for all* $t \in \mathbb{R}$.

A set N *is positively invariant set with respect to* $\dot{y} = f(y)$ *if* $y(0) \in M \quad \Rightarrow y(t) \in M$, *for all* $t \geq 0$ *[29].*

2.4.3 Equilibrium [3, 4, 5]

Consider the autonomous system of ordinary differential equations

$$\dot{x} = f(x) \quad y \in \mathbb{R}^n \tag{2.1}$$

Definition 2. x^* *is an equilibrium point if* $\dfrac{dx}{dt} = f(x)$ *and* $f(x^*) = 0$. *This applies to a continuous model or differential equation.*

Definition 3. *An equilibrium of the difference equation is a value* x^* *such that* $f(x^*) = x^*$, *so that* $x_n = x^*$ $(n = 0, 1, 2, ...)$ *is a constant solution of the difference equation.*

Definition 4. *An equilibrium point is said to be stable if all solutions sufficiently close to* x^* *remain close for all* $t \geq 0$, *otherwise it is unstable.*

Definition 5. ***(Asymptotic Stability)***

An equilibrium point of (2.1) is asymptotically stable if it is stable and there exists a constant $c > 0$ *such that if* $\mid y(t, x_0 - x^*) \mid \to 0$ *as* $t \to \infty$.

2.4.4 The basic reproduction number

Definition 6. *Basic reproduction number, denoted as* R_0 *is the average number of secondary infections resulting from introducing an infected individual into a disease-free population.*

If $R_0 < 1$, then on average a few infected individuals brought into a fully susceptible population will not be able to replace themselves and the disease will not spread. If $R_0 > 1$, then the number of infected individuals will increase with each generation and the disease will spread. For simple compartments with one infected class we can calculate R_0 simply by the definition of transmission rate multiplied by the infection period. However, for complex models with several infected classes, we need to make use of the next generation matrix method to determine R_0 as presented in Van den Driessche and Watmough [30].

2.4.5 The next generation matrix method

Van den Driessche and Watmough introduced the next generation matrix method for the discrete -time epidemic models to determine the reproduction number, R_0, where we have more than one infected class [31].

Let $Y = (y_1, y_2, ..., y_n)^T$ present population's n states corresponding to their disease status (susceptible, infectious, recovered, etc). Let

$$Y(t+1) = D(Y(t)), \quad t = 0, 1, ..., \tag{2.2}$$

define the population states variable dynamics over discrete time intervals, where D:$R_+^n \to R_+^n$ and $D \in C^1(R_+^n)$ for $R_+^n = \{Y = (y_1, y_2, ..., y_n) \mid y_j \geq 0, \quad j = 1, 2, ..., n\}$. Suppose the first m states, $m < n$, presented as $Y_0 = (y_1, ..., y_m)^T$, are infectious or exposed states and $n-m$ states are uninfected states presented as $Y_1 = (y_{m+1}, ..., y_n)^T$. Therefore, (2.2) can be expressed as

$$\begin{pmatrix} Y_0(t+1) \\ Y_1(t+1) \end{pmatrix} = \begin{pmatrix} D_0(X(t)) \\ D_1(Y(t)). \end{pmatrix} \tag{2.3}$$

We assume a unique disease-free equilibrium of a system (2.2) exists, where $Y_0 = 0$ and $Y_1 > 0$. We also assume that the discrete system (2.4) could be linearized about the disease free equilibrium and obtain the linearized system

$$X(t+1) = JX(t), \tag{2.4}$$

where J is the $n \times n$ Jacobian matrix evaluated at the disease free equilibrium. Matrix J is presented as

$$J = \begin{pmatrix} F+T & O \\ A & C \end{pmatrix}, \tag{2.5}$$

where F and T are positive $m \times m$ submatrices, $F + T$ is irreducible and O is the zero matrix. Through differentiation with respect to states Y_0 and evaluated at the disease free equilibrium we obtain the matrices F and T. Identify the terms in D_0 corresponding to those in T and those in F. Let $D_0(Y(t)) = \mathcal{F}(t) + \mathcal{T}(t)$, where the vector of new infections surviving the time interval is presented by $\mathcal{F}$ and the vector of any other transition leading to F and T is presented by $\mathcal{T}$. We

assume that the disease free equilibrium is locally asymptotically stable when there is no disease. Hence, the spectral radius of C is less than one. The spectral radius of T is required to be less than one. Hence, $\rho(T), \rho(C) < 1$. The stability of the linear system , $X(t+1) = JX(t)$, is dependent on the eigenvalues of $F + T$ and does not depend on matrix A, since $\rho(C) < 1$ and matrix J is block triangular. The matrix $G = F(I-T)^{-1}$ is the next generation matrix, where I is the $m \times m$ identity matrix. since the spectral radius of T is less than one, i.e $\rho(T) < 1$,

$$G = F(I + T + T^2 + ...).$$

Let I_0 be the density or initial number of infectious individuals vector, then during the lifespan of the population the distribution of all infections is represented by,

$$GI_0 = F(I_0 + TI_0 + T^2 I_0 + ...),$$

.

The basic reproduction number(R_0) is defined as the spectral radius of the matrix G,

$$R_0 = \rho(F[I-T]^{-1}) = \rho(G). \tag{2.6}$$

2.5 Summary

In this chapter we reviewed the literature on mathematical and economic epidemiology. The literature showed that the mathematical epidemiology is a very useful concept to present epidemic infectious diseases into simple and complex mathematical models which have to be solved and analyzed to produce the required results from the problem under study. However, the mathematical epidemiology models focus mostly on the dynamics and transmission of infectious diseases and gives less attention to effects of intervention strategies and implementation in terms of environmental, social and economic costs and benefits. The Economic epidemiology concept has not been used much in investigating the epidemics of infectious diseases but has proven to be vital in the analysis of social economic welfare and strategic implementation costs analysis. However, the economic epidemiology models give better results when the model under study is not too broad. Therefore, mathematical and economic models combined may capture a bigger scope of epidemic infectious disease problems and more accurate and

good results could be obtained. Preliminary concepts were also looked at in this chapter, where some types of mathematical models and tools to solve the mathematical tools were looked at in details. Some of the mathematical models and tools looked at in this chapter will be applied to the problem under study in the next chapter.

Chapter 3

Models of the formation of serodiscordant couples and the dynamics of HIV with treatment

3.1 Introduction

HIV/AIDS is one of the infectious diseases with a rapid spreading behavior in the society and in time it changes its distribution in space. Various factors and influences are responsible for an increased HIV infection risk. Recent research showed that the most heavily affected region by HIV/AIDS in the world is the sub-Saharan Africa [11]. The focus on preventing HIV in the first two decades of the HIV epidemic in sub Saharan Africa was on HIV negative individuals mainly prostitutes, individuals with more than one sexual partner and children and women. Most HIV transmission in sub-Saharan African region occurs amongst stable long term relationships, cohabitating and married serodiscordant couples [32, 33]. Standard mathematical models have been applied to model and analyze the spread of HIV amongst single individuals, cohabitating couples and married couples. Mathematical models have also been used to seek ways to minimize the risks of HIV infection [34, 35]. In this study we investigate the best intervention strategies that could minimize risks of HIV transmission among the HIV serodiscordant couples using mathematical and economic aspects. We formulate the two sub-models of single individuals and married couples HIV transmission dynamics and the main complex model which combines the single individuals and married couples HIV transmission

dynamics.

We consider the dynamics of HIV transmission and serodiscordant formation through three models, namely, serodiscordant couples formation from marriage of single individuals, formation of serodiscordant couples through infection of HIV concordant negative couples and single's and married couples HIV transmission and formation of serodiscordant couples. We have nine compartments in the dynamics, namely, the single HIV negative individuals, S_N, with high risk of getting HIV infection, the single HIV positive individuals, S_P, who are infectious and can actively transmit HIV to other individuals, the HIV negative concordant couples, M_{NN}, who are married susceptible couples free of HIV but at risk of getting HIV infection, the HIV-serodiscordant couples, M_{NP}, where one partner is HIV positive and infectious and one is HIV negative with high chances of getting HIV infection, the HIV concordant positive couples, M_{PP}, who are married and can transmit HIV infection to other individuals, the treated single HIV positive individuals, T_{S_P}, the treated HIV serodiscordant couples, $T_{M_{NP}}$, and the treated HIV concordant positive married couples, $T_{M_{PP}}$. The parameters and their description are presented in Table 3.1. In the HIV positive single individuals compartment one individual takes treatment. In the serodiscordant married couples compartment the seropositive partner takes treatment. In the HIV concordant positive married couples both partners in marriage take treatment.

We use proportions to indicate the number of individuals treated in each compartment. In the sub-models we assume that proportions are based on the the least number of infected individuals taking treatment in each compartment, out of the least case of total infected individuals in the same compartment. In, S_p, we have at least one taking treatment, for ,M_{NP}, we have one out of two taking treatment, $\frac{1}{2}$, and in, M_{PP}, we have, $\frac{2}{2}$, taking treatment. While in the main model proportions are based on the least case of infected individuals taking treatment per compartment, out of the least case of the total infected individuals in a population. In, S_P and M_{NP}, we have , $\frac{1}{4}$, and ,M_{PP}, we have , $\frac{2}{4}$. This is because we would like to incorporate treatment and use these proportions in determining the best strategies based on the least case of the total infected in the population rather than per compartment. However, the constant treatment rate implemented in each sub-model is the same.

We assume the population can mix homogeneously, meaning any member of the population is free to sexually commit to anyone in the population. We also assume that there is no re-infection of HIV

Table 3.1: Parameters and description

Parameters	Description
μ	Natural death rate
δ	HIV induced death rate
α	Marriage rate regardless of the HIV status
β	HIV infection rate
ϵ	Treatment rate
π	Recruitment rate

within the population. The change of HIV status with time of single individuals and married couples determine the classes they move to. We assume that the married couples stay married throughout the duration of study and there is no marriage dissolution. This is a simplifying assumption and we acknowledge that including marriage dissolution and remarriage will definitely alter the predictions of the current models. We assume that every individual or couple leaves the population through death only and there is no immigration of married couples. We further assume that the only allowed marriage dynamics of single individuals is the one that may lead to the formation of serodiscordant couples immediately or later due to infection.

3.2 Serodiscordant couples formation from marriage of single individuals

We consider a sub-model that shows HIV transmission amongst single individuals and the formation of serodiscordant couples. The sub-model consists of five compartments, namely, S_N, S_P, T_{S_P} where single individuals from these compartments could marry each other to form the serodiscordant couples compartment M_{NP} and $T_{M_{NP}}$. We assume that the subtotal population is

$$K = S_N + S_P + M_{NP} + T_{S_P} + T_{M_{NP}}. \tag{3.1}$$

When the single HIV negative individuals, S_N, get an infection from single HIV positive individuals they move to the class of single HIV positive individuals, S_P. When a single HIV negative individual gets married to the single HIV positive individual, the couple will join the HIV serodiscordant couples.

We assume that the constant rate of recruitment of all single susceptible individuals into the population is, π. Single HIV negative individuals are removed from the susceptible compartment , S_N, either through natural death at a constant death rate μ, or through union in marriage to HIV positive single individuals at a marriage rate α, and through HIV infection from infectious individuals with a force of infection, $\Lambda_N(S_P, M_{NP}, T_{S_P}, T_{M_{NP}})$ (see equation 3.2).

Single HIV positive individuals compartment, S_P, recruitment is through HIV infected individuals from the compartment, S_N. Single HIV positive individuals are removed from this class through blanket death at a rate, $(\mu + \delta)$. Blanket death is the combination of natural death, μ, and a disease induced death, δ. They are also removed when single HIV positive individuals get married to single HIV negative individuals to form HIV serodiscordant couples at a rate, α.

We assume that HIV serodiscordant couples compartment, M_{NP}, recruits couples when HIV negative individuals get married to HIV positive individuals, $\alpha(S_N + S_P)$. HIV Serodiscordant couples are removed from the compartment, M_{NP}, through change of status when the HIV negative partner gets infected and the couple is removed at a constant rate, ϕ, and through natural death at a constant death rate μ.

We assume that HIV positive individuals from the compartment who take treatment at a rate, ϵ, progress to the HIV single individuals treated compartment, T_{S_P}. Individuals are removed from this compartment through union in marriage to HIV negative single individuals at a rate, α, and through natural death at a constant death rate, μ.

We also assume that a seropositive partner in the serodiscordant couples compartment who take treatment progress to the HIV serodiscordant couples treated compartment, $T_{M_{NP}}$, at a rate, ϵ. The serodiscordant couples are also recruited into this compartment as result of a marriage union of individuals from the compartments, S_N and T_{S_P} at a rate α. The couples are removed from this compartment at a constant rate ϕ_{NP} through change of status when the seronegative partner gets infected and they are also removed through natural death at a rate, μ.

3.2.1 Force of infection for S_N

A force of infection is the rate at which susceptible individuals contract an infectious disease [36]. We have seven individuals in the model of serodiscordant couples formation from marriage of single individuals that are involved in the transmission dynamics of HIV at any particular time, one from each of the compartments, S_N, S_P, T_{S_P} and two from each of , M_{NP} and $T_{M_{NP}}$. Every HIV negative individual in the population has chances of being infected by HIV positive individuals from the four sources of infection compartments, S_P, T_{S_P}, M_{NP} and $T_{M_{NP}}$. There are four infectious individuals, one from the HIV positive single individuals compartment, one from the serodiscordant couple's compartment and each from the treated compartments, T_{S_P} and $T_{M_{NP}}$. Hence, the chances of an HIV negative individual to get infected with HIV from each source of infection compartment, S_P, T_{S_P}, $T_{M_{NP}}$ and M_{NP} are $\frac{1}{4}$ for each of the sources of infection. We assume that the infection rate, β, of each infected individual is the same.

We also assume that single individuals have high chances of having several regular and casual sexual partners and that HIV positive single individuals, S_P, have greater chances of spreading HIV than married couples, since they are not necessary bounded by any contractual obligation [37]. We assume that individuals who are taking treatment are more cautious than those who are not treated because of the intensive HIV counseling that they go through before they are given treatment. Hence, the transmission rate from S_P compared to the one from M_{NP}, T_{S_P} and $T_{M_{NP}}$ is , $\beta\eta$, where $\eta > 1$. η, is an amplification factor. Whilst the transmission rate from M_{NP}, T_{S_P} and $T_{M_{NP}}$ is β. The force of infection for HIV negative individuals, S_N, denoted by, Λ_N, is given by

$$\Lambda_N = \frac{\beta}{4K}(\eta S_P + M_{NP} + T_{S_P} + T_{M_{NP}}). \tag{3.2}$$

The HIV transmission dynamics illustrated in Figure 3.1 are presented by the continuous system as

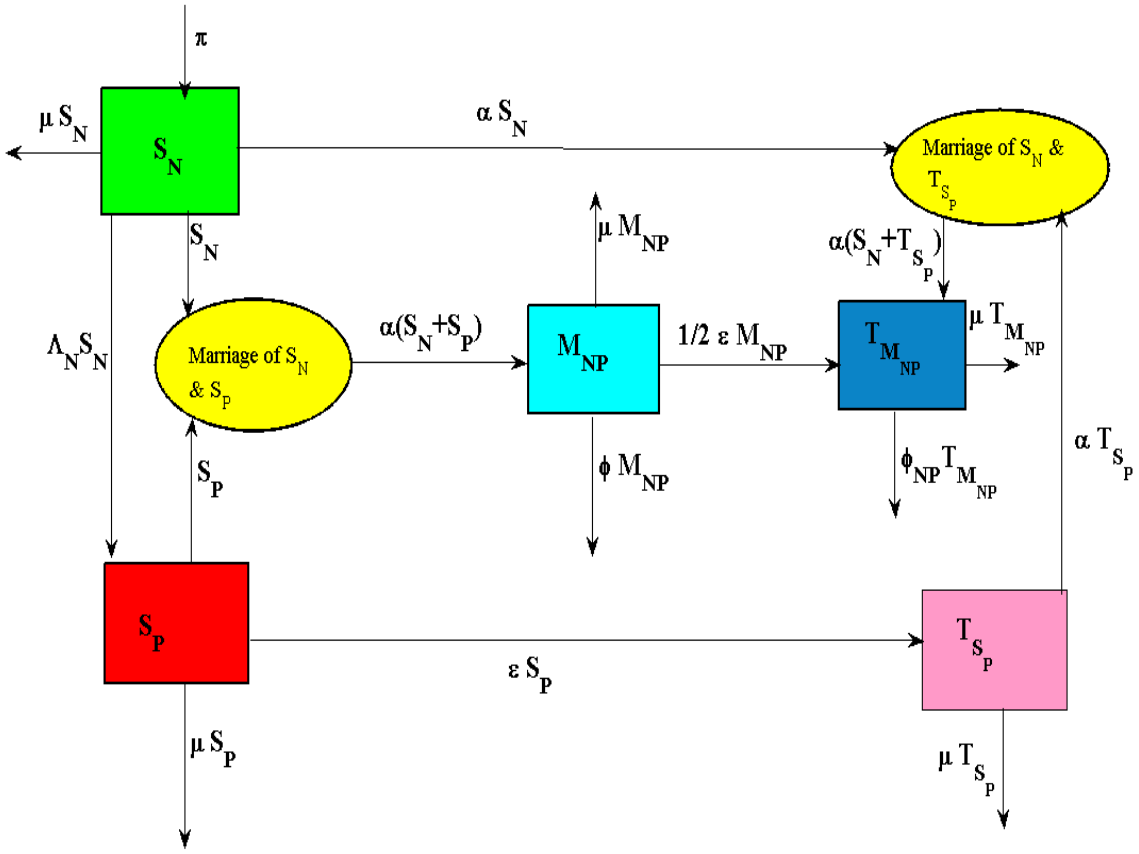

Figure 3.1: Schematic diagram that represents the formation of serodiscordant couples through marriage of single individuals.

follows:

$$\frac{dS_N}{dt} = \pi - \Lambda_N S_N - (2\alpha + \mu)S_N, \tag{3.3}$$

$$\frac{dS_P}{dt} = \Lambda_N S_N - (\alpha + \epsilon + \mu + \delta)S_P, \tag{3.4}$$

$$\frac{dM_{NP}}{dt} = \alpha(S_N + S_P) - (\phi + \frac{1}{2}\epsilon + \mu)M_{NP}, \tag{3.5}$$

$$\frac{T_{S_P}}{dt} = \epsilon S_P - (\alpha + \mu)T_{S_P}, \tag{3.6}$$

$$\frac{dT_{M_{NP}}}{dt} = \frac{1}{2}\epsilon M_{NP} + \alpha(S_N + T_{S_P}) - (\phi_{NP} + \mu)T_{M_{NP}}. \tag{3.7}$$

where $\phi > \phi_{NP}$ and the treatment rate is $0 \leq \epsilon \leq 1$.

3.2.2 Feasible region

The region $\Omega = \left\{(S_N, S_P, M_{NP}, T_{S_P}, T_{M_{NP}}) \in \mathbb{R}^5_+ | K(t) \leq \frac{\pi}{\mu}\right\}$, is feasible if it is positively invariant with respect to the system(3.3)-(3.7). Therefore, we have to prove that all the classes $S_N, S_P, M_{NP}, T_{S_P}$ and $T_{M_{NP}}$ are non-negative at all times ($t \geq 0$) and are bounded in the region Ω. We state and prove the positive invariance of solutions as in [38, 39]. The system of equations (3.3)-(3.7) has initial conditions given by $S_N(0) \geq 0, S_P(0) \geq 0$, $M_{NP}(0) \geq 0$, $T_{S_P}(0) \geq 0$ and $T_{M_{NP}}(0) \geq 0$.

Theorem 1. *The region $\Omega \in \mathbb{R}^5_+$ is positively invariant with respect to the system of equations (3.3)-(3.7) and a non-negative solution exists for all time $0 < t < \infty$.*

Proof. We can prove that the solutions in region Ω are positive by contradiction. Assume that there exits a first time,

t_N such that: $S_N(t_N) \leq 0$, and $S_N(t) > 0, S_P(t) > 0$, $M_{NP}(t) > 0$, T_{S_P} and $T_{M_{NP}}$ for $0 \leq t \leq t_N$, if we apply these conditions in the model system (3.3)-(3.7) we find that,

$$S'_N(t_N) = \pi > 0, \tag{3.8}$$

hence, if we integrate $S'_N(t_N)$ we get that $S_N(t_N) > 0$ which gives a contradiction to the assumption that $S_N(t_N) \leq 0$, hence S_N remains positive for all $t \in [0, t_N]$. If $t_N \to \infty$, then $S_N > 0 \; \forall \; t \in [0, \infty)$. Similarly, $S_P > 0$, $M_{NP} > 0$, $T_{S_P} > 0$ and $T_{M_{NP}} > 0 \; \forall \; t > 0$.

Therefore in all cases $S_N, S_P, M_{NP}, T_{S_P}$ and $T_{M_{NP}}$ remain positive for all $t \geq 0$, hence the region Ω has positive solutions. The change in total population, K, over time of model (3.3)-(3.7) is

$$\frac{dK}{dt} = \frac{d}{dt}(S_N + S_P + M_{NP} + T_{S_P} + T_{M_{NP}}) = \pi - \mu K - \delta(S_P) \tag{3.9}$$

since $K(t) \geq S_P(t)$, then

$$\pi - (\mu + \delta)K(t) \leq K'(t) \leq \pi - \mu K(t). \tag{3.10}$$

To determine the upperbound of $K(t)$ we integrate

$$\frac{dK}{dt} \leq \pi - \mu K,$$

that is,

$$\int_{K(0)}^{K} \frac{dV}{\pi - \mu V} \leq \int_0^t du,$$

hence,

$$-\frac{1}{\mu}\Big[ln|\pi - \mu V|\Big]_{K(0)}^{K} \leq \Big[u\Big]_0^t.$$

Hence we obtain,

$$K(t) \leq \frac{\pi}{\mu}(1 - e^{-\mu t}) + K(0)e^{-\mu t}, \tag{3.11}$$

for all $t > 0$. Consequently, $\limsup_{x\to\infty} K(t) \leq \frac{\pi}{\mu}$. If $K(0) \leq \frac{\pi}{\mu}$, then $\frac{\pi}{\mu}$ is the upperbound for K. This $K(t)$ is uniformly bounded, this means that $S_N, S_P, M_{NP}, T_{S_P}$ and $T_{M_{NP}}$ have a common upperbound.

To determine the lowerbound of $K(t)$ we integrate both sides of

$$\frac{dK}{dt} \geq \pi - (\mu + \delta)K,$$

that is,

$$\int_{K(0)}^{K} \frac{dP}{\pi - (\mu + \delta)P} \geq \int_0^t dr,$$

Hence we obtain,

$$K(t) \geq \frac{\pi}{\mu - \delta}(1 - e^{-(\mu+\delta)t}) + K(0)e^{-(\mu+\delta)t}, \tag{3.12}$$

for all $t > 0$. Consequently, $\liminf_{x\to\infty} K(t) \geq \frac{\pi}{\mu + \delta}$. If $K(0) \geq \frac{\pi}{\mu + \delta}$, then $\frac{\pi}{\mu + \delta}$ is the lowerbound for $K(t)$. $S_N, S_P, M_{NP}, T_{S_P}$ and $T_{M_{NP}}$ have a common lowerbound. Therefore, all solutions starting in the region Ω enter or remain in Ω for all time. Thus we conclude that the region

$$\Omega = \left\{(S_N, S_P, M_{NP}, T_{S_P}, T_{M_{NP}}) \in \mathbb{R}^3_+ | K(t) \leq \frac{\pi}{\mu}\right\} \tag{3.13}$$

is positively invariant for the model (3.3)-(3.7). The solutions of the model (3.3)-(3.7) are considered to be both biologically and mathematically feasible in the region Ω, hence it is sufficient to study the dynamics of the model in Ω. □

The system of continuous differential equations (3.3)-(3.7) can be transformed into the following system of discrete difference equations:

$$(S_N)_{t+1} = (S_N)_t + \pi - (\Lambda_N)_t(S_N)_t - (2\alpha + \mu)(S_N)_t, \tag{3.14}$$

$$(S_P)_{t+1} = (S_P)_t + (\Lambda_N)_t(S_N)_t - (\alpha + \epsilon + \mu + \delta)(S_P)_t, \tag{3.15}$$

$$(M_{NP})_{t+1} = (M_{NP})_t + \alpha((S_N)_t + (S_P)_t) - (\phi + \frac{1}{2}\epsilon + \mu)(M_{NP})_t, \tag{3.16}$$

$$(T_{S_P})_{t+1} = (T_{S_P})_t + \epsilon(S_P)_t - (\alpha + \mu)(T_{S_P})_t, \tag{3.17}$$

$$(T_{M_{NP}})_{t+1} = (T_{M_{NP}})_t + \frac{1}{2}\epsilon M_{NP} + \alpha(S_N + T_{S_P})_t - (\phi_{NP} + \mu)(T_{M_{NP}})_t. \tag{3.18}$$

3.2.3 Existence of equilibria and Invasion reproduction number

We shall determine the equilibrium points and the invasion reproduction number, R_{inv}, and the stability analysis of the discrete model (3.14)-(3.18). The discrete system has only one equilibrium point, the endemic equilibrium point E_1. We do not have a disease free equilibrium point for the discrete model (3.14)-(3.18) because we always have serodiscordant couples present in the population.

Endemic equilibrium point E_1

The endemic equilibrium point of the discrete system (3.14)-(3.18) is given by,

$$E_1 = (S_N^*, S_P^*, M_{NP}^*, T_{S_P}^*, T_{M_{NP}}^*). \tag{3.19}$$

where

$$S_N^* = \frac{\pi}{\Phi_1 + \Lambda_N^*}, \qquad S_P^* = \frac{\pi\Lambda_N^*}{\Phi_2(\Phi_1 + \Lambda_N^*)}, \tag{3.20}$$

$$M_{NP}^* = \frac{\pi(\Phi_2 + \Lambda_N^*)}{\Phi_2\Phi_3(\Phi_1 + \Lambda_N^*)}, \qquad T_{S_P}^* = \frac{\pi\Lambda_N^*}{\Phi_2\Phi_4(\Phi_1 + \Lambda_N^*)}, \tag{3.21}$$

$$T_{M_{NP}}^* = \frac{\Phi_6 + \Phi_7\Lambda_N^*}{\Phi_8(\Phi_1 + \Lambda_N^*)} \tag{3.22}$$

where,

$\Phi_1 = 2\alpha + \mu$, $\Phi_2 = \alpha + \epsilon + \mu + \delta$, $\Phi_3 = \dfrac{\alpha}{\phi + \dfrac{\epsilon}{2} + \mu}$, $\Phi_4 = \dfrac{\epsilon}{\alpha + \mu}$, $\Phi_5 = \phi_{NP} + \mu$,

$\Phi_6 = \Phi_2(2\pi\Phi_4\alpha + \epsilon)$, $\Phi_7 = 2\pi\Phi_4^2\alpha + \epsilon^2$, $\Phi_8 = 2\Phi_2\Phi_4\Phi_5\epsilon$

and

$$\Lambda_N^* = \frac{\beta}{4K^*}(\eta S_P^* + M_{NP}^* + T_{S_P}^* + T_{M_{NP}}^*) \tag{3.23}$$

We consider the following equation to solve for Λ_N^*

$$4K^*\Lambda_N^* - \beta(\eta S_P^* + M_{NP}^* + T_{S_P}^* + T_{M_{NP}}^*) = 0 \tag{3.24}$$

which when simplified we obtain, the equation

$$a_2\Lambda_N^2 + a_1\Lambda_N + a_0 = 0, \tag{3.25}$$

where

$$a_2 = 4(\pi(\Phi_3\Phi_4\Phi_8 + \Phi_4\Phi_8 + \Phi_3\Phi_8) + \Phi_2\Phi_3\Phi_4\Phi_7) \tag{3.26}$$

$$a_1 = 4(\pi\Phi_2\Phi_3\Phi_4\Phi_8 + \pi\Phi_2\Phi_4\Phi_8 + \Phi_2\Phi_3\Phi_4\Phi_6) - \beta(\pi\Phi_4\Phi_8 + \Phi_2\Phi_3\Phi_4\Phi_7) \tag{3.27}$$

$$a_0 = -\beta\Phi_4(\eta\pi\Phi_3\Phi_8 + \pi\Phi_2\Phi_8 + \Phi_2\Phi_3\Phi_6). \tag{3.28}$$

.

The nonnegative solution of (3.25) is

$$\Lambda_N^* = \frac{-a_1 + \sqrt{a_1^2 + 4a_2a_0}}{2a_2}. \tag{3.29}$$

Invasion Reproduction number

The invasion reproduction number is determined the same way as the basic reproduction number but using the endemic equilibrium point E_1 [40]. We will use the next generation matrix by Van den Driessche and Allen [41] to determine the invasion reproduction number of the discrete system (3.14)-(3.18). Since we have two infected compartments, we let $\mathcal{F}_i$ be the rate of appearance of new infections in compartment i and let $\mathcal{T}_i$ be the transfer rate of individuals into and out of compartment i by all other means. Then

$$\mathcal{F}_i = \begin{bmatrix} \Lambda_N S_N(t) \\ 0 \\ 0 \\ 0 \end{bmatrix}, \tag{3.30}$$

$$\mathcal{T}_i = \begin{bmatrix} (1-\alpha-\epsilon-\mu-\delta)S_P(t) \\ \alpha(S_N(t)+S_P(t)) + (1-\phi-\frac{\epsilon}{2}-\mu)M_{NP}(t) \\ \epsilon S_P + (1-\alpha-\mu)T_{S_P}(t) \\ \alpha(S_N+T_{SP}) + \frac{\epsilon}{2}M_{NP} - (1-\phi_{NP}-\mu)T_{M_{NP}}(t) \end{bmatrix}. \tag{3.31}$$

The matrices F and T are defined by;

$$F = \left[\frac{\partial \mathcal{F}_i(E_1)}{\partial x_j}\right] \quad and \quad T = \left[\frac{\partial \mathcal{T}_i(E_1)}{\partial x_j}\right], \tag{3.32}$$

for $1 \leq i, j \leq 4$. The state with no force of infection is represented by the vector $x_0 = E_1$. We determined F and $(I-T)^{-1}$ to be,

$$F = \begin{pmatrix} \frac{a}{4(\Lambda_N P_1 + P_2)} & \frac{b}{4(\Lambda_N P_1 + P_2)} & \frac{c}{4(\Lambda_N P_1 + P_2)} & \frac{d}{4(\Lambda_N P_1 + P_2)} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.33}$$

where

$$a = \pi(\alpha+\mu)(\alpha+\delta+\epsilon+\mu)(\epsilon+2(\phi+\mu))(\phi_{NP}+\mu)(\beta\eta - 4\Lambda_N) \tag{3.34}$$

$$b = c = d = \pi(\alpha+\mu)(\alpha+\delta+\epsilon+\mu)(\epsilon+2(\phi+\mu))(\phi_{NP}+\mu)(\beta - 4\Lambda_N) \tag{3.35}$$

and

$$\begin{aligned} P_1 &= \pi(\epsilon(\mu+2\phi_{NP})(\epsilon+2(\phi+\mu)) + \alpha((\epsilon+2\mu)(1+\alpha+\mu) + (\alpha+\mu)(\phi_{NP}+\mu)(\epsilon+2(\phi+\mu)) \\ &\quad + 2(\phi+\phi_{NP}(\alpha+\mu)))) \\ P_2 &= \pi(\alpha+\delta+\epsilon+\mu)(2\alpha(\epsilon+2\mu+\phi) + \mu(\epsilon+2(\phi+\mu)) + \phi_{NP}(2\alpha+\epsilon+2(\phi+\mu))) \end{aligned}$$

,

$$T = \begin{pmatrix} 1-\alpha-\epsilon-\delta-\mu & 0 & 0 & 0 \\ \alpha & 1-\phi-\frac{\epsilon}{2}-\mu & 0 & 0 \\ \epsilon & 0 & 1-\alpha-\mu & 0 \\ 0 & \frac{\epsilon}{2} & \alpha & 1-\phi_{NP}-\mu \end{pmatrix} \tag{3.36}$$

then,

$$(I-T)^{-1} = \begin{pmatrix} \frac{1}{\alpha+\delta+\epsilon+\mu} & 0 & 0 & 0 \\ \frac{2\alpha}{(\alpha+\delta+\epsilon+\mu)(\epsilon+2(\phi+\mu))} & \frac{1}{\frac{\epsilon}{2}+\phi+\mu} & 0 & 0 \\ \frac{\epsilon}{(\alpha+\mu)(\alpha+\delta+\epsilon+\mu)} & 0 & \frac{1}{\alpha+\mu} & 0 \\ m & \frac{\epsilon}{(\epsilon+2(\phi+\mu))(\phi_{NP}+\mu)} & \frac{\alpha}{(\alpha+\mu)(\phi_{NP}+\mu)} & \frac{1}{\phi_{NP}+\mu} \end{pmatrix} \tag{3.37}$$

where,

$$m = \frac{\alpha\epsilon(\alpha+\epsilon+3\mu+2\phi)}{(\alpha+\mu)(\alpha+\epsilon+\delta+\mu)(\epsilon+2(\phi+\mu))(\phi_{NP}+\mu)}.$$

The next generation matrix $F(I-T)^{-1}$ is given as

$$F(I-T)^{-1} = \begin{pmatrix} Q_1 & Q_2 & Q_3 & Q_4 \\ Q_5 & Q_6 & Q_7 & Q_8 \\ Q_9 & Q_{10} & Q_{11} & Q_{12} \\ Q_{13} & Q_{14} & Q_{15} & Q_{16} \end{pmatrix}, \tag{3.38}$$

where

$$\begin{aligned}
Q_1 &= \frac{q_1+q_2}{4(\Lambda_N r_1+r_2)}, \\
q_1 &= \pi(\beta-4\Lambda_N)(\alpha\epsilon(\alpha+\epsilon+3\mu+2\phi)+2\alpha(\alpha+\mu)(\phi_{NP}+\mu)+\epsilon(\epsilon+2(\phi+\mu))), \\
q_2 &= (\alpha+\mu)(\epsilon+2(\phi+\mu))(\phi_{NP}+\mu), \\
Q_2 &= \frac{\pi(\alpha+\mu)(\alpha+\delta+\epsilon+\mu)(\epsilon+2\mu+2\phi_{NP})(\beta-4\Lambda_N)}{4(\Lambda_N r_1+r_2)}, \\
Q_3 &= \frac{\pi(\alpha+\delta+\epsilon+\mu)(\epsilon+2(\phi+\mu))(\beta-4\Lambda_N)(\alpha+\phi_{NP}+\mu)}{4(\Lambda_N r_1+r_2)}, \\
Q_4 &= \frac{\pi(\alpha+\mu)(\alpha+\delta+\epsilon+\mu)(\epsilon+2(\phi+\mu))(\beta-4\Lambda)}{4(\Lambda_N r_1+r_2)}, \\
r_1 &= \pi\epsilon(\mu+2\phi_{NP})(\epsilon+2(\phi+\mu))+\pi\alpha((\epsilon+2\alpha)(1+\alpha+\mu)+2(\phi+\phi_{NP}(\alpha+\mu)), \\
&\quad +\pi(\alpha+\mu)(\phi_{NP})(\epsilon+2(\phi+\mu)), \\
r_2 &= \pi(\alpha+\delta+\epsilon+\mu)(2\alpha(\epsilon+2\mu+\phi)+\mu(\epsilon+2(\phi+\mu)))+\phi_{NP}(2\alpha+\epsilon+2(\phi+\mu)).
\end{aligned}$$

The invasion reproduction number is given by

$$R_{inv} = Q_1. \tag{3.39}$$

We require that the condition, $\beta - 4\Lambda_N > 0$, always hold for the invasion reproduction number to be greater than zero and be valid. Where, Λ_N, is the real value obtained in equation (3.29).

Stability of an endemic equilibrium point E_1

The system (3.14)-(3.18) also has an endemic equilibrium points, the jacobian matrix is given by

$$J(S_N^*, S_P^*, M_{NP}^*, T_{S_P}^*, T_{M_{NP}}^*) = \begin{pmatrix} a & b & c & d & e \\ f & g & h & i & j \\ k & l & m & n & o \\ p & q & r & s & t \\ u & v & w & x & y \end{pmatrix} \tag{3.40}$$

where

$a = 1 - \Lambda_N(1 - \frac{S_N}{K^*}) - 2\alpha - \mu$, $b = -\frac{S_N^*(\beta\eta - 4\Lambda_N)}{4K^*}$
$(c, d, e) = -\frac{S_N^*(\beta - 4\Lambda_N)}{4K^*}$, $f = \Lambda_N$, $g = \frac{S_N^*(\beta\eta - 4\Lambda_N) - 4K^*(\alpha + \epsilon + \delta + \mu)}{4K^*}$
$(h, i, j) = \frac{S_N^*(\beta - 4\Lambda_N)}{4K^*}$, $(k, l, x, u) = \alpha$, $m = 1 - \phi - \frac{\epsilon}{2} - \mu$, $(n, p, r, t, v) = 0$, $q = \epsilon$,
$s = 1 - \alpha - \mu$ $w = \frac{\epsilon}{2}$, $y = 1 - \phi_{NP} - \mu$

$$K^* = \frac{\pi(k_1^* + k_2^*)}{k_3^*}$$

$$k_1^* = \epsilon(\mu + 2\phi_{NP})(\epsilon + 2(\phi + \mu)) + \pi\alpha((\epsilon + 2\mu)$$
$$(1 + \alpha + \mu)2\phi + 2\phi_{NP}(\alpha + \mu) + \pi(\alpha + \mu)(\phi_{NP} + \mu)(\epsilon$$
$$+ 2(\phi + \mu)))$$

$$k_2^* = \pi(\alpha + \delta + \epsilon + \mu)(2\alpha(\epsilon + 2\mu + \phi) + \mu(\epsilon + 2(\mu + \phi))$$
$$+ \phi_{NP}(2\alpha + \epsilon + 2(\phi + \mu)))$$

$$k^* = (\alpha + \mu)(\alpha + \epsilon + \delta + \mu)(\epsilon + 2(\phi + \mu))(\phi_{NP} + \mu)$$
$$(2\alpha + \lambda_N + \mu)$$

The characteristic equation for the matrix is given by

$$z_0\lambda^5 - \lambda^4 z_1 - \lambda^3 z_2 - \lambda^2 z_3 - \lambda z_4 - z_5 = 0 \tag{3.41}$$

where

$$
\begin{aligned}
z_0 &= 1 \\
z_1 &= s + g + y + m + a \\
z_2 &= qi + c + lh - eu - bf - sg - sy - sm - sa - gy - mg - my - ag - ay - ma \\
z_3 &= lcf - lhy + w - cg - cy - sc + kbh + df - qiy + qxj - qmi + sgy + smg + sag \\
&\quad + smy + say + mas + mgy + gya + mag + may + bfs + bfm + bfy + eus + eum \\
&\quad - buj - eug \\
z_4 &= qkdh - qkli + qmiy - qmxj + aiyq - axjq - qdfm - dfy + duj + efx - skbh \\
&\quad + scg + scy - sew - kbhy + kbwj + cgy - ewg - slah - slcf + lwj - lcfy + lujc \\
&\quad + lefw - lhu - smgy - sagy - masg - masy - magy - smbf - smeu - bfys - bfym \\
&\quad + bujs + bujm + eugs + eugm \\
z_5 &= qkciy - qkcjx - qkdhy + qkdwj - qkewi - qmaiy + qmaxj + qdfym - qdujm \\
&\quad - qefxm + qeuim + skbhy - skbwj - scgy + sewg - slahy + slwja + slcfy \\
&\quad - slcuj - slefw + slehu + masgy - bfysm - smuj - smeug
\end{aligned}
$$

Table 3.2: Descartes rule of signs on the characteristic equation (3.41)

z_0	z_1	z_2	z_3	z_4	z_5	Possible outcomes of positive and negative real roots and imaginary roots
+	-	+	+	+	+	2 or 0 positive; or exactly 1 negative; and 4 or 2 or 0 imaginary
+	-	+	+	+	-	3 or 1 positive; or atleast 2 or 0 negative; and 4 or 2 or 0 imaginary
+	-	+	+	-	+	4 or 2 or 0 positive; or atleast 3 or 1 negative; and 4 or 2 or 0 imaginary
+	-	+	-	+	+	4 or 2 or 0 positive; or atleast 3 or 1 negative; and 4 or 2 or 0 imaginary
+	-	-	+	+	+	2 or 0 positive; or atleast 3 or 1 negative; and 4 or 2 or 0 imaginary
+	-	+	+	-	-	3 or 1 positive; or atleast 2 or 0 negative; and 4 or 2 or 0 imaginary
+	-	-	+	-	-	3 or 1 positive; or atleast 4 or 2 or 0; and 4 or 2 or 0 imaginary
+	-	-	-	+	-	3 or 1 positive; or atleast 4 or 2 or 0; and 4 or 2 or 0 imaginary
+	-	+	-	-	-	3 or 1 positive; or atleast 2 or 0 negative; and 4 or 2 or 0 imaginary
+	-	+	-	-	+	4 or 2 or 0 positive; or 3 or 1 negative; and 4 or 2 or 0 imaginary
+	-	-	-	-	+	2 or 0 positive; or atleast 3 or 1 negative; and 4 or 2 or 0 imaginary
+	-	-	+	-	+	4 or 2 or 0 positive; atleast 3 or 1 negative; and 4 or 2 or 0 imaginary
+	-	-	-	+	+	2 or 0 positive; or atleast 3 or 1 negative; and 4 or 2 or 0 imaginary
+	-	+	-	+	-	5 or 3 or 1 positive; or 4 or 2 or 0 negative; and 4 or 2 or 0 imaginary
+	-	-	+	+	-	3 or 1 positive; or 4 or 2 or 0 negative; and 4 or 2 or 0 imaginary
+	-	-	-	-	-	exactly 1 positive; or 2 or 0 negative; and 4 or 2 or 0 imaginary

The Table 1.1 shows the real and imaginary roots for each possible change of signs we could have in the characteristic equation (3.41). There is at least one positive real root, hence, an endemic equilibrium point is stable when $max\{|\lambda_1|, |\lambda_2|, |\lambda_3|, |\lambda_4|, |\lambda_5|\} < 1$.

3.3 Formation of serodiscordant couples through infection of HIV concordant negative married couples

We shall consider the model of the dynamics of HIV transmission amongst married couples and the formation of serodiscordant couples. This network consist of five compartments, namely, M_{NN}, M_{NP}, M_{PP}, $T_{M_{NP}}$ and $T_{M_{PP}}$. We assume the subtotal population to be

$$G = M_{NN} + M_{NP} + M_{PP} + T_{M_{NP}} + T_{M_{PP}}. \tag{3.42}$$

When one partner in the HIV concordant negative married couple, M_{NN}, gets infected with HIV, that couple progresses to join HIV serodiscordant couples in compartment, M_{NP}. When both partners from the HIV concordant negative couple, get infected with HIV, the couple progress to the HIV concordant positive couple's compartment, M_{PP} . The HIV concordant negative married couples are recruited at a constant rate, ζ. They are removed through infection with a force of infection, ω_{NN} (see equation 3.43) and through natural death at a rate, μ. Couples from this compartment are removed at the rate, τ_{NP}, to form serodiscordant couples and, τ_{PP}, to form HIV concordant positive couples so that $\tau = \tau_{NP} + \tau_{PP}$.

Serodiscordant couples recruitment is from the proportion of concordant negative married couple that is removed because one partner has been infected with HIV. When a seronegative partner in the serodiscordant couple gets infected with HIV, the couple will move to the HIV concordant positive couple's compartment, M_{PP},. Serodiscordant couples are also removed from the compartment, M_{NP}, when the HIV negative partner gets infected with a force of infection, ω_{NP}, (see equation 3.44) and move to the HIV positive concordant couple's compartment. When the seropositive partner in a serodiscordant couple takes treatment the couple moves to the treated serodiscordant compartment, $T_{M_{NP}}$, at a constant treatment rate, ϵ. We assume that when both partners in the HIV concordant positive couple, M_{PP}, take treatment the couple moves to the HIV concordant positive treated compartment at a constant treatment rate, ϵ, and also the couples are removed from this compartment through the blanket death at a rate $(\delta + \mu)$.

3.3.1 Forces of infection

The married couples HIV transmission network has a total number of ten individuals involved in the transmission dynamics of HIV at any particular time, two from each compartment M_{NN}, M_{NP}, M_{PP}, $T_{M_{NP}}$ and $T_{M_{PP}}$. The compartments M_{NP}, M_{PP}, $T_{M_{NP}}$ and $T_{M_{PP}}$ are the four sources of infection for every HIV negative individual in the population. Six individuals are infectious, one from each of the serodiscordant couples, M_{NP}, and $T_{M_{NP}}$, two from each of the HIV positive concordant couples, M_{PP} and $T_{M_{PP}}$. Hence, HIV negative individual's chances of getting infected with HIV from M_{NP} and $T_{M_{NP}}$ is $\frac{1}{6}$ and from M_{PP} and $T_{M_{PP}}$ is $\frac{1}{3}$.

Force of infection for M_{NN}

We assume that HIV concordant negative couples are also exposed to the risk of being infected with HIV by the HIV positive individuals from compartments, M_{NP}, M_{PP}, $T_{M_{NP}}$ and $T_{M_{PP}}$. We also assume that infectious individuals have the same HIV transmission rate. We assume that, $\theta > 1$, is amplification factor that indicates a greater chance that infectious individuals from M_{NP} and M_{PP} have to infect HIV negative individuals compared to infectious individuals from the compartments $T_{M_{NP}}$ and $T_{M_{PP}}$ who have less chances because of an intensive counseling they got before and after taking treatment. Therefore the force of infection of M_{NN}, is denoted by, ω_{NN}, given by

$$\omega_{NN} = \frac{\beta}{6G}(\theta M_{NP} + 2\theta M_{PP} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.43}$$

Force of infection for M_{NP}

We assume that the HIV negative partners in serodiscordant couples are exposed to more risk of contracting the disease from their HIV positive partners since couples stay together and have sex frequently and the use of prevention measures is very low [42, 32]. However, we assume that the HIV negative partners in serodiscordant couples are still at risk of contracting HIV from outside partners. The HIV negative individual in the serodiscordant couple have a risk of being infected by individuals from the compartments, M_{PP}, $T_{M_{NP}}$, $T_{M_{PP}}$. We assume that, γ, indicates greater chances that seropositive partner in the serodiscordant couple has to infect the seronegative partner compared to the other infectious individuals. However, infectious individuals from the compartment, M_{PP} have an amplification factor, ψ, indicating greater chances of infecting HIV negative individuals compared to individuals from the treated compartments, $T_{M_{NP}}$, $T_{M_{PP}}$. Therefore, the force of infection for the HIV negative individual in the serodiscordant couples, M_{NP}, denoted by, ω_{NP}, given by

$$\omega_{NP} = \frac{\beta}{6G}(\gamma M_{NP} + 2\psi M_{PP} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.44}$$

where $\gamma > \psi > 1$.

Force of infection for $T_{M_{NP}}$

We assume that the seronegative individuals from the treated serodiscordant couples compartment, $T_{M_{NP}}$, are also exposed to a risk of contracting HIV from the infectious individuals in the population.

However, we assume that individuals who are on treatment are more cautious than individuals who are not taking treatment because of counseling. Therefore, they will rather be engaged in an outside sexual relationship with an individual who is also treated for HIV because they could be both willing to protect each other but we do not neglect that there are possibilities that an individual from the treated compartment could be in a sexual relationship with someone outside the treated compartments. The chances in which individuals from the compartment, M_{NP} and M_{PP}, have to infect a seronegative individual from a treated serodiscordant couple is the same, while the amplification factor, κ, indicates that the treated HIV concordant positive couple has greater chances of infecting the seronegative individual in the treated serodiscordant couple compared to the compartments, M_{NP} and M_{PP}. However, the amplification factor, ϖ, indicates greater chances that seropositive partner in the treated serodiscordant couple has greater chances infecting the seronegative partner compared to all the infectious individuals in the population. We assume that ρ is the factor influencing the transmission rate.

$$\omega_T = \frac{\rho\beta}{6G}(M_{NP} + 2M_{PP} + \varpi T_{M_{NP}} + 2\kappa T_{M_{PP}}) \tag{3.45}$$

where $\varpi > \kappa > 1$.

The illustration in Figure 3.2 can be presented in continuous system of equation as follows:

$$\frac{dM_{NN}}{dt} = \zeta - \tau\omega_{NN}M_{NN} - \mu M_{NN}, \tag{3.46}$$

$$\frac{dM_{NP}}{dt} = \tau_{NP}\omega_{NN}M_{NN} - (\omega_{NP} + \frac{\epsilon}{2} + \mu)M_{NP}, \tag{3.47}$$

$$\frac{dM_{PP}}{dt} = \tau_{PP}\omega_{NN}M_{NN} + \omega_{NP}M_{NP} - (\mu + \delta + \epsilon)M_{PP} \tag{3.48}$$

$$\frac{dT_{M_{NP}}}{dt} = \frac{1}{2}\epsilon M_{NP} - \omega_T T_{M_{NP}} - \mu T_{M_{NP}}, \tag{3.49}$$

$$\frac{dT_{M_{PP}}}{dt} = \omega_T T_{NP} + \epsilon M_{PP} - \mu T_{M_{PP}}. \tag{3.50}$$

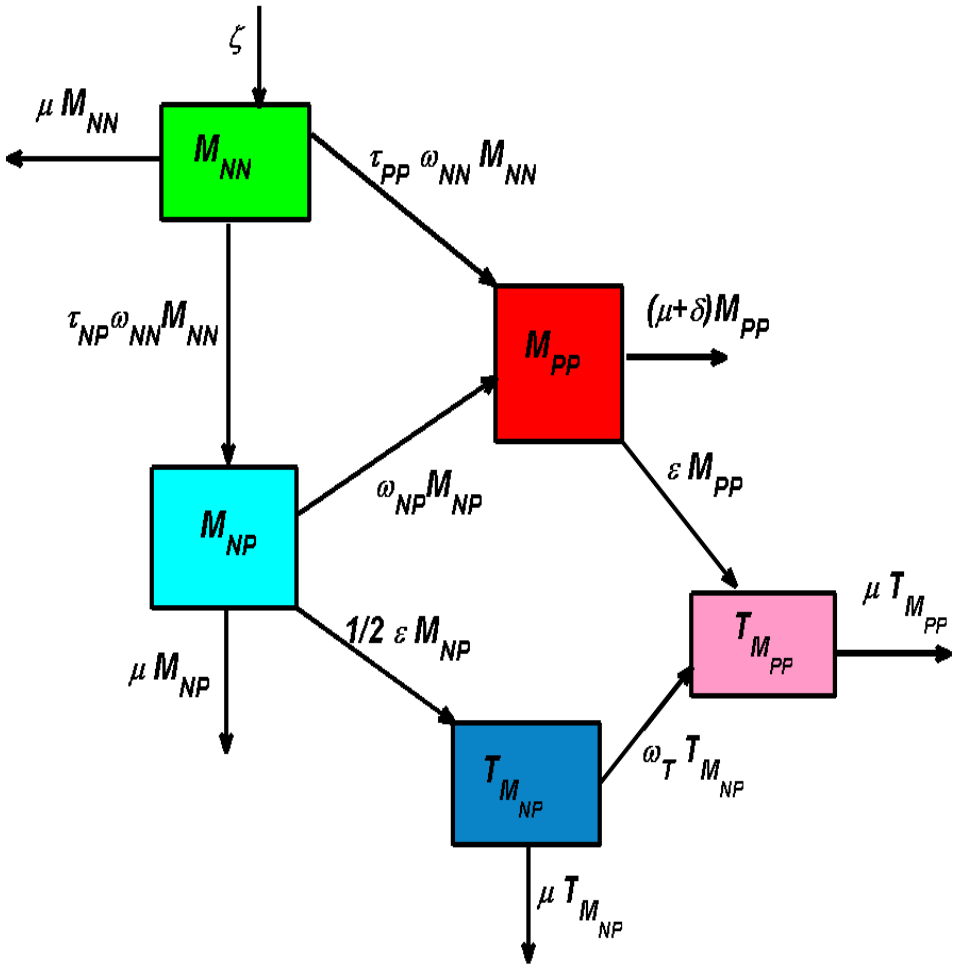

Figure 3.2: Schematic diagram that represents the formation and progression of serodiscordant couples.

3.3.2 Feasible region

The region, $\Gamma = \left\{(M_{NN}, M_{NP}, M_{PP}, T_{M_{NP}}, T_{M_{PP}}) \in \mathbb{R}^5_+ \mid G(t) \leq \frac{\zeta}{\mu}\right\}$, is feasible if it is positively invariant with respect to the model (3.46)-(3.50). Therefore, we have to prove that all the classes $M_{NN}, M_{NP}, M_{PP}, T_{M_{NP}}$ and $T_{M_{PP}}$ are non-negative at all times ($t \geq 0$) and are bounded in the region Γ. We state and prove the positive invariance of solutions as in [38, 39]. The system of equations (3.46-3.50) has initial conditions given by $M_{NN}(0) \geq 0, M_{NP} \geq 0, M_{PP} \geq 0, T_{M_{NP}}(0) \geq 0, T_{M_{PP}}(0) \geq 0$.

Theorem 2. *The region $\Gamma \in \mathbb{R}^5_+$ is positively invariant with respect to the system of equations (3.46)-(3.50) and non-negative solutions exist for all time $0 < t < \infty$.*

Theorem 5 can be proved using the same technique used in section 3.2.2 Thus, region

$$\Gamma = \left\{ (M_{NN}, M_{NP}, M_{PP}, T_{M_{NP}}, T_{M_{PP}}) \in \mathbb{R}^5_+; G(t) \leq \frac{\zeta}{\mu} \right\} \tag{3.51}$$

is positively invariant for the system (3.46)-(3.50). Therefore, it is sufficient to study the dynamics of the model in region Γ, since all the solutions of the model (3.46)-(3.50) are both epidemiologically and mathematically feasible.

The system of continuous differential equation (3.46)-(3.50) can be represented in the following discrete form,

$$(M_{NN})_{t+1} = (M_{NN})_t + \zeta - \tau(\omega_{NN})_t M_{NN} - \mu(M_{NN})_t, \tag{3.52}$$

$$(M_{NP})_{t+1} = (M_{NP})_t + \tau_{NP}(\omega_{NN})_t(M_{NN})_t - (\omega_{NP})_t(M_{NP})_t - \frac{1}{2}\epsilon(M_{NP})_t - \mu(M_{NP})_t, \tag{3.53}$$

$$(M_{PP})_{t+1} = (M_{PP})_t + \tau_{PP}(\omega_{NN})_t(M_{NN})_t + (\omega_{NP})_t(M_{NP})_t - \epsilon(M_{PP})_t - (\mu+\delta)(M_{PP})_t, \tag{3.54}$$

$$(T_{NP})_{t+1} = (T_{M_{NP}})_t + \frac{1}{2}\epsilon(M_{NP})_t - \omega_T(T_{M_{NP}})_t - \mu(T_{M_{NP}})_t, \tag{3.55}$$

$$(T_{M_{PP}})_{t+1} = (T_{M_{PP}})_t + \omega_T(T_{NP})_t + \epsilon(M_{PP})_t - \mu(T_{M_{PP}})_t. \tag{3.56}$$

3.3.3 Existence of equilibria and the basic reproduction number

We have to determine the equilibrium points and the threshold value, R_0, and the stability analysis on the difference equations (3.52)-(3.56). The discrete system has a disease free equilibrium E_0 and an endemic equilibrium E_1.

Disease free equilibrium point

The system of discrete model (3.52)-(3.56) has the disease free equilibrium given by,

$$E_0 = \left(\frac{\zeta}{\mu}, 0, 0, 0, 0 \right) \tag{3.57}$$

Basic reproduction number

The discrete system (3.52)-(3.56) has four infectious compartments, therefore we need to make use of the next generation matrix as in [41]. Therefore we have that,

$$\mathcal{F}_i = \begin{bmatrix} \tau_{NP}(\omega_{NN})_t(M_{NN})_t \\ \tau_{PP}(\omega_{NN})_t(M_{NN})_t + (\omega_{NP})_t(M_{NP})_t \\ 0 \\ \omega_T T_{M_{NP}} \end{bmatrix}, \tag{3.58}$$

and

$$\mathcal{T}_i = \begin{bmatrix} (1-\omega_{NP}-\mu-\frac{1}{2}\epsilon)(M_{NP})_t \\ (1-\epsilon-\mu-\delta)(M_{PP})_t \\ \frac{1}{2}\epsilon M_{NP} - (1-\rho-\mu)T_{M_{NP}} \\ \epsilon M_{PP} - \mu T_{M_{PP}} \end{bmatrix}. \tag{3.59}$$

To formulate the next generation matrix we need to generate the two 4×4 matrices, F and $(I-T)^{-1}$, for new infections and for transition, respectively. Where I is the identity matrix corresponding to the 4×4 matrix, T. The matrices F and T are defined by;

$$F = \left[\frac{\partial \mathcal{F}_i(E_0)}{\partial x_j}\right] \quad and \quad T = \left[\frac{\partial \mathcal{T}_i(E_0)}{\partial x_j}\right], \tag{3.60}$$

for $1 \leq i, j \leq 4$. The disease free state is represented by the vector $x_0 = E_0$. We determined F and $(I-T)^{-1}$ to be,

$$F = \begin{pmatrix} \frac{\beta\tau_{NP}\theta}{6} & \frac{\beta\theta\tau_{NP}}{3} & \frac{\beta\tau_{NP}}{6} & \frac{\beta\tau_{NP}}{3} \\ \frac{\beta\theta\tau_{PP}}{6} & \frac{\beta\theta\tau_{PP}}{3} & \frac{\beta\tau_{PP}}{6} & \frac{\beta\tau_{PP}}{3} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.61}$$

and

$$T = \begin{pmatrix} 1-\frac{1}{2}\epsilon-\mu & 0 & 0 & 0 \\ 0 & 1-\epsilon-\mu-\delta & 0 & 0 \\ \frac{1}{2}\epsilon & 0 & 1-\mu & 0 \\ 0 & \epsilon & 0 & 1-\mu \end{pmatrix} \tag{3.62}$$

therefore,

$$(I-T)^{-1}=\begin{pmatrix} \frac{2}{\epsilon+2\mu} & 0 & 0 & 0 \\ 0 & \frac{1}{\epsilon+\mu+\delta} & 0 & 0 \\ \frac{\epsilon}{\mu(\epsilon+2\mu)} & 0 & \frac{1}{\mu} & 0 \\ 0 & \frac{\epsilon}{\mu(\delta+\epsilon+\mu)} & 0 & \frac{1}{\mu} \end{pmatrix} \tag{3.63}$$

Then the next generation matrix $F(I-T)^{-1}$ is given as,

$$F(I-T)^{-1}=\begin{pmatrix} \frac{\beta\tau_{NP}(2\theta\mu+\epsilon)}{6\mu(\epsilon+2\mu)} & \frac{\beta\tau_{NP}(\theta\mu+\epsilon)}{3\mu(\delta+\epsilon+\mu)} & \frac{\beta\tau_{NP}}{6\mu} & \frac{\beta\tau_{NP}}{3\mu} \\ \frac{\beta\tau_{PP}(2\theta\mu+\epsilon)}{6\mu(\epsilon+2\mu)} & \frac{\beta\tau_{PP}(\epsilon+\theta\mu)}{3\mu(\delta+\epsilon+\mu)} & \frac{\beta\tau_{PP}}{6\mu} & \frac{\beta\tau_{PP}}{3\mu} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}. \tag{3.64}$$

The eigenvalues of the matrix $F(I-T)^{-1}$ are given by;

$\lambda_{1,2}=0$, or $\lambda^2-\lambda(a+f)+af-be=0$

where

$$a=\frac{\beta\tau_{NP}(2\theta\mu+\epsilon)}{6\mu(\epsilon+2\mu)}, \qquad b=\frac{\beta\tau_{NP}(\theta\mu+\epsilon)}{3\mu(\delta+\epsilon+\mu)}$$
$$e=\frac{\beta\tau_{PP}(2\theta\mu+\epsilon)}{6\mu(\epsilon+2\mu)}, \qquad f=\frac{\beta\tau_{PP}(\epsilon+\theta\mu)}{3\mu(\delta+\epsilon+\mu)}.$$

Note, $af-be=0$, so that $\lambda_{1,2,3}=0$ and $\lambda_4=a+f$. Hence,

$$R_0=\frac{\beta(\tau_{NP}(\epsilon+2\theta\mu)(\delta+\epsilon+\mu)+2\tau_{PP}(\epsilon+\theta\mu)(\epsilon+2\mu))}{6\mu(\epsilon+2\mu)(\delta+\epsilon+\mu)}. \tag{3.65}$$

Endemic equilibrium point

The endemic equilibrium point of the discrete system (3.52)-(3.56) is given by,

$$E_1=(M^*_{NN},M^*_{NP},M^*_{PP},T_{M_{NP}},T_{M_{PP}}).$$

where

$$M^*_{NN} = \frac{\zeta}{\tau\omega_{NN} + \mu}, \tag{3.66}$$

$$M^*_{NP} = \frac{\tau_{NP\omega_{NN}\zeta}}{(\tau\omega_{NN} + \mu)(\omega_{NP} + \frac{1}{2}\epsilon + \mu)}, \tag{3.67}$$

$$M^*_{PP} = \frac{\zeta\omega_{NN}(\tau_{PP}(\omega_{NP} + \frac{1}{2}\epsilon + \mu) + \tau_{NP}\omega_{NP})}{(\tau\omega_{NN} + \mu)(\omega + \frac{1}{2}\epsilon + \mu)(\epsilon + \delta + \mu)}, \tag{3.68}$$

$$T^*_{S_P} = \frac{\tau_{NP}\omega_{NN}\zeta\epsilon}{2(\tau\omega_{NN} + \mu)(\omega_{NP} + \frac{1}{2}\epsilon + \mu)(\omega_T + \mu)}, \tag{3.69}$$

$$T^*_{M_{PP}} = \frac{\zeta\omega_{NN}\epsilon(\tau_{NP}\omega_T(\epsilon + \delta + \mu) + 2(\tau_{PP}(\omega_{NP} + \frac{1}{2}\epsilon + \mu) + \tau_{NP}\omega_{NP})(\omega_T + \mu))}{2\mu(\tau\omega_{NN} + \mu)(\omega_{NP} + \frac{1}{2}\epsilon + \mu)(\epsilon + \delta + \mu)(\omega_T + \mu)}. \tag{3.70}$$

and

$$\omega_{NN} = \frac{\beta}{6G}(\theta M_{NP} + 2\theta M_{PP} + T_{M_{NP}} + 2T_{M_{PP}}), \tag{3.71}$$

$$\omega_{NP} = \frac{\beta}{6G}(\gamma M_{NP} + 2\psi M_{PP} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.72}$$

$$\omega_T = \frac{\rho\beta}{6G}(M_{NP} + 2M_{PP} + \varpi T_{M_{NP}} + 2\kappa T_{M_{PP}}). \tag{3.73}$$

We investigate the existence of endemic equilibrium points using the fixed point theory. Therefore, we express the endemic equilibrium point in terms of the forces of infection (ω_{NN},ω_{NP}, ω_T). We express the forces of infection in terms of M_{NN}, M_{NP}, M_{PP}, $T_{M_{NP}}$ and $T_{M_{PP}}$ and determine the equilibrium points of the model (3.52)-(3.56) by finding the fixed points of the functions

$$\varphi = \begin{pmatrix} \varphi_1(\omega_{NN}, \omega_{NP}, \omega_T) \\ \varphi_2(\omega_{NN}, \omega_{NP}, \omega_T) \\ \varphi_3(\omega_{NN}, \omega_T, \omega_T) \end{pmatrix}$$

given by

$$\begin{pmatrix} \varphi_1(\omega_{NN}, \omega_{NP}, \omega_T) \\ \varphi_2(\omega_{NN}, \omega_{NP}, \omega_T) \\ \varphi_3(\omega_{NN}, \omega_{NP}, \omega_T) \end{pmatrix} = \begin{pmatrix} A \\ B \\ C \end{pmatrix} \tag{3.74}$$

where

$$A = \frac{\beta\omega_{NN}a_1(\epsilon+\mu+\omega_{NP})}{b}$$

$$a_1 = 2\mu(\theta\tau_{NP}(\delta+\epsilon+\mu)+\theta\tau_{PP}(\epsilon+2\mu)+2\omega_{NP}(\tau_{NP}+\tau_{PP}))(\omega_T+\mu+\epsilon(2\tau_{PP}(\epsilon+2\mu+2\omega_{NP}))$$
$$(\omega_T+\mu)+\tau_{NP}(4\omega_{NP}(\omega_T+\mu)+\epsilon(2\tau_{PP}(\epsilon+2\mu+2\omega_{NP})(\omega_T+\mu)+\tau_{NP}(4\omega_{NP}(\omega_T+\mu)$$
$$+(\delta+\epsilon+\mu)(2\omega_T+\mu))))$$

$$b = 3(2\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)(\epsilon+2\mu+2\tau_{NP}\omega_{NN}+2\omega_{NP})(\omega_T+\mu)+\omega_{NN}(\tau_{PP}(\epsilon+2\mu+2\omega_{NP})$$
$$(\epsilon^2+4\epsilon\mu+2\mu^2+2\omega_{NP}(\epsilon+\mu))(\omega_T+\mu)+\tau_{NP}(2\omega_{NP}(\delta\epsilon+(2\epsilon+\mu)(\epsilon+2\mu))(\omega_T+\mu)+4\omega_{NP}^2$$
$$(\epsilon+\mu)(\omega_T+\mu)+\epsilon(\delta+\epsilon+\mu)(2\mu(\epsilon+\mu)+\omega_T(\epsilon+2\mu)))))$$

$$B = \frac{\beta\omega_{NN}a_2(\epsilon+\mu+\omega_{NP})}{b}$$

$$a_2 = 2\mu(\tau_{PP}\psi(\epsilon+2\mu+2\omega_{NP})+\tau_{NP}(\gamma(\delta+\epsilon+\mu)+2\psi\omega_{NP}))(\omega_T+\mu)+\epsilon(2\tau_{PP}(\epsilon+2\mu+\omega_{NP})$$
$$(\omega_T+\mu)+\tau_{NP}(4\omega_{NP}(\omega_T+\mu)+(\delta+\epsilon+\mu)(\omega_T+\mu)))$$

$$C = \frac{\beta\omega_{NN}a_3(\epsilon+\mu+\omega_{NP})}{b}$$

$$a_3 = \rho(2\mu\tau_{NP}(\delta+\epsilon+\mu)(\omega_T+\mu)+2\epsilon\kappa(\tau_{PP}(\epsilon+2\mu+2\omega_{NP})(\omega_T+\mu)+\tau_{NP}((\delta+\epsilon+\mu)\omega_T$$
$$+2\omega_{NP}(\omega_T+\mu)+\mu(2\tau_{PP}(\epsilon+2\mu+2\omega_{NP})(\omega_T+\mu)+\tau_{NP}(\epsilon\varpi(\delta+\epsilon+\mu)+4\omega_{NP}(\omega_T+\mu))))))$$

.

The fixed point $(\omega_{NN}, \omega_{NP}, \omega_T) = (0, 0, 0)$ of (3.74) corresponds to the disease free equilibrium point.

To determine the endemic equilibrium we consider the real valued function $\varphi_1^{(\omega_{NN},\omega_{NP})}(\omega_T)$ for a fixed $(\omega_{NP}, \omega_{NN})$ as follows:

$$\varphi_1^{(\omega_{NN},\omega_{NP})}(\omega_T) = A. \tag{3.75}$$

We have that,

$$\varphi^{(\omega_{NN},\omega_{NP})}(0) = \frac{q_1}{q_2} > 0 \tag{3.76}$$

where

$$q_1 = \beta\omega_{NN}(\epsilon + \omega_{NP} + \mu)(2\mu(\theta\tau_{NP}(\delta + \epsilon + \mu) + \theta\tau_{PP}(\epsilon + 2\mu) + 2\omega_{NP}(\tau_{NP} + \tau_{PP}))(\mu + \epsilon(2\tau_{PP}$$
$$(\epsilon + 2\mu + 2\omega_{NP}))\mu + \tau_{NP}(4\omega_{NP}(\mu + \epsilon(2\tau_{PP}(\epsilon + 2\mu + 2\omega_{NP})\mu + \tau_{NP}(4\omega_{NP}\mu + (\delta + \epsilon + \mu)\mu))))))$$
$$q_2 = 3(2\mu(\delta + \epsilon + \mu)(\epsilon + \omega_{NP} + \mu)(\epsilon + 2\mu + 2\tau_{NP}\omega_{NN} + 2\omega_{NP})\mu + \omega_{NN}(\tau_{PP}(\epsilon + 2\mu + 2\omega_{NP})$$
$$(\epsilon^2 + 4\epsilon\mu + 2\mu^2 + 2\omega_{NP}(\epsilon + \mu))\mu + \tau_{NP}(2\omega_{NP}(\delta\epsilon + (2\epsilon + \mu)(\epsilon + 2\mu))\mu + 4\omega_{NP}^2(\epsilon + \mu)\mu + \epsilon(\delta + \epsilon + \mu)$$
$$(2\mu(\epsilon + \mu))))$$

and

$$\lim_{\omega_T \to \infty} \varphi_1^{(\omega_{NN}, \omega_{NP})}(\omega_T) = \frac{q_3}{q_4} < \infty$$

where

$$q_3 = \beta\omega_{NN}(\epsilon + \omega_{NP} + \mu)(2\mu\theta(\tau_{NP}(\delta + \epsilon + \mu) + \tau_{PP}(\epsilon + 2\mu) + 2\omega_{NP}(\tau_{NP} + \tau_{PP}))$$
$$+ \epsilon(4\tau_{NP}\omega_{NP} + 2(\epsilon + \delta + \mu)))$$
$$q_4 = 3(2\mu(\delta + \epsilon + \mu)(\epsilon + \omega_{NP} + \mu)(\epsilon + 2\mu + 2\tau_{NP}\omega_{NN} + 2\omega_{NP}) + \omega_{NN}(\tau_{PP}(\epsilon + 2\mu + 2\omega_{NP})$$
$$(\epsilon^2 + 4\epsilon\mu + 2\mu^2 + 2\omega_{NP}(\epsilon + \mu)) + \tau_{NP}(2\omega_{NP}(\delta\epsilon + (2\epsilon + \mu)(\epsilon + 2\mu)) + \tau_{NP}(2\omega_{NP}$$
$$(\delta\epsilon + (2\epsilon + \mu)(\epsilon + 2\mu)) + 4\omega^2(\epsilon + \mu) + \epsilon(\delta + \epsilon + \mu)(\epsilon + 2\mu))))$$

Therefore, $0 < \varphi_1^{(\omega_{NN}, \omega_{NP})}(\omega_T) < \infty$, hence the function $\varphi^{(\omega_{NN}, \omega_{NP})}(\omega_T)$ is bounded for every fixed $(\omega_{NN}, \omega_{NP}) > 0$.

We determine if the function $\varphi_1^{(\omega_{NN}, \omega_{NP})}(\omega_T)$ is increasing or decreasing through the first derivative given by

$$\frac{\partial\varphi_1^{(\omega_{NN}^*, \omega_{NP}^*)}}{\partial\omega_T} = \frac{r_1}{r_2} > 0$$
$$r_1 = \beta\epsilon\tau_{NP}\omega_{NN}\mu(\delta + \epsilon + \mu)(\epsilon + \omega_{NP} + \mu)(2\mu(\theta\epsilon\omega_{NN}(\tau_{PP}(\epsilon + \mu) + 2\omega_{NP}(\tau_{NP} + \tau_{PP}))$$
$$+ (\delta + \epsilon + \mu)((\epsilon + 2\mu + 2\omega_{NP})(\epsilon + 2\mu + 2\omega_{NP}) + \tau_{NP}\omega_{NN}(2\epsilon + \epsilon\theta + 2\mu + 2\omega_{NP}))) + \omega_{NN}(\tau_{PP}$$
$$(\epsilon + 2\mu + 2\omega_{NP})(3\epsilon^2 + 4\epsilon\mu + 2\mu^2 + 2\omega_{NP}(\epsilon + \mu)) + \tau_{NP}(\epsilon(\delta + \epsilon + \mu)(3\epsilon + 2\mu)$$
$$+ 2\omega_{NP}(\epsilon(\delta + \epsilon + \mu)(3\epsilon + 2\mu) + 2\omega_{NP}(\epsilon(\delta + 4\epsilon) + 5\epsilon\mu + 2\mu^2 + \omega_{NP}(\epsilon + \mu))))))$$
$$r_2 = 3(2\mu(\delta + \epsilon + \mu)(\epsilon + \omega_{NP} + \mu)(\epsilon + 2\mu + 2\tau_{NP}\omega_{NN} + 2\omega_{NP})(\omega_T + \mu) + \tau_{NP}(2(\delta\epsilon + (2\epsilon + \mu)$$
$$(\epsilon + 2\mu))$$
$$(\omega_T + \mu)\omega_{NP} + 4\omega^2(\epsilon + \mu)(\omega_T + \mu) + \epsilon(\delta + \epsilon + \mu)(2\mu(\epsilon + \mu) + \omega_T(\epsilon + 2\mu))))^2$$

and the second derivative of $\varphi_1^{(\omega_{NN},\omega_{NP})}(\omega_T)$ with respect to ω_T is given by

$$\frac{\partial^2\varphi_1^{(\omega_{NN},\omega_{NP})}}{\partial\omega_T^2} = \frac{r_3}{r_4} < 0$$

$$\begin{aligned}
r_3 = &-(2\beta\epsilon\tau_{NP}\omega_{NN}\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)(2\mu(\epsilon\theta\omega_{NN}(\tau_{PP}(\epsilon+2\mu)+2\omega_{NP}(\tau_{NP}+\tau_{PP}))\\
&+(\delta+\epsilon+\mu)((\epsilon+\omega_{NP}+\mu)(\epsilon+2\mu+2\omega_{NP})+\tau_{NP}\omega_{NN}(2\epsilon+\epsilon\theta+2\mu+2\omega_{NP})))\\
&+\omega_{NN}(\tau_{PP}(\epsilon+2\omega_{NP}+2\mu)(3\epsilon^2+4\epsilon\mu+2\mu^2+\omega_{NP}(\epsilon+\mu))+\tau_{NP}(\epsilon(\delta+\epsilon+\mu)\\
&(3\epsilon+2\mu)+2\omega_{NP}(\epsilon(\delta+4\epsilon)+5\epsilon\mu+2\mu^2+2\omega_{NP}(\epsilon+\mu))))(2\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)\\
&(\epsilon+2\tau_{NP}\omega_{NN}+2\omega_{NP})+\omega_{NN}(\tau_{PP}(\epsilon+2\mu+2\omega_{NP})(\epsilon^2+4\epsilon\mu+2\mu^2+2\omega_{NP}(\epsilon+\mu)\omega_{NP})\\
&+\tau_{NP}(\epsilon(\delta+\epsilon+\mu)(\epsilon+2\mu)+2\omega_{NP}(\delta\epsilon+(2\epsilon+\mu)(\epsilon+2\mu)+2\omega_{NP}(\epsilon+\mu)))))))\\
r_4 = &\,3(2\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)(\epsilon+2\mu+2\tau_{NP}\omega_{NN}+2\omega_{NP})(\omega_T+\mu)+\tau_{NP}(2(\delta\epsilon+(2\epsilon+\mu)\\
&(\epsilon+2\mu))(\omega_T+\mu)\omega_{NP}+4\omega_{NP}^2(\epsilon+\mu)(\omega_T+\mu)+\epsilon(\delta+\epsilon+\mu)(2\mu(\epsilon+\mu)+\omega_T(\epsilon+2\mu))))^3.
\end{aligned}$$

Since $\dfrac{\partial\varphi_1^{(\omega^*_{NN},\omega^*_{NP})}}{\partial\omega_T} > 0$ and $\dfrac{\partial^2\varphi_1^{(\omega^*_{NN},\omega^*_{NP})}}{\partial\omega_T^2} < 0$, the function $\varphi_1^{(\omega_{NN},\omega_{NP})}(\omega_T)$ is an increasing concave down function. Hence, there exist a unique point $\omega_T > 0$ satisfying $\dfrac{\partial^2\varphi_1^{(\omega^*_{NN},\omega^*_{NP})}}{\partial\omega_T^2} = \omega_T$.

For $(\omega_{NP}, \omega_T^*)$ we consider the real valued-function that depends on ω_{NN}.

$$\varphi_2^{(\omega_{NP},\omega_T^*)}(\omega_{NP}) = B. \tag{3.77}$$

Clearly

$$\varphi_2^{(\omega_{NP},\omega_T^*)}(0) = 0, \tag{3.78}$$

and

$$\lim_{\omega_{NN}\to\infty}\varphi_2^{(\omega_{NP},\omega_T^*)}(\omega_{NN}) = \frac{q_5}{q_6} < \infty.$$

$$q_5 = \beta(\epsilon + \omega_{NP} + \mu)(2\mu(\tau_{PP}\psi(\epsilon + 2\omega_{NP} + 2\mu) + \tau_{NP}(\gamma(\delta + \epsilon + \mu)))(\omega_T^* + \mu) + \epsilon$$
$$(2\tau_{PP}(\epsilon + 2\omega_{NP} + 2\mu)(\omega_T^* + \mu) + \tau_{NP}(4\omega_{NP}(\omega_T^* + \mu) + (\delta + \epsilon + \mu)(\omega_T^* + \mu))))$$
$$q_6 = 3(4\tau_{NP}\mu(\delta + \epsilon + \mu)(\epsilon + \omega_{NP} + \mu)(\omega_T^* + \mu) + \tau_{PP}(\epsilon + 2\mu + 2\omega_{NP})$$
$$(\epsilon^2 + 4\epsilon\mu + 2\mu^2 + 2\omega_{NP}(\epsilon + \mu))(\omega_T^* + \mu) + \tau_{NP}(2\omega_{NP}(\delta\epsilon + (2\epsilon + \mu)(\epsilon + 2\mu))(\omega_T^* + \mu) + 4\omega_{NP}^2$$
$$(\epsilon + \mu)(\omega_T^* + \mu) + \epsilon(\delta + \epsilon + \mu)(2\mu(\epsilon + \mu) + \omega_T^*(\epsilon + 2\mu))))$$

Therefore, $0 \leq \varphi_2^{(\omega_{NP}, \omega_T^*)}(\omega_{NN}) < \infty$, hence the function $\varphi_2^{(\omega_{NP}, \omega_T^*)}(\omega_{NN})$ is bounded for every fixed $(\omega_{NP}, \omega_T^*) > 0$

We also consider the first derivative with respect to ω_{NN} of the function $\varphi_2^{(\omega_{NP}, \omega_T^*)}(\omega_{NN})$ and is given as

$$\frac{\partial \varphi_2}{\partial \omega_{NN}} = \frac{q_7}{3(q_8)^2} < 0 \tag{3.79}$$

$$q_7 = -(4\beta\tau_{NP}\mu(\epsilon + \delta + \mu)(\epsilon + \omega_{NP} + \mu)(\omega_T^* + \mu)(2\gamma\tau_{NP}\mu(\delta + \epsilon + \mu)(\omega_T^* + \mu) + 2\psi\omega_{NN}\mu$$
$$(\tau(\epsilon + 2\mu) + 2\omega_{NP}(\tau_{NP} + \tau_{PP}))(\omega_T^* + \mu) + \epsilon\omega_{NN}(2\tau_{PP}(\epsilon + 2\mu + 2\omega_{NP})(\omega_T^* + \mu) + \tau_{NP}$$
$$(4\omega_{NP}(\omega_T^* + \mu) + (\delta + \epsilon + \mu)(2\omega_T^* + \mu)))))$$
$$q_8 = 2\mu(\delta + \epsilon + \mu)(\epsilon + \omega_{NP} + \mu)(\epsilon + 2\tau_{NP}\omega_{NN} + 2\mu)(\omega_T^* + \mu) + \omega_{NN}(\tau_{PP}(\epsilon + 2\omega_{NP} + 2\mu)$$
$$(\epsilon^2 + 4\epsilon\mu + 2\mu^2 + 2\omega_{NP}(\epsilon + \mu))(\omega_T^* + \mu) + \tau_{NP}(2\omega_{NP}(\delta\epsilon + (2\epsilon + \mu)(\epsilon + 2\mu))(\omega_T^* + \mu)$$
$$+ 4\omega_{NP}^2(\epsilon + \mu)(\omega_T^* + \mu) + \epsilon(\delta + \epsilon + \mu)(2\mu(\epsilon + \mu) + \omega_T^*(\epsilon + 2\mu))))$$

and the second derivative of the function $\varphi_2^{(\omega_{NP}, \omega_T^*)}(\omega_{NN})$ with respect to ω_{NN} is

$$\frac{\partial^2 \varphi_2}{\partial \omega_{NN}^2} = \frac{q_9}{3(q_8)^3} > 0 \tag{3.80}$$

$$q_9 = 32\beta\tau_{NP}^2\mu^2(\delta + \epsilon + \mu)^2(\epsilon + \omega_{NP} + \mu)(\omega_T^* + \mu)^2(2\gamma\omega_{NN}\tau_{NP}\mu(\delta + \epsilon + \mu)(\omega_T^* + \mu)$$
$$2\psi\omega_{NN}\mu(\tau_{PP}(\epsilon + 2\mu) + 2\omega_{NN}(\tau_{NP} + \tau_{PP}))(\omega_T^* + \mu) + \epsilon\omega_{NN}(2\tau_{PP}(\epsilon + 2\omega_{NP} + 2\mu)(\omega_T^* + \mu)$$
$$+ \tau_{NP}(4\omega_{NP}(\omega_T^* + \mu) + (\delta + \epsilon + \mu)(2\omega_T^* + \mu))))$$

Since $\dfrac{\partial\varphi_2^{(\omega_{NP},\omega_T^*)}}{\partial\omega_{NN}} < 0$ and $\dfrac{\partial^2\varphi_2^{(\omega_{NP},\omega_T^*)}}{\partial\omega_{NN}^2} > 0$, therefore the real valued function $\varphi_2^{(\omega_{NP},\omega_T^*)}(\omega_{NN})$ is a decreasing concave up function. This means that there exist a unique point $\omega_{NN}^* > 0$ satisfying $\varphi_2^{(\omega_{NP},\omega_T^*)}(\omega_{NN}^*) = \omega_{NN}^*$.

For $(\omega_{NN}^*, \omega_T^*)$ we consider the real valued-function that depends on ω_{NP}.

$$\varphi_3^{(\omega_{NN}^*,\omega_T^*)}(\omega_{NP}) = C \tag{3.81}$$

Clearly

$$\varphi_3^{\omega_{NN}^*,\omega_T^*}(0) = \frac{q_{10}}{q_{11}} > 0 \tag{3.82}$$

$$\begin{aligned}
q_{10} &= \beta\omega_{NN}^*(\epsilon+\mu)(\rho(2\mu\tau_{NP}(\delta+\epsilon+\mu)(\omega_T^*+\mu) + 2\epsilon\kappa(\tau_{PP}(\epsilon+2\mu)(\omega_T^*+\mu) + \tau_{NP}((\delta+\epsilon+\mu)\omega_T^* \\
&\quad + \mu(2\tau_{PP}(\epsilon+2\mu)(\omega_T^*+\mu) + \tau_{NP}(\epsilon\varpi(\delta+\epsilon+\mu) + 4\omega_{NP}^*(\omega_T^*+\mu)))))))) \\
q_{11} &= 3(2\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}^*+\mu)(\epsilon+2\mu+2\tau_{NP}\omega_{NN}^*+2\omega_{NP}^*)(\omega_T^*+\mu) + \omega_{NN}^*(\tau_{PP}(\epsilon+2\mu+2\omega_{NP}^*) \\
&\quad (\epsilon^2+4\epsilon\mu+2\mu^2)(\omega_T^*+\mu) + \tau_{NP}((\omega_T^*+\mu)(\epsilon+\mu)(\omega_T^*+\mu) + \epsilon(\delta+\epsilon+\mu)(2\mu(\epsilon+\mu)+\omega_T^*(\epsilon+2\mu)))))
\end{aligned}$$

and

$$\lim_{\omega_{NP}\to\infty} \varphi_3^{(\omega_{NN}^*,\omega_T^*)}(\omega_{NP}) = \frac{q_{12}}{q_{13}} < \infty.$$

$$\begin{aligned}
q_{12} &= \beta\omega_{NN}^*\rho(2\mu\tau_{NP}(\delta+\epsilon+\mu)(\omega_T^*+\mu) + 2\epsilon\kappa(\tau_{PP}(\epsilon+2\mu)(\omega_T^*+\mu) + \tau_{NP}((\delta+\epsilon+\mu)\omega_T^* \\
&\quad + \mu(2\tau_{PP}(\epsilon+2\mu)(\omega_T^*+\mu) + \tau_{NP}(\epsilon\varpi(\delta+\epsilon+\mu)))))) \\
q_{13} &= 3(2\mu(\delta+\epsilon+\mu)(\epsilon+\mu)(\epsilon+2\mu+2\tau_{NP}\omega_{NN}^*)(\omega_T^*+\mu) + \omega_{NN}^*(2\tau_{PP}\omega_{NP}(\epsilon^2+4\epsilon\mu+2\mu^2)(\omega_T^*+\mu) \\
&\quad + \tau_{NP}(2(\delta\epsilon+(2\epsilon+\mu)(\epsilon+2\mu))(\omega_T^*+\mu))))
\end{aligned}$$

Therefore, $0 < \varphi_2^{(\omega_{NN}^*,\omega_T^*)}(\omega_{NP}) < \infty$, hence the function $\varphi_2^{(\omega_{NN}^*,\omega_T^*)}(\omega_{NP})$ is bounded for every fixed $(\omega_{NN}^*, \omega_T^*) > 0$

We also consider the first derivative of the function $\varphi_3^{(\omega^*_{NN},\omega^*_T)}(\omega_{NP})$ with respect to ω_{NP} and is given as

$$\frac{\partial\varphi_3^{(\omega^*_{NN},\omega^*_T)}}{\partial\omega_{NP}} = \frac{q_{14}}{3(q_8)^2}$$

$$\begin{aligned}
q_{14} = &-(\beta\rho(8\mu\tau_{NP}(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)^2(\omega_T+\mu)(\omega_{NN}\mu(\delta+\epsilon+\mu)(\omega_T+\mu)\\
&-\epsilon\kappa\omega_{NN}(\mu(\epsilon+2\mu)+\omega_T(\mu-\delta)+2\tau_{PP}\omega_{NN}(\omega_T+\mu)))+\omega^2\mu(2\epsilon^2\tau^2\\
&(\epsilon+2\mu+\omega_{NP})^2(\omega_T+\mu)^2-\tau_{NP}\tau_{PP}(\omega_T+\mu)(-4\omega_{NP}^2(\epsilon\varpi+2(1+\varpi))\mu+\mu^2(\epsilon\varpi-2\epsilon)\\
&+\delta\epsilon(\epsilon\varpi-2\mu+\varpi\mu)+2\epsilon\omega_T(\epsilon-\delta-\mu))-8\omega_{NP}(\epsilon^3(\epsilon\varpi-\mu)+\epsilon^2\mu(3\epsilon\varpi-2\mu)\\
&+\epsilon(3\epsilon\varpi-2\mu)\mu^2+\epsilon\varpi\mu^3+\delta(\epsilon+\mu)(\epsilon(\epsilon\varpi-2\mu)+\epsilon\varpi\mu)-\epsilon\omega_T(\delta+\mu)(\epsilon+2\mu)\\
&+(\delta+\epsilon+\mu)(4\epsilon\mu^2(2\mu-3\epsilon\varpi)-4\epsilon\varpi\mu^3)+4\epsilon^2\mu(4\mu-3\epsilon\varpi)+\epsilon^3(8\mu-3\epsilon\varpi)+\epsilon^3\\
&(8\mu-3\epsilon\varpi)+2\epsilon\omega_T(\epsilon+2\mu)^2))+\tau_{NP}^2(4\omega_{NP}^2(\omega_T+\mu)(\epsilon^2\varpi(\delta+\epsilon)+\mu(2\epsilon^2\varpi+\delta\\
&(\epsilon\varpi-2\epsilon))+\mu^2(\epsilon\varpi-2\epsilon)-2\epsilon\omega_T(\delta+\mu))+8\omega_{NP}(\delta+\epsilon+\mu)(\omega_T+\mu)((\epsilon+\mu)\\
&(\epsilon^2\varpi-2\epsilon\varpi\mu)-\epsilon\omega_T(\epsilon+2\mu))+(\delta+\epsilon+\mu)(2\mu(\epsilon+\mu)(\epsilon^2(\epsilon\varpi-4\mu)+4\epsilon\mu(\epsilon\varpi-\mu)\\
&+2\epsilon\varpi\mu^2)+\omega_T(\delta\epsilon^3\varpi+(\epsilon+\mu)(3\epsilon^2(\epsilon\varpi-4\mu)+8\epsilon\mu(\epsilon\varpi-2\mu)+4\epsilon\varpi\mu^2)-4\epsilon\\
&(\epsilon+\mu)(\epsilon+2\mu)\omega_T))))+2\omega_{NN}(\epsilon^3\kappa\omega_{NN}\tau_{PP}^2(\epsilon+2\mu+\omega_{NP})^2(\omega_T+\mu)^2-\tau_{NP}(\omega_T+\mu)\\
&(2\epsilon\kappa\omega_{NN}\tau_{PP}(2\epsilon\mu((\epsilon+\mu)^2(\delta+\epsilon+\mu)+\omega_{NP}(\epsilon(2\delta+\epsilon)+2\mu(\delta+\epsilon+2\mu^2+\omega_{NP}\\
&(\delta+\mu-\epsilon)))-((\delta+\epsilon+\mu)(\epsilon^3+4\epsilon^2\mu-4\epsilon\mu^2+2\mu^3)+2\omega_{NP}(\epsilon^2(\delta+2\epsilon)+\epsilon\mu(2\delta+5\epsilon)+2\mu^2\\
&(\delta+2\epsilon)+2\mu^3+\omega_{NP}(2\epsilon^2+\mu(\delta+\mu)+\mu^2))\omega_T)-\mu(\delta+\epsilon+\mu)(\tau_{PP}\omega_{NN}(3\epsilon^3+4\epsilon^2\mu-4\epsilon\mu^2\\
&-4\mu^3+\omega_{NP}(\epsilon-\mu)(2(\epsilon+\mu)+\omega_{NP}))(\omega_T+\mu)+2\mu(\epsilon+\omega_{NP}+\mu)^2(\epsilon\varpi(\delta+\epsilon)+\mu(\epsilon\varpi-2\epsilon)\\
&-4\mu^2-2(\epsilon+2\mu)\omega_T)))+\tau_{NP}^2(\mu\omega_{NN}(\delta+\epsilon+\mu)(\omega_T+\mu)(2\mu(\epsilon+\mu)(\epsilon^2-2\mu^2)+(\delta\epsilon^2+(\epsilon+\mu)\\
&(3\epsilon^2-4\mu^2))\omega_T+8\omega_{NP}(\epsilon-\mu)(\omega_T+\mu)+4\omega^2(\epsilon-\mu)(\omega_T+\mu)+\epsilon\kappa\omega_{NN}(4\omega_{NP}^2(\omega_T+\mu)(\mu^2+\mu\\
&(\delta+\epsilon)-\epsilon\mu(\delta+\mu))-4\omega_{NP}(\omega_T+\mu)(\delta+\epsilon+\mu)(2\epsilon\mu(\epsilon+\mu)-\omega_T(\epsilon^2+2\epsilon\mu+2\mu^2))+(\delta+\epsilon+\mu)\\
&(-4\epsilon\mu^2(\epsilon+\mu)^2-4\mu(\epsilon-\mu)(\epsilon+\mu)^2)\omega_T+(\delta\epsilon^2+(\epsilon+\mu)(\epsilon+2\mu)^2\omega_T^2)))))))
\end{aligned}$$

and the second derivative of the function $\varphi_3^{(\omega^*_{NN},\omega^*_T)}(\omega_{NP})$ with respect to ω_{NP} is

$$\frac{\partial^2\varphi_3^{(\omega^*_{NN},\omega^*_T)}}{\partial\omega_{NP}^2} = \frac{2\beta\rho(q_{15})}{q_{16}}$$

$$q_{15} = -2\tau_{NP}(\epsilon+2\mu+2\omega_{NP})\Bigg(\frac{8\tau_{NP}\omega_{NN}}{(\epsilon+2\mu+2\omega_{NP})^2} - \frac{2\epsilon\omega_{NN}(\tau_{NP}+\tau_{PP})}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)} -$$

$$\frac{4\omega_{NN}(\tau_{NP}+\tau_{PP})}{(\delta+\epsilon+\mu)(\epsilon+2\mu+2\omega_{NP})} + \frac{2\omega_{NN}(\tau_{NP}\omega_{NP}+\tau_{PP}(\frac{\epsilon}{2}+\mu+\omega_{NP}))}{(\delta+\epsilon+\mu)(\frac{\epsilon}{2}+\mu+\omega_{NP})^2}$$

$$\frac{4\epsilon+\tau_{NP}\omega_{NN}}{(\epsilon+2\mu+2\omega_{NP})^2(\omega_T+\mu)} + \frac{\epsilon\omega_{NN}(\tau_{NP}\omega_T(\delta+\epsilon+\mu)+2(\tau_{NP}\omega_{NP}+\tau_{PP}(\frac{\epsilon}{2}+\omega_{NP}+\mu))(\omega_T+\mu))}{\mu(\delta+\epsilon+\mu)(\epsilon+\mu+\omega_{NP})^2(\omega_T+\mu)}\Bigg)$$

$$\Bigg(2+\frac{4\tau_{NP}\omega_{NN}}{\epsilon+2\mu+2\omega_{NP}} + \frac{2\omega_{NN}(\tau_{NP}\omega_{NP}+\tau_{PP}\big(\frac{\epsilon}{2}+\mu+\omega_{NP}\big))}{(\delta+\epsilon+\mu)\big(\frac{\epsilon}{2}+\omega_{NP}+\mu\big)} + \frac{\epsilon\omega_{NN}\tau_{NP}}{\big(\frac{\epsilon}{2}+\omega_{NP}+\mu\big)(\omega_T+\mu)} +$$

$$\frac{\epsilon\omega_{NN}(\tau_{NP}\omega_T(\delta+\epsilon+\mu)+2(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\omega_{NP}+\mu))(\omega_T+\mu))}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)(\omega_T+\mu)}\Bigg)(\mu\omega_{NN}(\epsilon(\delta\varpi+\epsilon-2\mu+\mu\varpi-$$

$$4\mu^2-2\omega_T(\epsilon+2\mu))+2((\mu\omega_{NN}(\delta+\epsilon+\mu)(\omega_T+\mu)-\epsilon\kappa\omega_{NN}(\mu(\epsilon+2\mu)+\omega_T(\mu-\delta))))))+4\tau_{NP}\Big($$

$$2+\frac{4\tau_{NP}\omega_{NN}}{\epsilon+2\mu+2\omega_{NP}} + \frac{2\omega_{NN}(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\mu+\omega_{NP}))}{(\delta+\epsilon+\mu)(0.5\epsilon+\omega_{NP}+\mu)} + \frac{\epsilon\omega_{NN}\tau_{NP}}{(0.5\epsilon+\omega_{NP}+\mu)(\omega_T+\mu)}$$

$$\frac{\epsilon\omega_{NN}(\tau_{NP}\omega_T(\delta+\epsilon+\mu)+2(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\omega_{NP}+\mu))(\omega_T+\mu))}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)(\omega_T+\mu)}\Big)^2(\mu\omega_{NN}(\epsilon(\delta\varpi+\epsilon\varpi-2\mu+$$

$$\varpi\mu-4\mu^2-2\omega_T(\epsilon+2\mu)))+2(\mu\omega_{NN}(\delta+\epsilon+\mu)(\omega_T)-\epsilon\kappa\omega_{NN}(\mu(\epsilon+2\mu)+\omega_T(\mu-\delta))))+(\epsilon+2\mu+2\omega_{NP})^2$$

$$\Big(\frac{8\epsilon\omega_{NN}\tau_{NP}}{(\epsilon+2\mu+2\omega_{NP})^2} - \frac{2\epsilon\omega_{NN}(\tau_{NP}+\tau_{PP})}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\epsilon)} - \frac{4\omega_{NN}(\tau_{NP}+\tau_{PP})}{(\delta+\epsilon+\mu)(\epsilon+2\mu+2\omega_{NP})} +$$

$$\frac{2\omega_{NN}(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\mu+\omega_{NP}))}{(\delta+\epsilon+\mu)(0.5\epsilon+\omega_{NP}+\mu^2)} + \frac{4\epsilon\omega_{NN}\tau_{NP}}{(\epsilon+2\mu+2\omega_{NP})^2(\omega_T+\mu)}$$

$$\frac{\epsilon\omega_{NN}(\tau_{NP}\omega_T(\delta+\epsilon+\mu)+2(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\mu+\omega_{NP}))(\omega_T+\mu))}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)^2(\omega_{T+\mu})}\Big)^2(\mu\omega_{NN}(2\tau_{PP}(\epsilon+2\mu+2\omega_{NP})(\omega_T+$$

$$\mu)+\tau_{NP}(\epsilon\varpi(\delta+\epsilon+\mu)+4\omega_{NP}(\omega_T+\mu)))+2(\mu\tau_{NP}\omega_{NN}(\delta+\epsilon+\mu)(\omega_T+\mu)+\epsilon\kappa\omega_{NN}(\tau_{PP}(\epsilon+2\mu+$$

$$2\omega_{NP})(\omega_T+\mu)+\tau_{NP}(\omega_T(\delta+\epsilon+\mu)+2\omega_{NP}(\omega_T+\mu)))))-(\epsilon+2\mu+2\omega_{NP})^2$$

$$\Big(\frac{2\tau_{NP}\omega_{NN}}{(0.5\epsilon+\mu+\omega_{NP})^3} - \frac{2\epsilon\omega_{NN}(\tau_{NP}+\tau_{PP})}{\mu(\delta+\epsilon+\mu)(\epsilon+\mu+\omega_{NP})^2} - \frac{8\omega_{NN}(\tau_{NP}+\tau_{PP})}{(\delta+\epsilon+\mu)(\epsilon+2\mu+2\omega_{NP})^2}$$

$$\frac{2\omega_{NN}(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\omega_{NP}+\mu))}{(\delta+\epsilon+\delta+\mu)(0.5\epsilon+\omega_{NP}+\mu)^3} + + \frac{\epsilon\omega_{NN}\tau_{NP}}{(\omega_T+\mu)}$$

$$+\frac{\epsilon\omega_{NN}(\tau_{NP}\omega_T(\delta+\epsilon+\mu)+2(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\omega_{NP}+\mu))(\omega_T+\mu))}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)^3(\omega_T+\mu)}\Big)$$

$$\Big(2+\frac{4\tau_{NP}\omega_{NN}}{\epsilon+2\mu+2\omega_{NP}} + \frac{2\omega_{NN}(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\mu+\omega_{NP}))}{(\delta+\epsilon+\mu)(0.5\epsilon+\mu+\omega_{NP})} + \frac{\epsilon\omega_{NN}\tau_{NP}}{(0.5\epsilon+\omega_{NP}+\mu)(\omega_T+\mu)}$$

$$\frac{\epsilon\omega_{NN}(\tau_{NP}\omega_T(\delta+\epsilon+\mu)+2(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\mu+\omega_{NP}))(\omega_{T+\mu}))}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)(\omega_T+\mu)}\Big)(\mu\omega_{NN}(2\tau_{PP}(\epsilon+2\mu+2\omega_{NP})(\omega_T+$$

$$\mu)+\tau_{NP}(\epsilon\varpi(\delta+\epsilon+\mu)+4\omega_{NP}(\omega_T+\mu)))+2(\mu\tau_{NP}\omega_{NN}(\delta+\epsilon+\mu)(\omega_T+\mu)+\epsilon\kappa\omega_{NN}(\tau_{PP}(\epsilon+2\mu+$$

$2\omega_{NP})(\omega_T+\mu)+\tau_{NP}(\omega_T(\delta+\epsilon+\mu)+2\omega_{NP}(\omega_T+\mu)))))$

$$q_{16}=3\mu(\delta+\epsilon+\mu)(\epsilon+2\mu+2\omega_{NP})^3(\omega_T+\mu)\Big(2+\frac{4\tau_{NP}\omega_{NN}}{\epsilon+2\mu+2\omega_{NP}}+$$
$$\frac{2\omega_{NN}(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\mu+\omega_{NP}))}{(\delta+\epsilon+\mu)(0.5\epsilon+\omega_{NP}+\mu)}+\frac{\epsilon\omega_{NN}\tau_{NP}}{(0.5\epsilon+\omega_{NP}+\mu)(\omega_T+\mu)}$$
$$\frac{\epsilon\omega_{NN}(\tau_{NP}\omega_T(\delta+\epsilon+\mu)+2(\tau_{NP}\omega_{NP}+\tau_{PP}(0.5\epsilon+\omega_{NP}+\mu))(\omega_T+\mu))}{\mu(\delta+\epsilon+\mu)(\epsilon+\omega_{NP}+\mu)(\omega_T+\mu)}\Big)$$

It is not clear whether the first and second derivatives are less than zero, or greater than zero, or equal to zero because of the complexity of the derivatives and different signs of parameters. However, the function $\varphi_3^{(\omega^*_{NN},\omega^*_T)}(\omega_{NP})$ could be one of the following possibilities,

Table 3.3: Slope and concavity of the function $\varphi_3^{(\omega^*_{NN},\omega^*_T)}(\omega_{NP})$

$\frac{\partial\varphi_3^{(\omega^*_{NN},\omega^*_{NP})}}{\partial\omega_{NP}}$	$\frac{\partial^2\varphi_3^{(\omega^*_{NN},\omega^*_{NP})}}{\partial\omega^2_{NP}}$	Possible outcomes of $\varphi_3^{(\omega^*_{NN},\omega^*_T)}(\omega_{NP})$
(i). <0	<0	Decreasing concave down function
(ii). >0	>0	Increasing concave up function
(iii). <0	>0	Decreasing concave up function
(iv). >0	<0	Increasing concave down function
(v). >0	$=0$	Increasing but no concavity
(vi). <0	$=0$	Decreasing but no concavity
(vii). $=0$	$=0$	neither increasing nor decreasing and no concavity

Therefore, we require that the function $\varphi_3^{(\omega^*_{NN},\omega^*_T)}(\omega_{NP})$ be any of (i)-(iv) of the possible outcomes in table 3.3, that would mean that there exist a unique point $\omega^*_{NP}>0$ satisfying $\varphi_3^{(\omega^*_{NN},\omega^*_T)}(\omega^*_{NP})=\omega^*_{NP}$. The possibilities (v)-(vii) allows the chance for change of convexity in the function.

3.3.4 Stability of equilibria

We determine the stability using the forces of infection equations (3.52)-(3.56). The Jacobian matrix is,

$$J^* = \begin{pmatrix} \frac{\partial \varphi_1}{\partial \omega_{NN}} & \frac{\partial \varphi_1}{\partial \omega_{NP}} & \frac{\partial \varphi_1}{\partial \omega_T} \\ \frac{\partial \varphi_2}{\partial \omega_{NN}} & \frac{\partial \varphi_2}{\partial \omega_{NP}} & \frac{\partial \varphi_2}{\partial \omega_T} \\ \frac{\partial \varphi_3}{\partial \omega_{NN}} & \frac{\partial \varphi_3}{\partial \omega_{NP}} & \frac{\partial \varphi_3}{\partial \omega_T} \end{pmatrix}. \tag{3.83}$$

Stability of the disease free equilibrium point

We set forces of infection to equal to zero and the corresponding Jacobian matrix of the equations (3.52)-(3.56) is given by,

$$J(0,0,0) = \begin{pmatrix} \frac{\beta(\tau_{NP}(\delta+\epsilon+\mu)(2\theta\mu+\epsilon)+2\tau_{PP}(\epsilon+2\mu)(\theta\mu+\epsilon))}{6\mu(\delta+\epsilon+\mu)(\epsilon+2\mu)} & 0 & 0 \\ \frac{\beta(2\mu\gamma\tau_{NP}(\delta+\epsilon+\mu)+2\mu\psi\tau_{PP}(\epsilon+2\mu)+\epsilon(2\tau_{PP}(\epsilon+2\mu)+\tau_{NP}(\delta+\epsilon+\mu)))}{6\mu(\epsilon+2\mu)(\delta+\epsilon+\mu)} & 0 & 0 \\ \frac{\beta\rho(\tau_{NP}(\delta+\epsilon+\mu)(2\mu+\epsilon\varpi)+2\tau_{PP}(\epsilon\kappa+\mu)(\epsilon+2\mu))}{6\mu(\delta+\epsilon+\mu)(\epsilon+2\mu)} & 0 & 0 \end{pmatrix} \tag{3.84}$$

The eigenvalues are given by, $\lambda_{1,2} = 0$ and $\lambda_3 = \frac{\beta(\tau_{NP}(\delta+\epsilon+\mu)(2\theta\mu+\epsilon)+2\tau_{PP}(\epsilon+2\mu)(\theta\mu+\epsilon))}{6\mu(\delta+\epsilon+\mu)(\epsilon+2\mu)}$. To determine stability we require that $max\{|\lambda_1|, |\lambda_2|, |\lambda_3|\} < 1$. Hence, the fixed point $(0,0,0)$ is stable when the dominant eigenvalue $|\lambda_3| = R_0 < 1$.

Stability of the endemic equilibrium E_1

The Jacobian matrix of the function $\varphi(\omega_{NN}, \omega_{NP}, \omega_T)$ at the unique equilibrium point $(\omega^*_{NN}, \omega^*_{NP}, \omega^*_T)$ is given as

$$J(\omega^*_{NN}, \omega^*_{NP}, \omega^*_T) = \begin{pmatrix} \frac{\partial \varphi_1}{\partial \omega_{NN}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} & \frac{\partial \varphi_1}{\partial \omega_{NP}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} & \frac{\partial \varphi_1}{\partial \omega_T}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} \\ \frac{\partial \varphi_2}{\partial \omega_{NN}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} & \frac{\partial \varphi_2}{\partial \omega_{NP}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} & \frac{\partial \varphi_2}{\partial \omega_T}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} \\ \frac{\partial \varphi_3}{\partial \omega_{NN}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} & \frac{\partial \varphi_3}{\partial \omega_{NP}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} & \frac{\partial \varphi_3}{\partial \omega_T}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} \end{pmatrix}. \tag{3.85}$$

where

$$\frac{\partial \varphi_1}{\partial \omega_{NN}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} = \frac{a_1}{a_2}$$

$$a_1 = \beta(\epsilon + \omega^*_{NP} + \mu)(2\mu(\mu + \omega^*_T)(\theta\tau_{NP}(\delta + \epsilon + \mu) + \theta(\tau_{PP}(\epsilon + 2\mu) + 2\omega^*_{NP}(\tau_{NP} + \tau_{PP}))))$$
$$+ \epsilon(2\tau_{PP}(\mu + \omega^*_T)(\epsilon + 2\mu + 2\omega^*_{NP})) + \tau_{NP}(4\omega^*_{NP}(\mu + \omega^*_T) + (\delta + \epsilon + \mu)(\omega^*_T + \mu))$$

$$a_2 = 6\mu(\delta + \epsilon + \mu)(\epsilon + \omega^*_{NP} + \mu)(\epsilon + 2\mu + 2\omega^*_{NP})(\omega^*_T + \mu)$$

$$\frac{\partial \varphi_2}{\partial \omega_{NN}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} = \frac{a_3}{a_2}$$

$$a_3 = \beta(\epsilon + \omega^*_{NP} + \mu)(2\gamma\tau_{NP}\mu(\omega^*_T)(\delta + \epsilon + \mu) + 2\psi\mu(\tau_{PP}(\epsilon + 2\mu) + 2\omega^*_{NP}(\tau_{NP} + \tau_{PP})))$$
$$+ \epsilon(2\tau_{PP}(\omega^*_T + \mu)(\epsilon + 2\omega^*_{NP} + 2\mu) + \tau_{NP}(4\omega^*_{NP}(\omega^*_T + \mu) + (\delta + \epsilon + \mu)(\omega^*_T + \mu)))$$

$$\frac{\partial \varphi_3}{\partial \omega_{NN}} = \frac{a_4}{a_2}$$

$$a_4 = \beta\rho(\epsilon + \omega^*_{NP} + \mu)(2\tau_{NP}\mu(\delta + \epsilon + \mu)(\omega^*_T + \mu) + 2\epsilon\kappa(\tau_{PP}(\epsilon + 2\omega^*_{NP} + 2\mu)(\omega^*_T + \mu)))$$
$$\tau_{NP}(\omega^*_T(\delta + \epsilon + \mu) + 2\omega^*_{NP}(\omega^*_T + \mu)) + \mu(2\tau_{PP}(\omega^*_T + \mu)(\epsilon + 2\mu + 2\omega^*_{NP}) + \tau_{NP}(\epsilon\varpi$$
$$(\delta + \epsilon + \mu) + 4\omega^*_{NP}(\omega^*_T + \mu)))$$

$$\frac{\partial \varphi_1}{\partial \omega_{NP}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} = \frac{a_5}{a_6}$$

$$a_5 = 6\beta\mu((\epsilon + 2\mu)(2\mu(\epsilon + \mu)(\delta + \epsilon + \mu) + (\epsilon^2 + 4\epsilon\mu + \mu^2)\tau_{PP}\omega^*_{NN})(\omega^*_T + \mu) + \tau_{NP}\omega^*_{NN}$$
$$(\delta + \epsilon + \mu)(2\mu(\epsilon + \mu)(\epsilon + 2\mu) + \omega^*_T(\epsilon^2 + 6\epsilon\mu + 4\mu^2))(\theta\tau_{NP}\omega^*_{NN}(\delta + \epsilon + \mu)$$
$$+ 2\theta\tau_{NP}\omega^*_{NP} + \theta\tau_{PP}(\epsilon + 2\omega^*_{NP} + 2\mu) + (\delta + \epsilon + \mu)(\mu + 2\omega^*_T)) + \omega^*_{NN}(\theta\tau_{NP}(\delta + \epsilon + \mu)$$
$$+ \theta\tau_{PP}(\epsilon + 2\mu)(\omega^*_T + \mu) + \epsilon(2\omega^*_{NP}(\mu(\delta + \epsilon + \mu) + \tau_{PP}\omega^*_{NN}(\epsilon + \mu))))$$
$$(\tau_{NP}\omega^*_{NN}(\delta\epsilon + (2\epsilon + \mu)(\epsilon + 2\mu) + 4\omega^*_{NP}(\epsilon + \mu)(\omega^*_T + \mu))$$
$$- 6(\epsilon + \mu)(\mu + \omega^*_T)(2\omega^*_{NP}(\mu(\delta + \epsilon + \mu) + \tau_{PP}\omega^*_{NN}(\epsilon + \mu)))))$$

$$a_6 = 9((\omega^*_T + \mu)(2(\delta + \epsilon + \mu)(\mu(\epsilon + \mu)(\epsilon + 2\mu) + 2\omega^{*2}\mu)$$
$$+ \tau_{PP}\omega^*_{NN}((\epsilon + 2\mu)(\epsilon^2 + 4\epsilon\mu + \mu^2) + 4\omega^{*2}_{NP}(\epsilon + \mu)) + \tau_{NP}\omega^*_{NN}(2\omega^*_{NP}(\omega^*_T + \mu)$$
$$(\delta\epsilon + (2\epsilon + \mu)(\epsilon + 2\mu)) + 8\omega^{*2}_{NP}(\epsilon + \mu)(\omega^{*2}_T + \mu) + (\delta + \epsilon + \mu)(2\mu(\epsilon + \mu)(\epsilon + 2\mu)$$
$$+ \omega^*_T(\epsilon^2 + 6\epsilon\mu + 4\mu^2)))))^2$$

$$\frac{\partial \varphi_2}{\partial \omega_{NP}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} = \frac{a_7}{a_8}$$

$$a_7 = \beta(2\gamma\tau_{NP}\omega^*_{NN}\mu(\omega^*_T+\mu)(\delta+\epsilon+\mu)+2\psi\mu\omega^*_{NN}(2\omega^*_{NP}(\omega^*_T+\mu)(\tau_{NP}+\tau_{PP}))$$
$$+\epsilon(2\tau_{PP}(2\omega^*_{NP}\mu+\omega^*_T)+4\tau_{NP}\omega^*_{NP}(\omega^*_T+\mu)))(3(2\mu(\delta+\epsilon+\mu)(\epsilon+\mu)(\omega^*_T+\mu)(\epsilon+2\mu$$
$$+2\tau_{NP}\omega^*_{NN})\omega^*_{NN}(\tau_{PP}(\epsilon+2\mu)(\mu+\omega^*_T)(\epsilon^2+4\epsilon\mu+\mu^2)+\tau_{NP}(\epsilon(\delta+\epsilon+\mu)(2\mu$$
$$(\epsilon+\mu)+\omega^*_T(\epsilon+2\mu))))))$$
$$-(3(4\omega_{NP}\mu(\omega^*_T+\mu)(\delta+\epsilon+\mu)+\omega^*_{NN}(4\tau_{PP}\omega^*_{NP}(\omega^*_T+\mu)(\epsilon+\mu)+\tau_{NP}(2(\omega^*_T+\mu)$$
$$(\delta\epsilon+(2\epsilon+\mu)(\epsilon+2\mu)+4\omega^*_{NP}(\epsilon+\mu)(\omega^*_T+\mu)))))(\beta(\epsilon+\mu)(2\gamma\tau_{NP}\omega^*_{NN}\mu)(\omega^*_T+\mu)(\delta+\epsilon$$
$$+\mu)2\tau_{PP}\mu(\omega^*_T+\mu)(\epsilon+2\mu)+\epsilon\omega^*_{NN}(2\tau_{PP}(\epsilon+2\mu)(\omega^*_T+\mu)+\tau(\delta+\epsilon+\mu)(2\omega^*_T+\mu))))$$

$$a_8 = (\omega^*_{NP}(3(4\omega^*_{NP}\mu(\omega^*_T+\mu)(\delta+\epsilon+\mu)+\omega^*_{NN}(4\tau_{PP}\omega^*_{NP}(\omega^*_T+\mu)(\epsilon+\mu)+\tau_{NP}(2(\omega^*_T+\mu)$$
$$(\delta\epsilon+(2\epsilon+\mu)(\epsilon+2\mu)+4\omega^*_{NP}(\epsilon+\mu)(\omega^*_T+\mu)))))+\beta(2\gamma\tau_{NP}\omega^*_{NN}\mu(\omega^*_T+\mu)(\delta+\epsilon+\mu)$$
$$+2\psi\mu\omega^*_{NN}(2\omega^*_{NP}(\omega^*_T+\mu)(\tau_{NP}+\tau_{PP}))$$
$$+\epsilon(2\tau_{PP}(2\omega^*_{NP}\mu+\omega^*_T)+4\tau_{NP}\omega^*_{NP}(\omega^*_T+\mu)))(3(2\mu(\delta+\epsilon+\mu)(\epsilon+\mu)(\omega^*_T+\mu)$$
$$(\epsilon+2\mu+2\tau_{NP}\omega^*_{NN}\omega^*_{NN}(\tau_{PP}(\epsilon+2\mu)(\mu+\omega^*_T)(\epsilon^2+4\epsilon\mu+\mu^2)+\tau_{NP}(\epsilon(\delta+\epsilon+\mu)$$
$$(2\mu(\epsilon+\mu)+\omega^*_T(\epsilon+2\mu)))))))^2$$

$$\frac{\partial \varphi_3}{\partial \omega_{NP}}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} = \frac{a_9}{a_8}$$

$$a_9 = \beta\rho(2\mu\tau_{NP}\omega^*_{NN}(\mu+\omega^*_T)(\delta+\epsilon+\mu)+2\epsilon\kappa\omega^*_{NN}(\tau_{PP}(\epsilon+2\mu+\omega^*_{NP})$$
$$(\omega^*_T+\mu)+\tau_{NP}(\omega^*_T(\delta+\epsilon+\mu)+2\omega^*_{NP}(\omega^*_T+\mu)))+\mu\omega^*_{NN}(2\tau_{PP}(\omega^*_T+\mu)(\epsilon$$
$$+2\mu+2\omega^*_{NP})+\tau_{NP}(\epsilon\varpi(\delta+\epsilon+\mu)+4\omega^*_{NP}(\omega^*_T+\mu)))(\beta(2\gamma\tau_{NP}\omega^*_{NN}\mu$$
$$(\omega^*_T+\mu)(\delta+\epsilon+\mu)+2\psi\mu\omega^*_{NN}(2\omega^*_{NP}(\omega^*_T+\mu)(\tau_{NP}+\tau_{PP}))+\epsilon(2\tau_{PP}(2\omega^*_{NP}$$
$$\mu+\omega^*_T)+4\tau_{NP}\omega^*_{NP}(\omega^*_T+\mu)))(3(2\mu(\delta+\epsilon+\mu)(\epsilon+\mu)(\omega^*_T+\mu)(\epsilon+2\mu+2\tau_{NP}\omega^*_{NN})$$
$$\omega^*_{NN}(\tau_{PP}(\epsilon+2\mu)(\mu+\omega^*_T)(\epsilon^2+4\epsilon\mu+\mu^2)+\tau_{NP}(\epsilon(\delta+\epsilon+\mu)(2\mu(\epsilon+\mu)$$
$$+\omega^*_T(\epsilon+2\mu))))))-(\epsilon+\mu)(3(4\omega^*_{NP}\mu(\omega^*_T+\mu)(\delta+\epsilon+\mu)+\omega^*_{NN}(4\tau_{PP}\omega^*_{NP}(\omega^*_T+\mu)$$
$$(\epsilon+\mu)+\tau_{NP}(2(\omega^*_T+\mu)(\delta\epsilon+(2\epsilon+\mu)(\epsilon+2\mu)+4\omega^*_{NP}(\epsilon+\mu)(\omega^*_T+\mu))))))$$

$$\frac{\partial \varphi_1}{\partial \omega_T}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} = \frac{a_{10}}{a_{11}}$$

$$a_{10} = \beta\epsilon\tau_{NP}\omega^*_{NN}(\epsilon+\omega^*_{NP}+\mu)(\delta+\epsilon+\mu)(2\mu(\epsilon\theta\omega^*_{NN}(\tau_{PP}(\epsilon+2\mu)+2\omega^*_{NP}(\tau_{NP}+\tau_{PP}))$$
$$+(\delta+\epsilon+\mu)((\epsilon+\omega^*_{NP}+\mu)(\epsilon+2\mu+2\omega^*_{NP})+\tau_{NP}\omega^*_{NN}(2\epsilon+\epsilon\theta+2\omega^*_{NP}))$$
$$+\omega^*_{NN}(\tau_{PP}(\epsilon+2\mu+2\omega^*_{NP})(3\epsilon^2+4\epsilon\mu+2\mu^2+2\omega^*_{NP}(\epsilon+\mu))+\tau_{NP}(\epsilon(\delta+\epsilon+\mu)(3\epsilon+2\mu)$$
$$+2\omega^*_{NP}(\epsilon(\delta+4\epsilon)+5\epsilon\mu+2\mu^2+2\omega^*_{NP}(\epsilon+\mu))))))$$
$$a_{11} = 3(2\mu(\delta+\epsilon+\mu)(\epsilon+\omega^*_{NP}+\mu)(\epsilon+2\mu+2\tau_{NP}\omega^*_{NN}+2\omega^*_{NP}(\omega^*_T+\mu)+\omega^*_{NN}(\omega^*_T+\mu)$$
$$(\tau_{PP}(\epsilon+2\mu+2\omega^*_{NP})(\epsilon^2+4\epsilon\mu+2\mu^2+2\omega^*_{NP}(\epsilon+\mu)))+\tau_{NP}(2\omega^*_{NP}(\omega^*_T+\mu)$$
$$(\delta\epsilon+(2\epsilon+\mu)(\epsilon+2\mu))+4\omega^{*2}_{NP}(\epsilon+\mu)(\mu+\omega^*_T)+\epsilon(\delta+\epsilon+\mu)(2\mu(\epsilon+\mu)+\omega^*_T(\epsilon+2\mu)))))^2$$
$$\frac{\partial\varphi_2}{\partial\omega_T}|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)} = \frac{a_{12}}{a_{11}}$$
$$a_{12} = \beta\epsilon\tau_{NP}\omega^*_{NN}\mu(\epsilon+\mu+\omega^*_{NP})(2\epsilon\gamma\mu\tau_{NP}+2\mu(\epsilon\psi\omega^*_{NN}(\epsilon+2\mu+2\omega^*_{NP})$$
$$+(\delta+\epsilon+\mu)(\epsilon+2\mu+2\omega^*_{NP})(\epsilon+\omega^*_{NP}+\mu)+2\tau_{NP}(\epsilon\psi\omega^*_{NN}\omega^*_{NP}$$
$$+\omega^*_{NN}(\delta+\epsilon+\mu)(\epsilon+\omega^*_{NP}+\mu))+\omega^*_{NN}(\tau_{PP}(\epsilon+2\omega^*_{NP}+2\mu)(3\epsilon^2+4\epsilon\mu+2\mu^2+2\omega^*_{NP}$$
$$(\epsilon+\mu))+\tau_{NP}(\epsilon(\delta+\epsilon+\mu)(3\epsilon+2\mu)+2\omega^*_{NP}(\epsilon(\delta+4\epsilon)+5\epsilon\mu+2\mu^2+2\omega^*_{NP}(\epsilon+\mu))))))$$
$$\frac{\partial\varphi_3}{\partial\omega_T}|_{(\omega_{NN},\omega_{NP},\omega_T)} = \frac{a_{13}}{a_{14}}$$
$$a_{13} = \beta\rho\tau_{NP}\omega^*_{NN}\mu(\frac{\epsilon}{2}+\omega^*_{NP}+\mu)(\epsilon+\omega^*_{NP}+\mu)(\epsilon+2\omega^*_{NP}+2\mu)(2\mu\tau_{NP}\omega^*_{NN}(\delta+\epsilon+\mu)$$
$$+\epsilon\tau_{NP}\omega^*_{NN}(\delta\epsilon\varpi-(\delta+\mu)(\epsilon\varpi+4\mu))+(\epsilon+\omega^*_{NP}+\mu)(\tau_{PP}\mu(2\epsilon-3\epsilon\varpi-2\mu\varpi)+$$
$$2\omega^*_{NN}(2\epsilon(2\mu\epsilon-\epsilon\varpi(\delta+\mu))+4\kappa\mu(\delta+\epsilon+\mu)(\epsilon+2\mu+2\tau_{NP}\omega^*_{NN})$$
$$+2(2\kappa\omega^*_{NN}(\epsilon\tau_{NP}(\delta+\epsilon+\mu)+\tau_{PP}(\epsilon+\mu)(\epsilon+2\mu)))-\epsilon\varpi\mu(\delta+\epsilon+\mu)(\epsilon+2\mu+2\tau_{NP}\omega^*_{NN}))))$$
$$-4(\varpi-2\kappa)(\omega^*_T+\mu)(\mu(\delta+\epsilon+\mu)+\omega^*_{NN}(\epsilon+\mu)(\tau_{NP}+\tau_{PP}))$$
$$a_{14} = \epsilon\tau_{NP}\omega^*_{NN}\mu(\delta+\epsilon+\mu)(\epsilon+\mu+\omega^*_{NP})(\epsilon+2\omega^*_{NP}+2\mu)+(\frac{\epsilon}{2}+\omega^*_{NP}+\mu)(\epsilon+\omega^*_{NP}+\mu)$$
$$(\omega^*_T+\mu)+2\mu\tau_{NP}\omega^*_{NN}(\delta+\epsilon+\mu)(\epsilon+\omega^*_{NP}+\mu)(\epsilon+2\mu+2\omega^*_{NP})(\mu+\omega^*_T)+2\mu\omega^*_{NN}(\epsilon+\omega^*_{NP}+$$
$$\mu)(\epsilon+2\mu+2\omega^*_{NP})\tau_{NP}\omega^*_{NP}+\tau_{PP}(\frac{\epsilon}{2}+\mu+\omega^*_{NP})(\omega^*_T+\mu)+\frac{\epsilon}{2}\omega^*_{NN}(\epsilon+2\mu+2\omega^*_{NP})^2$$
$$(2\tau_{PP}(\epsilon+2\mu+2\omega^*_{NP})(\omega^*_T+\mu)+\tau_{NP}(\omega^*_T(2+\delta+\epsilon+\mu)+4\omega^*_{NP}(\omega^*_T+\mu)))$$

The characteristic equation is given as

$$\lambda^3-\lambda^2P_1|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)}-\lambda P_2|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)}+P_3|_{(\omega^*_{NN},\omega^*_{NP},\omega^*_T)}=0 \tag{3.86}$$

where,

$$
\begin{aligned}
P_0 &= 1 \\
P_1 &= \frac{\partial\varphi_1}{\partial\omega_{NN}} + \frac{\partial\varphi_2}{\partial\omega_{NP}} + \frac{\partial\varphi_3}{\partial\omega_T} + \frac{\partial\varphi_3}{\partial\omega_{NN}} - \frac{\partial\varphi_1}{\partial\omega_{NP}}\frac{\partial\varphi_2}{\partial\omega_{NN}} \\
P_2 &= \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_2}{\partial\omega_{NP}} + \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_T} + \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_{NN}} + \frac{\partial\varphi_2}{\partial\omega_{NP}}\frac{\partial\varphi_3}{\partial\omega_T} + \frac{\partial\varphi_3}{\partial\omega_{NN}}\frac{\partial\varphi_1}{\partial\omega_{NP}}\frac{\partial\varphi_2}{\partial\omega_T} \\
&\quad - \frac{\partial\varphi_1}{\partial\omega_{NP}}\frac{\partial\varphi_2}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_T} - \frac{\partial\varphi_3}{\partial\omega_{NN}}\frac{\partial\varphi_2}{\partial\omega_{NP}} + \frac{\partial\varphi_1}{\partial\omega_T}\frac{\partial\varphi_2}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_{NP}} - \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_1}{\partial\omega_{NP}}\frac{\partial\varphi_2}{\partial\omega_{NN}} \\
P_3 &= \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_2}{\partial\omega_{NP}}\frac{\partial\varphi_3}{\partial\omega_T} - \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_{NN}}\frac{\partial\varphi_2}{\partial\omega_{NP}} + \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_1}{\partial\omega_T}\frac{\partial\varphi_2}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_{NP}} \\
&\quad - \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_{NN}}\frac{\partial\varphi_2}{\partial\omega_T}\frac{\partial\varphi_1}{\partial\omega_{NP}} - \frac{\partial\varphi_1}{\partial\omega_{NN}}\frac{\partial\varphi_1}{\partial\omega_{NP}}\frac{\partial\varphi_2}{\partial\omega_{NN}}\frac{\partial\varphi_3}{\partial\omega_T}
\end{aligned}
$$

Every possibility we have on table 3.4 shows that there exist at least one positive real root. Hence,

Table 3.4: Descartes rule of signs on the characteristic equation 3.86

P_0	P_1	P_2	P_3	Possible outcomes of roots
+	+	+	+	0 positive; or atleast 1 negative; and 2 imaginary
+	+	+	-	exactly 1 positive; or at least 2 or 0 negative; and 2 or 0 imaginary
+	+	-	+	2 or 0 positive; or at least 3 or 1 negative; and 2 or 0 imaginary
+	+	-	-	exactly 1 positive; or at least 2 or 0 negative; and 2 or 0 imaginary
+	-	+	+	2 or 0 positive; or at least 1 negative; and 2 or 0 imaginary
+	-	+	-	3 or 1 positive; or at least 2 or 0 negative; and 2 or 0 imaginary
+	-	-	+	2 or 0 positive; or exactly 1 negative; and 2 or 0 imaginary
+	-	-	-	exactly 1 positive; or 0 negative; and 2 imaginary

for possibilities where we have one positive real valued root we require that $|\lambda| < 1$ for the fixed point to be stable, and for possibilities where we have more than one positive real root the fixed point is stable when $max\{|\lambda_1|, |\lambda_2|, |\lambda_3|\} < 1$.

3.4 Sensitivity analysis of parameters

The successful implementation of possible intervention strategies requires that we know the parameters which the reproduction number, R_0, and the invasion reproduction number, R_{inv}, are highly sensitive to. We investigate the effect that the transmission rate β and the treatment rate ϵ has on the reproduction number and the invasion reproduction number by performing the sensitivity analysis.

3.4.1 Sensitivity with respect to the transmission rate ,β,

We determine the change in R_0 and R_{inv} obtained in the sub-models (3.14)-(3.18) and (3.52)-(3.56), respectively, with respect to β. We have that

$$\frac{\partial R_0}{\partial \beta} = \frac{(\tau_{NP}(\epsilon + 2\theta\mu)(\delta + \epsilon + \mu) + 2\tau_{PP}(\epsilon + \theta\mu)(\epsilon + 2\mu))}{6\mu(\epsilon + 2\mu)(\delta + \epsilon + \mu)} > 0 \tag{3.87}$$

and

$$\frac{\partial R_{inv}}{\partial \beta} = \frac{r_1}{r_2} > 0 \tag{3.88}$$

where

$$r_1 = \pi(\alpha\epsilon(\alpha + \epsilon + 3\mu + 2\phi) + \epsilon(\epsilon(\epsilon + 2(\phi + \mu)) + 2\alpha(\alpha + \mu)(\phi_{NP} + \mu)))$$

$$r_2 = 4(\pi(\alpha + \delta + \epsilon + \mu)((2\alpha + \mu)(\epsilon + 2\mu) + 2\phi(\alpha + \mu)) + \phi_{NP}(2\alpha + \epsilon + 2(\phi + \mu)) + \lambda$$
$$(\pi\epsilon(\epsilon + 2(\phi + \mu))(2\phi_{NP} + \mu) + \pi\alpha((2\alpha + \epsilon)(1 + \alpha + \mu) + 2\phi + (\alpha + \mu)((\epsilon + 2(\phi + \mu))\pi$$
$$\phi_{NP} + 2\phi_{NP}))))$$

Since ,$\frac{\partial R_0}{\partial \beta} > 0$ and $\frac{\partial R_{inv}}{\partial \beta} > 0$, this means that the basic reproduction number, R_0, and the invasion reproduction number ,R_{inv}, increases with the transmission rate, β, in their respective subpopulations. If the transmission rate is high, we expect to have a high number new infections produced by an infectious individual introduced into the population. Therefore, the intervention strategies should target to lower the transmission rate.

3.4.2 Sensitivity with respect to the treatment rate, ϵ,

We determine the change in R_0 and R_{inv} obtained in the sub-models (3.14)-(3.18) and (3.52)-(3.56), respectively, with respect to ϵ. For

$$\frac{\partial R_0}{\partial \epsilon} = \frac{\beta(\tau_{NP}(\mu(1-\theta)) + \tau_{PP}(\delta + \mu(1-\theta)))}{3\mu(\epsilon + 2\mu)^2(\delta + \epsilon + \mu)^2} \tag{3.89}$$

where $\theta > 1$. If $\delta < \mu c_n$, where $c_n = \theta - 1$ is a positive constant term, then ,$\frac{\partial R_0}{\partial \epsilon} < 0$, this means that an increase in treatment rate, ϵ, decreases the basic reproduction number, R_0. This implies that given the condition that the HIV induced death rate is less than the natural death rate, the treatment rate is highly and positively effective on R_0. Each new infectious individual can only produce few number of new infections. If $\mu < b_n\delta$, where $b_n = \frac{\tau_{PP}}{\alpha}$ is a positive constant term, then, $\frac{\partial R_0}{\partial \epsilon} > 0$, this means that the treatment rate is not effective. This implies that given the condition that the HIV induced death rate times some positive constant, b_n, is greater than the natural death rate, the treatment rate would not be effective in reducing the number of new infections.

The rate of change of the invasion reproduction number with respect to the treatment rate is found as

$$\frac{\partial R_{inv}}{\partial \epsilon} = \frac{r_3}{r_4} \tag{3.90}$$

where

$$\begin{aligned}
r_3 = &-(\pi(2\alpha+\mu)(\alpha+\delta+2\epsilon+3\mu) + \Lambda_N\pi\alpha(1+\alpha+\mu) + \Lambda_N\pi\epsilon\mu + 2\pi\phi(\alpha+\mu) \\
&+ \Lambda_N\pi\alpha\phi_{NP}(\alpha+\mu) + \phi_{NP}(1+2\Lambda_N\epsilon\pi))((\alpha+\mu)(\epsilon+2(\phi+\mu))(\phi_{NP}+\mu) + \pi(\beta-4\Lambda_N) \\
&(\alpha\epsilon(\alpha+\epsilon+3\mu+2\phi) + \epsilon(\epsilon+2(\phi+\mu)) + 2\alpha(\alpha+\mu)(\phi_{NP}+\mu))) + (\pi(\beta-4\Lambda_N)(\alpha\epsilon \\
&2(\epsilon+\phi+\mu) + (\alpha+\mu)(\phi_{NP}+\mu))(\pi(\alpha+\delta+\epsilon+\mu)((2\alpha+\mu)(\epsilon+2\mu) + 2\phi(\alpha+\mu)) + \phi_{NP} \\
&(2\alpha+\epsilon+2(\phi+\mu)) + \Lambda_N(\pi\epsilon(\epsilon+2(\phi+\mu))(2\phi_{NP}+\mu) + \pi\alpha((2\alpha+\epsilon)(1+\alpha+\mu) + 2\phi \\
&+ (\alpha+\mu)((\epsilon+2(\phi+\mu))\pi\phi_{NP} + 2\phi_{NP})))) \\
r_4 = &\ 4(\pi(\delta+\alpha+\epsilon+\mu)((2\alpha+\mu)(\epsilon+2\mu) + 2\phi(\alpha+\mu)) + \phi_{NP}(2\alpha+\epsilon+2(\phi+\mu)) + \Lambda_N \\
&(\pi\epsilon(\epsilon+2(\phi+\mu))(2\phi_{NP}+\mu) + \pi\alpha((2\alpha+\epsilon)(1+\alpha+\mu) + 2\phi + (\alpha+\mu)((\epsilon+2(\phi+\mu))\pi\phi_{NP} \\
&+ 2\phi_{NP})))))^2.
\end{aligned}$$

Equation (3.90) indicates that the change in the invasion reproduction number with respect to the treatment rate indicates that , $\frac{\partial R_{inv}}{\partial \epsilon} < 0$ or $\frac{\partial R_{inv}}{\partial \epsilon} > 0$, depending on the values of parameters. If $\frac{\partial R_{inv}}{\partial \epsilon} < 0$, then the treatment rate is highly effective in reducing the number of new infections produced by an infectious individuals introduced into the population that is not entirely susceptible.

If $\frac{\partial R_{inv}}{\partial \epsilon} > 0$, then the treatment rate is not effective in reducing ,R_{inv}, an alternative intervention strategy should be considered.

When, $\frac{\partial R_0}{\partial \epsilon} < 0$, and ,$\frac{\partial R_{inv}}{\partial \epsilon} < 0$, the treatment rate has a positive effect on reducing the number of secondary infections and this is a desired outcome. Therefore, intervention strategies target must be to increase the treatment rate in the population.

3.5 Single's and married couples HIV transmission and serodiscordant couples formation model

In this section we present the main model which combines the HIV transmission dynamics of single individuals and married couples networks and formation of serodiscordant couples. The assumptions and description of parameters made in section 3.1 still hold in the main model. The main model consist of eight compartments, $S_N, S_P, M_{NN}, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}$ and $T_{M_{PP}}$, and the state variables definitions are still as in section 3.1. The total population size, R, is given by

$$R = S_N + S_P + M_{NN} + M_{NP} + M_{PP} + T_{S_P} + T_{M_{NP}} + T_{M_{PP}}.$$

We assume the state variables $S_N, S_P, M_{NN}, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}}$ are all positive since they represent compartments of the population which are assumed to have at least one or zero individual present in each compartment. We assume that single individuals and married couples could have sexual relations. We also assume that only the marriage dynamics that will lead to the formation of HIV serodiscordant couple is allowed or the marriage dynamic that may lead to the formation of serodiscordant couple in future. When the single HIV negative individuals from the compartment, S_N, get infected they progress to the compartment of single HIV positive individuals, S_P,. When a single HIV negative individual gets married to the single HIV positive individual, the couple will progress to the HIV serodiscordant couple's compartment. When two single HIV negative individuals get married to each other, they join the concordant HIV negative compartment. We assume that two HIV positive single individuals are restricted from marrying each other since they do not form serodiscordant couples and since there is no possibility that the couple may ever form serodiscordant couple. When single HIV positive individuals take treatment they move to the treated single HIV

positive individuals compartment, T_{S_P}, . individuals from the treated single HIV positive compartment could get married to HIV negative single individual from the compartment, S_N. When one partner from the HIV negative concordant couples, M_{NN}, gets HIV infection the couple moves to the HIV serodiscordant couples compartment, M_{NP}, and when both partners get infected they move to the HIV concordant positive couples compartment, M_{PP},. When the seronegative partner takes treatment the couple moves to the HIV serodiscordant treated compartment, $T_{M_{NP}}$. When a HIV negative partner from the serodiscordant couples gets the HIV infection the couple moves to the HIV positive concordant couple's compartment. When HIV positive concordant couple takes treatment the couple moves to the treated HIV positive concordant couple's compartment , $T_{M_{PP}}$. We assume the treatment rate to be a function of the demand for treatment rather than a constant treatment rate as in the sub-models.

We assume that the description of the recruitment rate of all single individuals and that of the proportion of HIV negative individuals recruited is the same as in section 3.2. Therefore the constant recruitment rate for single susceptible individuals is, π. Single HIV negative individuals are removed from the susceptible class , S_N, either through natural death at a constant death rate μ, or through union in marriage to HIV negative single individuals or HIV positive single individuals or the treated HIV positive single individual at a marriage rate α, and through HIV infection from infectious individuals with a force of infection, $\lambda_N(S_P, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}})$ (see equation 3.91). We note that in the case of single individuals who leave the class due to marriage, we have two HIV negative individual marrying one HIV positive single individual and one treated HIV positive single to form a serodiscordant couple that joins, M_{NP} and $T_{M_{NP}}$, respectively and also we have two HIV negative singles getting married to each other forming a HIV negative concordant couple. Therefore we have a total number of four individuals going out of this compartment at a constant marriage rate α, so that the rate of removal through marriage is, $4\alpha S_N$.

We assume that the description of the dynamics that occur to the compartment, S_P, is the same as that explained in section 3.2.. The recruitment of S_P is dependent on HIV infected individuals from S_N. They are removed through blanket death, $(\mu + \delta)$, and through marriage of HIV negative single individuals to form serodiscordant couples at a rate, α. They are also removed when a HIV single individuals takes treatment and move to the compartment, T_{S_P}, at a treatment rate, ϵ,. We assume that individuals in the treated compartment, T_{S_P}, are removed at a constant natural death rate, μ.

HIV negative concordant couples, M_{NN}, are recruited when two single HIV negative individuals get married to each other. They are removed from this compartment through infection of one partner with a force of infection, $\lambda_{NN}(S_P, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}})$ (see equation 3.93). We still assume that the proportion of M_{NN} removed is, τ, and , $\tau = \tau_{NP} + \tau_{PP}$, as in section 3.3. They are also removed through natural death at a rate, μ.

The serodiscordant couples are recruited when a single HIV negative individual, S_N, marries single HIV positive individual, S_P, and when one of the HIV negative concordant couple partner gets infected. Serodiscordant couples are removed from the compartment M_{NP} if the seronegative partner gets infected with a force of infection, $\lambda_{NP}(S_P, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}})$ (see equation 3.92), they move to HIV positive concordant couple's compartment. When the seropositive partner takes treatment the couple moves to the treated HIV serodiscordant compartment, $T_{M_{NP}}$ at a treatment rate, ϵ. We assume that married couples in the treated HIV serodiscordant compartment are removed at a constant natural death rate, μ. We also assume that when the seronegative partner in the treated HIV serodiscordant couple gets infected with a force of infection , $\lambda_T(S_P, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}})$, that partner takes treatment immediately and the couples moves to the treated HIV positive concordant couple's compartment.

The HIV positive concordant married couples, M_{PP}, are recruited from the HIV infection of the HIV negative individual from the HIV serodiscordant couple, infection of both partners in the HIV concordant negative couples single HIV positive, and also through marriage of two HIV positive single individuals. We assume that for HIV positive concordant couples both partners take treatment at the same time so that they move to the treated HIV positive concordant couple's compartment. The couples are also removed from this compartment through the blanket deaths at a rate, $(\mu + \delta)$. We assume that couples from the treated HIV positive concordant compartment, $T_{M_{PP}}$, are removed at a constant natural death rate, μ.

3.5.1 Forces of infection

We assume that out of a total population R, for an infection to be possible, at most thirteen individuals are involved in the HIV transmission event at any particular time one from each compartment,

S_N, S_P and T_{S_P}, and two from each class $M_{NP}, M_{NN}, M_{PP}, T_{M_{NP}}$ and $T_{M_{PP}}$. There are six compartments that are sources of infection for every HIV negative individual in the population namely , $S_P, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}}$ and eight individuals are infectious, one from the HIV positive single's and one from the treated HIV positive single's, one from the HIV serodiscordant couple and one from the treated HIV serodiscordant couple, and two from the HIV positive concordant couple and two form the treated HIV positive concordant couple. Therefore, an HIV negative individual's chances of getting HIV infection from S_P and T_{S_P} is $\frac{1}{6}$, from M_{NP} and $T_{M_{NP}}$ is also $\frac{1}{6}$ and from M_{PP} and $T_{M_{PP}}$ is $\frac{2}{6}$.

Force of infection for HIV Negative Individuals, S_N,

We assume that the assumptions made in subsection 3.2.1 about the force of infection for, S_N, holds. We also assume that HIV positive single individuals from the compartment, S_P, have greater chances of spreading HIV to other single HIV negative individuals from the compartment, S_N, because of the same reasons stated in subsection 3.2.1. As a result S_P's rate of infecting S_N is amplified by a factor $\eta > 1$. We assume that HIV positive married individuals from the compartment, M_{NP}, M_{PP}, $T_{M_{NP}}$ and $T_{M_{PP}}$ have equal and less chances of transmitting the disease to the HIV negative single individuals, S_N, since they are restricted by the wedlock obligation. The force of infection for, S_N, denoted by, λ_N, is given by

$$\lambda_N = \frac{\beta}{4R}(\eta S_P + M_{NP} + 2M_{PP} + T_{M_{NP}} + 2T_{M_{PP}}). \tag{3.91}$$

Force of infection for HIV Serodiscordant Couples, M_{NP},

The HIV negative individuals in the serodiscordant couples also have chances of being infected by the three sources of infection. Evidence from the study in [32] showed that about 25% - 29% of HIV transmission within the serodiscordant couples was from outside partners. Therefore, we assume that outside partners have an equal chance to have sexual relationship with the HIV negative individual in the serodiscordant couple. The force of infection for, M_{NP}, denoted by, λ_{NP}, is given by

$$\lambda_{NP} = \frac{\beta}{6R}(S_P + \gamma M_{NP} + 2\psi M_{PP} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.92}$$

where $\gamma > 1$ indicates the higher chances the HIV seropositive partner have to infect the HIV seronegative partner within the serodiscordant couples and $\psi > 1$ also indicates better chances that HIV

positive concordant couples have to infect the HIV seronegative partner in the HIV serodiscordant couple.

Force of infection for HIV Concordant negative couples, M_{NN},

The susceptible individuals from the the HIV concordant negative couples also have chances of being infected with HIV by outside partners. The evidence available in [43] showed that in some countries with poor resource settings most man in HIV concordant negative relationships spend most time in bars and trading centres and most of them engage in multiple sexual relationships of which the level of condom use is low mostly because of high alcohol consumption. Therefore, the compartment M_{NN} is also exposed to infection transmission from the six sources of infection. Assume that individuals from the compartment, S_P, have high chances of engaging and infecting individuals from the compartment, M_{NN}, because the single individuals are free to take decisions based on their interests without the influence and pressure from any partner. We also assume that M_{NP}, $M_{PP}, T_{M_{NP}}$ and $T_{M_{PP}}$ have an equal rate of infecting, M_{NN}. As evidenced in [33, 42, 43, 32], where individuals have been found to have a similar sexual behavior and both partners are most likely going to have sexual partners outside their marriage, preferably single individuals. This still supports our assumption that M_{NP}, $M_{PP}, T_{M_{NP}}$ and $T_{M_{PP}}$ have less rate of infection than S_P to transmit the infection to M_{NN}. The force of infection of, M_{NN}, is denoted by, λ_{NN}, given by

$$\lambda_{NN} = \frac{\beta}{6R}(\sigma S_P + M_{NP} + M_{PP} + T_{S_P} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.93}$$

where $\sigma > 1$ indicates the increased rate of infection that individuals from the class S_P have to transmit infection to M_{NN}.

Force of infection for treated serodiscordant couples, $T_{M_{NP}}$,

We assume that seronegative partners from the treated HIV serodiscordant are also exposed to the risk of being infected by the HIV positive individuals from the sources of infection compartments. We assume that the seropositive partner in the treated HIV serodiscordant couple has chances of infecting the seronegative partner because of the frequency of sexual relation. We also assume that the transmission rate of HIV to treated individuals is influenced by some term, ρ, indicating that

treated individuals tend to be more cautious. The treated HIV positive concordant couple also has better chances of infecting the seronegative partner in the treated HIV serodiscordant couple compared to others who do not take treatment. The force of infection of, $T_{M_{NP}}$, is denoted by, λ_T, given by

$$\lambda_T = \frac{\beta\rho}{6R}(S_P + M_{NP} + M_{PP} + T_{S_P} + \varpi T_{M_{NP}} + 2\kappa T_{M_{PP}}) \tag{3.94}$$

where $\varpi > \kappa > 1$ are amplification factors and $0 < \rho < 1$.

Comparison of η, γ, σ, ψ, ϖ, κ

The parameters, η, γ, σ, ψ, ϖ and κ indicate the amplification factors that HIV positive individuals may have to transmit HIV infection to HIV negative individuals. The amplification factor, γ, corresponds to the HIV seropositive partner in the serodiscordant married couple in the force of infection for serodiscordant married couples, individuals can easily transmit the HIV infection to each other since individuals are married and likely to have sex frequently. The amplification factor, η, corresponds to a single HIV positive individual in the force of infection for a single HIV negative individual, single individuals have a greater rate of infection towards each other but their rate of infection is not as high as that of married couples since they may not be able to have sex as frequently as the married couples. The amplification factor, σ, corresponds to the single HIV positive individual in the force of infection for HIV negative concordant couple. A single HIV positive individual has a greater rate of infecting individuals from the HIV negative concordant couple class compared to, M_{NP} and M_{PP}, since the married couples are more restricted than the single individuals in terms of engaging with different sexual partners. The amplification factor, ψ, correspond to the HIV positive concordant couples in the force of infection for HIV serodiscordant married couples indicating the greater chances that infectious individuals from the compartment, M_{PP}, have to infect seronegative partner in the serodiscordant married couple compared to all other compartments except for, M_{NP},. The amplification factor, ϖ, corresponds to the treated HIV serodiscordant married couple indicating greater chances that the HIV seropositive partner have to infect the HIV seronegative partner for the same reason given to HIV serodiscordant married couple without treatment. However, we assume that a treated HIV seropositive partner is more cautious than untreated HIV seropositive partner but this does not change the assumption that they have sex frequently with their HIV seronegative partners than any other partner outside their marriage. The amplification factor, κ, correspond to the treated HIV positive concordant married couple indicating a high chance that they have in in-

fecting the seronegative partner in the treated HIV serodiscordant married couple. This is because we assumed that individuals from the treated compartment mostly prefer to have sexual relations with someone who has been exposed to HIV counseling and taking treatment.

In comparison, we assume that the amplification factors weights are, $\gamma > \varpi > \eta > \sigma > \psi > \kappa > 1$.

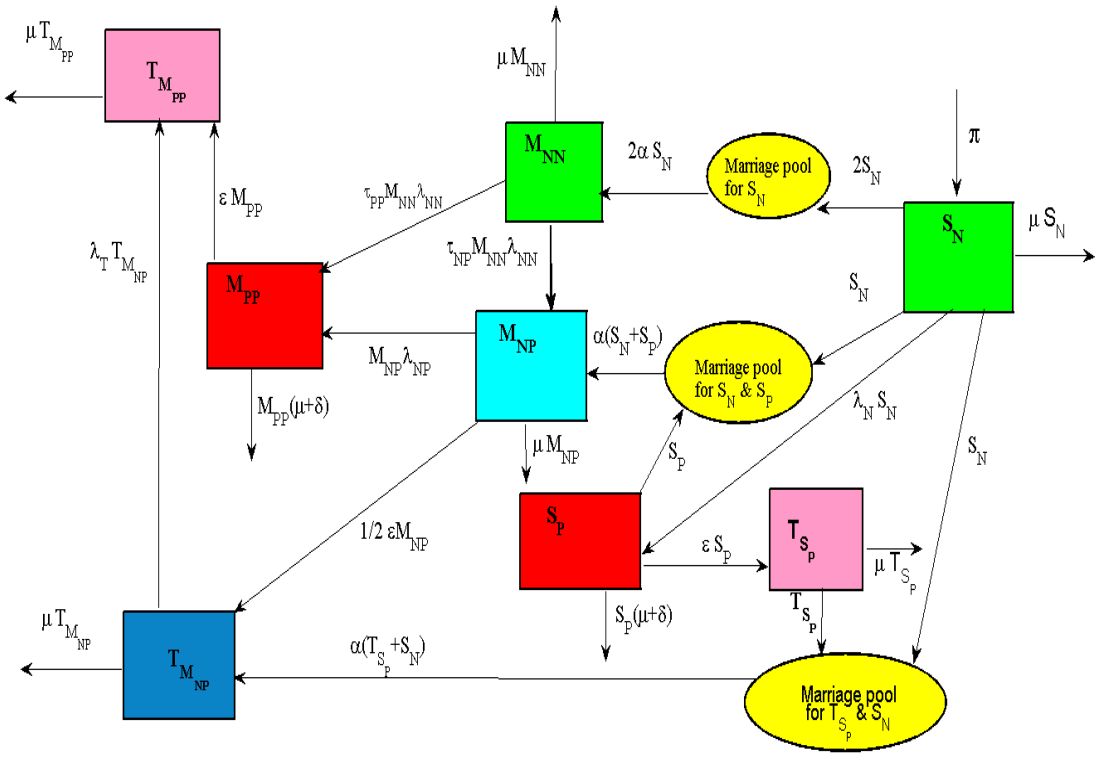

Figure 3.3: Schematic diagram that represent HIV transmission dynamics amongst single individuals and married couples.

The HIV transmission dynamics explained in section 3.5 and illustrated in Figure 3.3 is described by the system of continuous differential equations as follows;

$$\frac{dS_N}{dt} = \pi - \mu(S_N) - (\lambda_N)(S_N) - 4\alpha(S_N) - \mu(S_N), \tag{3.95}$$

$$\frac{dS_P}{dt} = (\lambda_N)(S_N) - \alpha(S_P) - \frac{\epsilon}{4}(S_P) - (\mu+\delta)(S_P), \tag{3.96}$$

$$\frac{dM_{NN}}{dt} = 2\alpha(S_N) - \tau(M_{NN})(\lambda_{NN}) - \mu(M_{NN}) \tag{3.97}$$

$$\frac{dM_{NP}}{dt} = \tau_{NP}(M_{NN})(\lambda_{NN}) + \alpha(S_N + S_P) - \frac{1}{4}\epsilon M_{NP} - M_{NP}\lambda_{NP} - \mu(M_{NP}), \tag{3.98}$$

$$\frac{dM_{PP}}{dt} = M_{NP}\lambda_{NP} + \tau_{PP}M_{NN}\lambda_{NN} - \frac{\epsilon}{2}(M_{PP})_t - (\mu+\delta)M_{PP} \tag{3.99}$$

$$\frac{dT_{S_P}}{dt} = \frac{\epsilon}{4}S_P - \alpha T_{S_P} - \mu T_{S_P}, \tag{3.100}$$

$$\frac{dT_{M_{NP}}}{dt} = \frac{1}{4}\epsilon M_{NP} + \alpha(S_N + T_{S_P}) - \lambda_T T_{M_{NP}} - \mu T_{M_{NP}} \tag{3.101}$$

$$\frac{dT_{M_{PP}}}{dt} = \frac{\epsilon}{2}M_{PP} + \lambda_T T_{M_{NP}} - \mu T_{M_{PP}}. \tag{3.102}$$

3.5.2 Feasible region

The region $\Psi = \left\{(S_N, S_P, M_{NN}, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}}) \in \mathbb{R}^8_+; R(t) \leq \frac{\pi}{\mu}\right\}$ is feasible if it is positively invariant with respect to the model (3.95)-(3.102). Therefore, we have to prove that all the classes $S_N, S_P, M_{NN}, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}$ and $T_{M_{PP}}$ are non-negative at all times ($t \geq 0$) and are bounded in the region Ψ. We state and prove the positive invariance of solutions as in [38, 39]. The system of equations (3.95)-(3.102) has initial conditions given by $S_N(0) \geq 0, S_P(0) \geq 0, M_{NN}(0) \geq 0, M_{NP}(0) \geq 0, M_{PP}(0) \geq 0, T_{S_P}(0) \geq, T_{M_{NP}}(0) \geq 0, T_{M_{PP}}(0) \geq 0$.

Theorem 3. *The region $\Psi \in \mathbb{R}^8_+$ is positively invariant with respect to the system of equations (3.95)-(3.102) and a non-negative solution exists for all time $0 < t < \infty$.*

Theorem 3 can be proved using the same technique used in subsection 3.2.2. Thus, the region

$$\Psi = \left\{(S_N, S_P, M_{NN}, M_{NP}, M_{PP}, T_{S_P}, T_{M_{NP}}, T_{M_{PP}}) \in \mathbb{R}^8_+; R(t) \leq \frac{\pi}{\mu}\right\} \tag{3.103}$$

is positively invariant for the model (3.95)-(3.102). The solutions of the model (3.95)-(3.102) are considered to be both biologically and mathematically feasible in the region Ψ, hence it is sufficient to study the dynamics of the model in Ψ.

The continuous model system of equations $(3.95) - (3.102)$ is transformed into the following discrete model:

$$(S_N)_{t+1} = (S_N)_t + \pi - (\lambda_N)_t(S_N)_t - 4\alpha(S_N)_t - \mu(S_N)_t, \tag{3.104}$$

$$(S_P)_{t+1} = (S_P)_t + (\lambda_N)_t(S_N)_t - \alpha(S_P)_t - \frac{\epsilon}{4}(S_P)_t - (\mu+\delta)(S_P)_t, \tag{3.105}$$

$$(M_{NN})_{t+1} = (M_{NN})_t + 2\alpha(S_N)_t - \tau(M_{NN})_t(\lambda_{NN})_t - \mu(M_{NN})_t \tag{3.106}$$

$$(M_{NP})_{t+1} = (M_{NP})_t + \tau_{NP}(M_{NN})_t(\lambda_{NN})_t + \alpha((S_N)_t + (S_P)_t) - \frac{1}{4}\epsilon(M_{NP})_t - (M_{NP})_t(\lambda_{NP})_t - \mu(M_{NP})_t, \tag{3.107}$$

$$(M_{PP})_{t+1} = (M_{PP})_t + (M_{NP})_t(\lambda_{NP})_t + \tau_{PP}(M_{NN})_t(\lambda_{NN})_t - \frac{\epsilon}{2}(M_{PP})_t - (\mu+\delta)(M_{PP})_t \tag{3.108}$$

$$(T_{S_P})_{t+1} = (T_{S_P})_t + \frac{\epsilon}{4}(S_P)_t - \alpha(T_{S_P})_t - \mu(T_{S_P}), \tag{3.109}$$

$$(T_{M_{NP}})_{t+1} = (T_{M_{NP}})_t + \frac{1}{4}\epsilon(M_{NP})_t + \alpha((S_N)_t + (T_{S_P})_t) - (\lambda_T)_t(T_{M_{NP}})_t - \mu(T_{M_{NP}})_t \tag{3.110}$$

$$(T_{M_{PP}})_{t+1} = (T_{M_{PP}})_t + \frac{\epsilon}{4}(M_{PP})_t + (\lambda_T)_t(T_{M_{NP}})_t - \mu(T_{M_{PP}})_t, \tag{3.111}$$

where

$$\lambda_N = \frac{\beta}{6R}(\eta S_P + M_{NP} + 2M_{PP} + T_{S_P} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.112}$$

$$\lambda_{NN} = \frac{\beta}{6R}(\sigma S_P + M_{NP} + 2M_{PP} + T_{S_P} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.113}$$

$$\lambda_{NP} = \frac{\beta}{6R}(S_P + \gamma M_{NP} + 2\psi M_{PP} + T_{S_P} + T_{M_{NP}} + 2T_{M_{PP}}) \tag{3.114}$$

$$\lambda_T = \frac{\beta}{6R}(S_P + M_{NP} + 2M_{PP} + T_{S_P} + \varpi T_{M_{NP}} + 2\kappa T_{M_{PP}}) \tag{3.115}$$

3.6 Existence of Equilibria

We have to determine the existence of the equilibrium points of the system (3.104)-(3.111).

3.6.1 Existence of equilibria

The discrete model (3.104)-(3.111) does not have a disease-free equilibrium point since the forces of infections are never zero and the serodiscordant couples always appear at equilibrium which shows the presence of the disease. Therefore, this system only has an endemic equilibrium point.

Endemic equilibrium point E_1

The model (3.104)-(3.115) has the endemic equilibrium point given by,

$E_1 = (S_N^*, S_P^*, M_{NN}^*, M_{NP}^*, M_{PP}^*, T_{S_P}, T_{M_{NP}}, T_{M_{PP}})$. where

$$S_N^* = \frac{\pi}{4\alpha + \lambda_N^* + \mu}, \tag{3.116}$$

$$S_P^* = \frac{\lambda_N^* \pi}{(4\alpha + \lambda_N^* + \mu)(\alpha + \epsilon + \mu + \delta)}, \tag{3.117}$$

$$M_{NN}^* = \frac{2\alpha\pi}{(4\alpha + \lambda_N^* + \mu)(\tau\lambda_{NN}^* + \mu)}, \tag{3.118}$$

$$M_{NP}^* = \frac{2\tau_{NP}\alpha\pi\lambda_{NN}^*(\alpha + \delta + \epsilon + \mu) + (\pi(\alpha + \epsilon + \delta + \mu) + \pi\lambda_N^*)(\tau\lambda_{NN}^* + \mu)}{(4\alpha + \lambda_N^* + \mu)(\tau\lambda_{NN}^* + \mu)(\alpha + \epsilon + \delta + \mu)} \tag{3.119}$$

$$M_{PP}^* = \frac{a_0}{(4\alpha + \lambda_N^* + \mu)(\tau\lambda_{NN}^* + \mu)(\alpha + \epsilon + \delta + \mu)} \tag{3.120}$$

$$T_{S_P}^* = \frac{\pi\lambda_N^*\epsilon}{\alpha + \mu} \tag{3.121}$$

$$T_{M_{NP}}^* = \frac{a_1}{2(4\alpha + \lambda_{NN}^* + \mu)(\tau\lambda_{NN}^* + \mu)(\alpha + \epsilon + \delta + \mu)(\lambda_T^* + \mu)} \tag{3.122}$$

$$T_{M_{PP}}^* = \frac{a_2}{2\mu(4\alpha + \lambda_{NN}^* + \mu)(\tau\lambda_{NN}^* + \mu)(\alpha + \epsilon + \delta + \mu)(\lambda_T^* + \mu)}, \tag{3.123}$$

where

$$\begin{aligned}
a_0 &= 2\alpha\pi\tau_{NP}\lambda_{NN}^*(\alpha + \epsilon + \delta + \mu) + \lambda_{NP}^*(2\tau\lambda_{NN}^*\alpha\pi(\alpha + \epsilon + \delta + \mu) \\
&\quad + (\pi(\alpha + \epsilon + \delta + \mu) + \pi\lambda_N^*)(\tau\lambda_{NN}^* + \mu)) \\
a_1 &= \epsilon(2\tau_{NP}\lambda_{NN}^*\alpha\pi(\alpha + \epsilon + \delta + \mu) + (\pi(\alpha + \epsilon + \delta + \mu) + \pi\lambda_N^*)(\tau\lambda_{NN} + \mu)) \\
&\quad + 2(\tau\lambda_{NN}^* + \mu)(\delta + \epsilon + \alpha + \mu)(\alpha\pi(\alpha + \mu) + \pi\lambda_N^*\epsilon(4\alpha + \lambda_N^* + \mu)) \\
a_2 &= 2\epsilon(\lambda_T^* + \mu)(2\alpha\pi\tau_{NP}\lambda_{NN}^*(\alpha + \epsilon + \delta + \mu) + \lambda_{NP}^*(2\tau\lambda_{NN}^*\alpha\pi \\
&\quad (\alpha + \epsilon + \delta + \mu) + (\pi(\alpha + \epsilon + \delta + \mu) + \pi\lambda_N^*)(\tau\lambda_{NN}^* + \mu))) + \lambda_T^*(\epsilon(2\tau_{NP} \\
&\quad \lambda_{NN}^*\alpha\pi(\alpha + \epsilon + \delta + \mu) + (\pi(\alpha + \epsilon + \delta + \mu) + \pi\lambda_N^*)(\tau\lambda_{NN} + \mu)) \\
&\quad + 2(\tau\lambda_{NN}^* + \mu)(\delta + \epsilon + \alpha + \mu)(\alpha\pi(\alpha + \mu) + \pi\lambda_N^*\epsilon(4\alpha + \lambda_N^* + \mu)))
\end{aligned}$$

3.6.2 Incorporating economic aspects

We consider and incorporate the economic aspects in the discrete system (3.104)-(3.111) to get an economic understanding of the system. We assumed the treatment rate to be a constant parameter in the sub-models, in this section we assume that it is an economic demand function of the prevalence, I_t, of the disease and the treatment price, p_t. This means that, $\epsilon = D(I^t, p^t)$. We also assume that everyone who is infected and take treatment reduces the HIV transmission rate in the population. We normalize the total population to unity,

$$\frac{(S_N)_t}{R(t)} + \frac{(S_P)_t}{R(t)} + \frac{(M_{NN})_t}{R(t)} + \frac{(M_{NP})_t}{R(t)} + \frac{(M_{PP})_t}{R(t)} + \frac{T_{S_P}}{R(t)} + \frac{T_{M_{NP}}}{R(t)} + \frac{T_{M_{PP}}}{R(t)} = 1, \tag{3.124}$$

we assume that the state variables are presented as,

$$\begin{aligned}
\frac{(S_N)_t}{R(t)} &= s_n(t), & \frac{S_P}{R(t)} &= s_p(t),\\
\frac{M_{NN}}{R(t)} &= m_{nn}(t), & \frac{M_{NP}}{R(t)} &= m_{np}(t),\\
\frac{M_{PP}}{R(t)} &= m_{pp}(t), & \frac{T_{S_P}}{R(t)} &= T_{s_p}(t),\\
\frac{T_{M_{NP}}}{R(t)} &= T_{m_{np}}(t), & \frac{T_{M_{PP}}}{R(t)} &= T_{m_{pp}}(t)
\end{aligned}$$

we also assume that the prevalence, I_t, of the disease is the total fraction of all the infected in the population

$$I_t = s_p(t) + m_{np}(t) + m_{pp}(t) + T_{s_p}(t) + T_{m_{np}}(t) + T_{m_{pp}}(t). \tag{3.125}$$

We assume that, $I^t \equiv \{I_j; j \geq t\}$, represents the prevalence future path and that, $p^t \equiv \{p_j; j \geq t\}$, represents a price future path. Therefore, the demand for treatment at time t as a function of the

two paths is given as $D(I^t, p^t)$. The discrete system (3.104)-(3.111) is transformed to be

$$(s_n)_{t+1} = (s_n)_t + \pi - (\overline{\lambda}_n)_t(s_n)_t - 4\alpha(s_n)_t - \mu(s_n)_t, \tag{3.126}$$

$$(s_p)_{t+1} = (s_p)_t[1 - \frac{1}{4}D(I^t, p^t)] + (\overline{\lambda}_n)_t(s_n)_t - \alpha(s_p)_t - (\mu + \delta)(s_p)_t, \tag{3.127}$$

$$(m_{nn})_{t+1} = (m_{nn})_t + 2\alpha(s_n)_t - \tau(m_{nn})_t(\overline{\lambda}_{nn})_t - \mu(m_{nn})_t \tag{3.128}$$

$$(m_{np})_{t+1} = (m_{np})_t[1 - \frac{1}{4}D(I^t, p^t)] + \tau_{np}(m_{nn})_t(\overline{\lambda}_{nn})_t + \alpha((s_n)_t + (s_p)_t) - (m_{np})_t(\overline{\lambda}_{np})_t - \mu(m_{np})_t, \tag{3.129}$$

$$(m_{pp})_{t+1} = (m_{pp})_t[1 - \frac{1}{2}D(I^t, p^t)] + (m_{np})_t(\overline{\lambda}_{np})_t + \tau_{pp}(m_{nn})_t(\overline{\lambda}_{nn})_t - (\mu + \delta)(M_{PP})_t \tag{3.130}$$

$$(T_{s_p})_{t+1} = (T_{s_p})_t + \frac{1}{4}(s_p)_t D(I^t, p^t) - \alpha(T_{s_p})_t - \mu(T_{s_p}), \tag{3.131}$$

$$(T_{m_{np}})_{t+1} = (T_{m_{np}})_t + \frac{1}{4}(m_{np})_t D(I^t, p^t) + \alpha((s_n)_t + (T_{s_p})_t) - (\overline{\lambda}_{tn})_t(T_{m_{np}})_t - \mu(T_{m_{np}})_t \tag{3.132}$$

$$(T_{m_{pp}})_{t+1} = (T_{m_{pp}})_t + \frac{1}{2}(m_{pp})_t D(I^t, p^t) + (\overline{\lambda}_{tn})_t(T_{m_{np}})_t - \mu(T_{m_{pp}})_t, \tag{3.133}$$

where

$$\overline{\lambda}_n = \frac{\beta}{6\overline{R}}\left(\overline{\eta}s_p + m_{np} + 2m_{pp} + T_{s_p} + T_{m_{np}} + 2T_{m_{pp}}\right), \tag{3.134}$$

$$\overline{\lambda}_{nn} = \frac{\beta}{6\overline{R}}\left(\overline{\sigma}s_p + m_{np} + 2m_{pp} + T_{s_p} + T_{m_{np}} + 2T_{m_{pp}}\right), \tag{3.135}$$

$$\overline{\lambda}_{np} = \frac{\beta}{6\overline{R}}\left(s_p + \overline{\gamma}m_{np} + 2\overline{\psi}m_{pp} + T_{s_p} + T_{m_{np}} + 2T_{m_{pp}}\right), \tag{3.136}$$

$$\overline{\lambda}_{tn} = \frac{\beta}{6\overline{R}}\left(s_p + m_{np} + 2m_{pp} + T_{s_p} + \overline{\varpi}T_{m_{np}} + 2\overline{\kappa}T_{m_{pp}}\right), \tag{3.137}$$

and

$$\overline{R}_t = (s_n)_t + (s_p)_t + (m_{nn})_t + (m_{np})_t + (m_{pp})_t + (T_{s_p})_t + (T_{m_{np}})_t + (T_{m_{pp}})_t. \tag{3.138}$$

The amplification factors have similar definitions and weights compared to each other as in subsection (3.5.1), $\overline{\gamma} > \overline{\varpi} > \overline{\eta} > \overline{\sigma} > \overline{\psi} > \overline{\kappa}$, but each amplification factor is now between zero and one.

3.6.3 Influence of prevalence and price on the demand for treatment

The HIV treatments have shown positive and effective results on prolonging human lives when taken accordingly. In regions like the sub-Saharan Africa mortality rates are very high due to HIV/AIDS and one of the main reasons for that is that people do not have an easy access to treatment because of high market prices of treatment. We focus on the assumption that the demand for treatment

is determined by the increase or decrease of prevalence in the population and also of prices in the medicine market and neglect all other economic factors which may also influence the demand for treatment. We assume that there is a positive relationship between the prevalence and treatment market prices. If the prevalence of HIV increases, the demand for treatment increases. Hence, the treatment market price also increase to a certain level then remains constant for any further increase in the prevalence. If the prevalence of HIV decreases, the demand for treatment also decreases in the population. Hence, the treatment market price decreases to a certain level then remains constant for any further decrease in the prevalence . Therefore, the demand for HIV treatment is said to be prevalence dependent.

3.6.4 The value function

We formulate the value function for the system (3.104)-(3.111) to illustrate the idea of benefit and costs of taking treatment. We assume we have a utility function $u(h, d)$. We assume that, d, is a binary demand for treatment. The binary demand means that either all the infected individuals demand treatment, $d = 1$, or none of them do, $d = 0$. We also assume that, h, is the state variable that represents the susceptible, $s = s_n + m_{nn}$, or infected, $i = s_p + m_{np} + m_{pp} + T_{s_p} + T_{m_{np}} + T_{m_{pp}}$. We evaluate the value function in the infected state since we want to investigate the costs and benefits of treatment and only the infected take treatment, then we have

$$V(i) = max\{u(i, 1) + \varsigma V(i), u(i, 0) + \varsigma[\beta I_t V(i) + (1 - \beta I_t)V(s)]\} \tag{3.139}$$

where ς is the discount rate. Discount rate quantifies benefits and costs relative to time that allows for an individual to choose the health state that has greater present value than at some time in future. We assume that we could restrict the infected, i, into the following possibilities:

- $i = s_p$,
- $i = m_{np}$,
- $i = m_{pp}$,
- $i = s_p + m_{np}$,
- $i = s_p + m_{pp}$,
- $i = m_{np} + m_{pp}$.

We assume that infected individuals weigh the costs and benefits of demanding treatment. If the current benefits of demanding treatment outweigh the cost of demanding treatment in the future, then they would take treatment now and that could reduce the risk of infecting the susceptible's. If the current cost of demanding treatment outweighs the benefits of demanding treatment in the future, then they might forgo treatment and expose the susceptible individuals to HIV.

3.6.5 Price dependent deterministic demand functions

We explore the different types of price dependent deterministic demand functions because price is the most dominant and a crucial economic factor that affects demand directly. There is a negative relationship between demand and price when there is no other external factor influencing the demand. Therefore, the demand function, $d(p)$, is the decreasing function of price, p, given the absence of external factors. The following are the different types of demand functions, where $a_1, a_2, \gamma, \phi, \alpha$ are constant terms [44],

1. Price-dependent linear models of demand

   Quantitative problems in economics and most other fields, patterns of crucial variables are described well by linear models. The linear models are very useful in determining optimal solutions for economic problems pertaining demand and supply of resources and products and their prices.

   - $d(p) = a_1 - a_2 p$ where $a_1, a_2 > 0$
   - $d(p) = a_1(t) - a_2 p(t)$ where $a_1(t), a_2 > 0, t \in [0, T]$
   - $d(p) = a_1(t) - a_2(t)p(t)$ where $t \in [0, T]$
   - $d(p, r) = a_1 - \phi p - \gamma(p - r), a_1, \gamma, \phi > 0$

2. Price-dependent power models of demand

   These models are mostly applied in microeconomics and social sciences. Also applied in power law which is the procedure taken by significant number of regularities in finance and economics.

   - $d(p) = a_1 p^{-a_2}$, where $a_1, a_2 > 0$
   - $d(p) = (a_1 p + a_2)^{-\gamma}$ where $a_1, a_2 > 0, \gamma > 1$
   - $d(p) = (a_1 - a_2 p^{\gamma})^{\gamma}$ where $a_1, a_2 > 0, \gamma \in (-\infty, -1) \cup (0, \infty)$

- $d(p) = a_1 - a_2 p^{\gamma}$ where $a_1, a_2 > 0, \gamma \geq 1$
- $d(p) = (a_1 - a_2 p^{\alpha})^{\gamma}$ where $a_1, a_2, \alpha \geq 1, \gamma \leq 1$
- $d(p) = \dfrac{a_1}{a_1 + a_2 p^{\gamma}}$ where $a_1, a_2, \gamma > 0$
- $d(p) = \phi(a_1 - a_2 p) + (1 - \phi) a_2 p^{-\gamma}$ where $a_1, a_2, a_3 > 0, \gamma > 1, 0 \leq \phi \leq 1$

3. Price-dependent exponential models of demand

   Exponential models are among important models that could well describe nonlinear patterns of change. These models are very useful in modelling and analysis of change in, pollution, population, radioactive material, bank savings, etc.

   - $d(p) = a_1 exp(-a_2 p)$ where $a_1, a_2 > 0$
   - $d(p) = exp(a_1 - a_2 p)$ where $a_1, a_2 > 0$
   - $d(p) = a_1 - exp(a_2 p)$ where $a_1, a_2 > 0$

4. Price-dependent logarithmic model of demand

   The logarithmic models have a close relation with exponential models. These models are useful in studying demands in econometrics. There are also used in expansion of the Cobb-Douglas production function, the Baumol money demand function, etc [45].

   - $d(p) = ln(a_1 - a_2 p)^{\gamma}$ where $a_1, a_2 \gamma > 0$

5. Price-dependent logit models of demand

   Logit models sparked significant attention to researchers from different fields, economics, marketing, transportation science and operations management, to name a few. In economics, these models are very useful for pricing purposes in firms offering products that are differentiated and substitutable[46].

   - $d(p) = \dfrac{a_1 exp(-a_2 p)}{1 + exp(-a_2 p)}$ where $a_1, a_2 > 0$
   - $d(p) = \dfrac{1}{1 + exp(a_1 + a_2 p)}$ where $a_1, a_2 > 0$
   - $d(p(t)) = \dfrac{1}{1 + exp(a_1 \pm a_2 p(t))}$ where $a_1, a_2 > 0, t \in [0, T]$

The linear models, exponential model, power models and logarithmic models are mostly used in economics, however, there are not applicable in this study. The price dependent demand function that is of interest to us in this work is the price-dependent logit model of demand. This is because

in our model we assumed that there is a positive relationship between price and the prevalence. However, there is a maximum point in which the price is allowed to reach, beyond that price level the market prices remain constant for any further increase in prevalence. The demand for treatment is dependent on the prevalence and the market price as mentioned in subsection (3.62) and both the prevalence and market price depend on time. Hence, the demand for treatment varies with time. We then assume that the treatment rate as a demand function increases significantly in the first few years of implementation, and start increasing at a decreasing rate and then remain constant over time. This means we assume that after some years the treatment rate reaches a highest point that the sub-Saharan region health authorities could afford to implement into the population given that every economic factor remains constant in all these years.

3.7 Summary

In this chapter we formulated the two sub-models, the model of formation of serodiscordant married couples through marriage and the model of formation of serodiscordant married couples through HIV infection. We analyzed each sub-model analytically and found that, the model of the formation of serodiscordant married couples through marriage did not have a disease free equilibrium point and we could only determine the invasion reproduction number, R_{inv}. While, the model of the formation of serodiscordant married couples through infection had the disease free and the endemic equilibrium points. Hence, we could determine the basic reproduction number, R_0. We used the fixed point theory to determine the existence of the endemic equilibrium point. We also investigated the sensitivity of the invasion reproduction number and the basic reproduction number with respect to the HIV transmission rate and the constant treatment rate. We then combined the two sub-models to form a complex model of singles and married couples HIV transmission and serodiscordant couples formation model and incorporated economic aspects through the treatment rate. We assumed that the treatment rate is the demand function of price and prevalence. We presented the value function of taking treatment and stated that we could restrict prevalence into six different cases. We also looked different types of price-dependent demand functions. We will use the singles and married couples HIV transmission and serodiscordant couples formation model to investigate intervention strategies that could reduce the rate of HIV transmission amongst serodiscordant married couples in the next chapter.

Chapter 4

Numerical Simulations

4.1 Introduction

In chapter 3 we formulated and solved the sub-models analytically to get an understanding of the dynamics of the formation of the serodiscordant married couples and the transmission of HIV in the sub-population of single individuals and that of married couples. We also combined the two sub-models to formulate the main complex model that represents the dynamics of marriage and transmission of HIV. Due to the model complexity and the objectives, in the main model we opt to use the numerical techniques where we could use reasonable parameter values that could best fit our strategic scenarios. We then use the results to provide an understanding of the strategies and determine the best strategy that could be used to reduce the HIV transmission to serodiscordant couples. We use the Matlab programming languages for the simulations. The focus of our analysis is based on the effects of HIV treatment on the serodiscordant couples under different strategies. In this chapter simulations are based on the model $(3.126) - (3.133)$ where the treatment rate is a price and prevalence dependent demand function rather than a constant as in the sub-models in chapter 3.

4.2 Intervention strategies

We use the initial conditions and the parameter values from Table 4.1 and Table 4.2 for illustration and to create representative figures. In all simulations, the state variables initial conditions are as

stated in Table 4.1. In all simulations we assumed that every infected individual and married couples who take treatment reduces the transmission rate of HIV in the population since they go through an intense counseling as mentioned in chapter 3. Hence, their sexual behavior changes drastically in a positive manner. The treatment rate function is given by, $D(I(t), P(t)) = \dfrac{1}{1 + exp(1-t)}$, and the treatment profile is shown in Figure 4.1

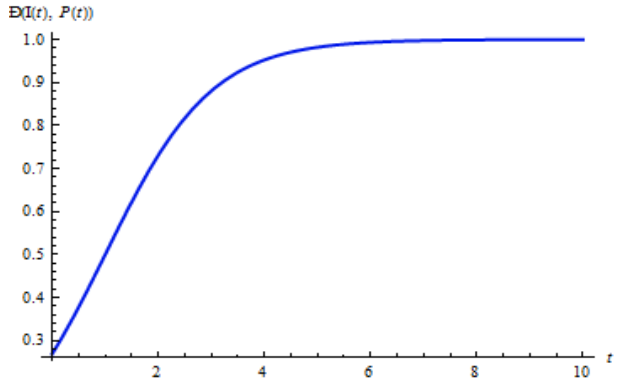

Figure 4.1: Profile presenting the treatment rate as a function of time-dependent demand.

Table 4.1: State variables initial conditions

$s_n(0)$	$s_p(0)$	$m_{nn}(0)$	$m_{np}(0)$	$m_{pp}(0)$	$T_{s_p}(0)$	$T_{m_{np}}(0)$	$T_{m_{pp}}(0)$
0.6870	0.14364	0.009960	0.05370	0.1057	0	0	0

In this study we investigate the effects of treatment under eight different intervention strategic scenarios . We first consider the behavior of the population's compartments when there is no treatment introduced into the population. We use this strategy as a reference scenario to compare the trends of other intervention strategies. The second strategy is to investigate the effects of treating the HIV positive single individuals, s_p. The third strategy is to investigate the effects of treating the serodiscordant couples, m_{np}. The fourth strategy is to investigate the effects of treating the HIV positive concordant positive married couples, m_{pp}. The fifth strategy is to investigate the effects of treating, s_p and m_{np}. The sixth strategy is to investigate the effects of treating, s_p and m_{pp}. The seventh strategy is to investigate the effects of treating, m_{np} and m_{pp}. The eighth strategy is to investigate the effects of treating the entire infective compartments in the population.

Table 4.3 indicates the effects that each intervention strategy has in the population compartments. We use arrows to show the trends, where an upward arrow indicates an increase, a downward arrow

Table 4.2: Parameter values

Parameters	Value	Source
π	0.029	[47]
α	0.0035	[13]
μ	0.02	[48]
δ	0.044	[11]
β	0.0890	[11]
τ	0.2257	[14]
τ_{NP}	0.225	[14]
τ_{PP}	0.00070	[14]
ρ	0.0098	estimated
$\overline{\eta}$	0.520	estimated
$\overline{\sigma}$	0.420	estimated
$\overline{\gamma}$	0.780	estimated
$\overline{\psi}$	0.400	estimated
$\overline{\varpi}$	0.580	estimated
$\overline{\kappa}$	0.320	estimated

indicates a decrease, a downward and upward arrows indicates a decrease then increase until it stabilizes, upward and downward arrows indicates an increase then decrease and a dash indicates that there are no dynamics in that compartment.

We explore the effects of not introducing treatment in the population in Figure 4.2. The HIV negative single individuals, s_n, decrease over time. The HIV concordant negative married couples compartment, m_{nn}, increases for some time and then decreases over time. The infective compartments, s_p, m_{np} and m_{pp}, all increase over time. The HIV concordant positive married couples, m_{pp}, decrease slightly before they start increasing. The serodiscordant married couples compartment, m_{np}, increases significantly than, s_p and m_{pp}.

We explore the effects of treating the HIV positive single individuals, s_p, in Figure 4.3. The HIV

Table 4.3: Intervention strategic scenarios

Strategies	**Effects of the strategy**							
	s_n	s_p	m_{nn}	m_{np}	m_{pp}	T_{s_p}	$T_{m_{np}}$	$T_{m_{pp}}$
No treatment	$\downarrow$	$\uparrow$	$\uparrow,\downarrow$	$\uparrow$	$\downarrow,\uparrow$	–	–	–
Treat s_p	$\downarrow$	$\downarrow$	$\uparrow,\downarrow$	$\uparrow,\downarrow$	$\downarrow,\uparrow$	$\uparrow$	–	–
Treat m_{np}	$\downarrow$	$\uparrow$	$\uparrow$	$\downarrow,\uparrow$	$\downarrow,\uparrow$	–	$\uparrow$	–
Treat m_{pp}	$\downarrow$	$\uparrow$	$\uparrow,\downarrow$	$\uparrow,\downarrow$	$\downarrow$	–	–	$\uparrow$
Treat s_p **and** m_{np}	$\downarrow$	$\downarrow$	$\uparrow$	$\downarrow$	$\downarrow$	$\uparrow$	$\uparrow$	–
Treat s_p **and** m_{pp}	$\downarrow$	$\downarrow$	$\uparrow$	$\uparrow$	$\downarrow$	$\uparrow$	–	$\uparrow$
Treat m_{np} **and** m_{pp}	$\downarrow$	$\uparrow$	$\uparrow$	$\downarrow$	$\downarrow$	–	$\uparrow$	$\uparrow,\downarrow$
Treat the entire infected compartments	$\downarrow$	$\downarrow$	$\uparrow$	$\downarrow$	$\downarrow$	$\uparrow$	$\uparrow$	$\uparrow,\downarrow$

single individual's compartment decreases sharply over a short period of time and remains constant at some level. The HIV concordant negative married couples compartment increases sharply and start decreasing a bit faster than in Figure 4.2. The HIV positive single individuals compartment decreases sharply and that effect reflects through an increase in the treated HIV positive single individuals compartment, T_{s_p}. The serodiscordant married couples compartment increases as in Figure 4.2 then decreases after some time until it remains constant. The HIV concordant positive married couples compartment decreases initially as in Figure 4.2 then increases until it reaches some point than remains constant over time.

We investigate the effects of treating the serodiscordant married couples, m_{np}, in figure 4.4. The HIV negative single individuals compartment decreases in a similar way to Figure 4.2. The HIV concordant negative married couples compartment increases more compared to, m_{nn}, in Figure 4.2 and then remains constant over time. The HIV positive single individuals compartment increases to some point but lower than that of, s_p, in Figure 4.2 then remains constant over time. The serodiscordant married couples compartment decrease significantly in a very short period of time until it is or very close to zero and then start increasing and then remains constant. The effect of the decrease in, m_{np}, reflects through the increase of the treated serodiscordant married couples compartment, $T_{m_{np}}$. The HIV concordant positive married couples compartment decreases significantly to some point then increases slightly and remain constant.

We investigate the effects of treating only the HIV positive concordant married couples, m_{pp}, in Figure 4.5. The compartment, s_n, decreases and then reach equilibrium. The compartment, m_{nn}, increases and then start decreasing. The compartment, s_p, increases and then remains constant over time. The compartment, m_{np}, also increases to similarly to Figure 4.2 but decreases after some time. The compartment, m_{pp}, decreases significantly to some point and start to increase and then remains constant. The effect is reflected through the increase of the treated HIV concordant positive married couples compartment, $T_{m_{pp}}$.

We study the effects of treating both the HIV positive single, s_p, individuals and serodiscordant married couples, m_{np}, in Figure 4.6. The compartment, s_n, decreases significantly over time and then remains constant. The compartment, m_{nn}, increases to some point but not as high as in Figure 4.2 and then remains constant over time. The compartments, s_p and m_{np}, decreases significantly over a short period of time and then remain constant. The effects of the decrease in, s_p and m_{np}, are reflected through the increase in the compartments, T_{s_p} and $T_{m_{np}}$. The compartment, m_{pp}, also decreases over time to some level and then remains constant.

We study the effect of treating both HIV positive single individuals, s_p, and the HIV positive concordant married couples, m_{pp}, in Figure 4.7. The compartment, s_n, decreases significantly in Figure 4.7 compared to Figure 4.2. The compartment, m_{nn}, increases to some level lower than that in Figure 4.2 and remains constant over time. The compartments, s_p and m_{pp}, decrease significantly over a short period of time and reach equilibrium. The effect of a decrease in the compartments, s_p and m_{pp}, is reflected through an increase in the treatment compartments, T_{s_p} and $T_{m_{pp}}$. The compartment, m_{np}, increases initially as in Figure 4.2 and then decreases and remains constant over time.

We examine the effects of treating serodiscordant married couples, m_{np}, and HIV positive concordant positive married couples, m_{pp}, in Figure 4.8. The compartment, s_n, decreases significantly over time. The compartments, s_p and m_{nn}, increase over time and then level off. The compartments, m_{np} and m_{pp}, decrease significantly and remain constant at some level. This effect is reflected through an increase in the compartments, $T_{m_{np}}$ and $T_{m_{pp}}$.

We explore the effect of treating the entire infective class in Figure 1.9. This strategy reduces significantly every infective compartment, s_p, m_{np}, m_{pp}, in the population. The effect of an increase in these compartments is reflected through the increase in the treatment compartments, $T_{s_p}, T_{m_{np}}, T_{m_{pp}}$. The compartments, s_n, decreases significantly and m_{nn} increases to some level less than that in Figure 4.2 and then remain constant.

4.2.1 Best intervention strategies

The different scenarios of the intervention strategies gave us an idea of comparing the effectiveness of each of the strategies. The Table 4.3 and Figure 4.2 - Figure 4.9 give us ideas of the overall effects of strategies in each compartment. By comparing the strategies we can draw best strategies that could be used to reduce the HIV transmission rate amongst the serodiscordant married couples and other infective compartments. A strategy is deemed best if it reduces HIV transmission rate amongst the serodiscordant married couples significantly and in other infected individuals from other compartments, and when the least number of individuals could be treated and the required effects reflect on most infected individuals. This condition allows us to take into consideration the expectations of implementation costs of each strategy.

Our results illustrate that the most effective strategy is treating the serodiscordant married couples, m_{np}. This strategy reduces the HIV transmission rate amongst the serodiscordant married couples and the HIV concordant positive married couples compartments. At least one HIV seropositive partner is treated and the required effects reflect on three infected individuals. Hence, costs of implementing this strategy are expected to be low since at least one out of four infected individuals demands treatment. The second effective strategy is treating the HIV positive single individuals, s_p, and the serodiscordant married couples, m_{np}. This strategy reduces the HIV transmission rate in every infective compartment in the population. At least two infected individuals are treated from each of the compartments, s_p and m_{np}, and the required effects reflect on at least four infected individuals. Therefore, costs of implementing this strategy are expected to be a bit higher than the first since at least two out of four infected individuals demand treatment. The third effective strategy is treating the HIV positive single individuals, s_p. This strategy reduces the HIV transmission rate amongst the serodiscordant married couples and the HIV positive single individuals. At least one infected individual is treated in, s_p, and the required effects reflect on at least two infected individuals. This

strategy is expected to be the same as the first in terms of treatment costs. However, this strategy is not considered to be the most effective as the first because it does not reduce HIV transmission rate amongst the HIV concordant positive married couples, which has a huge influence in the rate of infecting the serodiscordant couples. The fourth effective strategy is treating the HIV positive single individuals, s_p, and the HIV concordant positive married couples, m_{pp}. This strategy reduces the HIV transmission rate in every infected compartment in the population. At least three individuals are treated from the compartments, s_p and m_{pp}, and the required effects reflect on at least four infected individuals. This strategy is more costly to implement compared to the most effective strategy since at least three infected individuals demand treatment. The fifth effective strategy is treating the serodiscordant married couples, m_{np}, and the HIV positive concordant married couples, m_{pp}. This strategy reduces the HIV transmission rate amongst the serodiscordant married couples and the HIV concordant positive married couples. At least three infected individuals are treated from, m_{np} and m_{pp}, and the required effects reflect on at least three infected individuals. This strategy is expected to be similar to the fourth strategy in terms of implementation costs, since in both at least three infected individuals demand treatment. The sixth effective strategy is treating every infected individual in the population. This strategy is also very effective since it reduces the HIV transmission rate in every infected compartment in the population. At least four infected individuals are treated and the required effects reflect on at least four infected individuals. The implementation costs of this strategy are expected to be more than any of the best strategies.

These best strategies imply that single individuals and married couples benefits of taking treatment increase their overall utility since their health authorities can afford to provide treatment in time and at reasonable costs. Hence, they continue to take treatment and further increase their utilities and the value function since benefits would overweight costs.

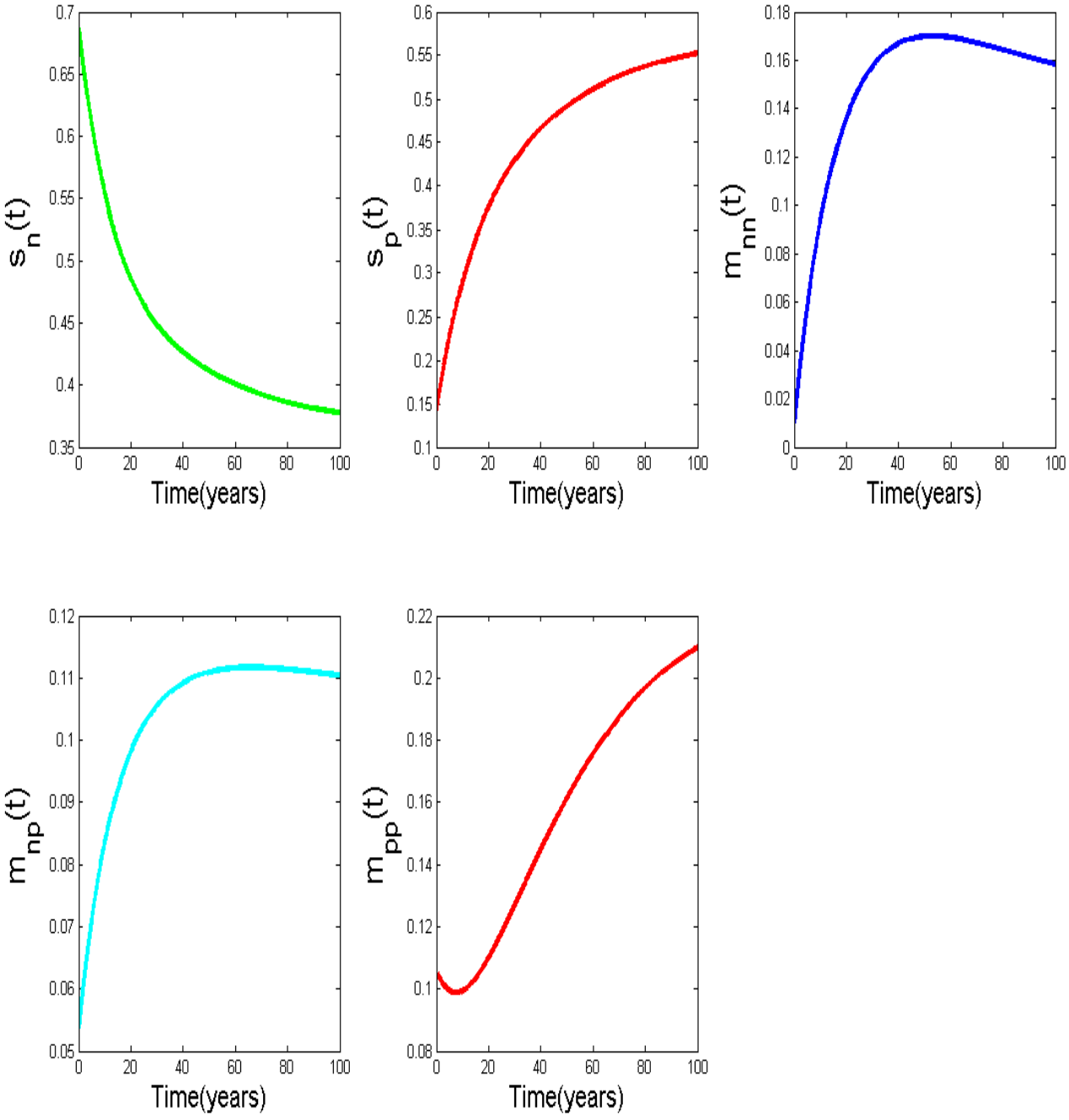

Figure 4.2: Profiles presenting population compartments without treatment and the state variables are dimensionalized.

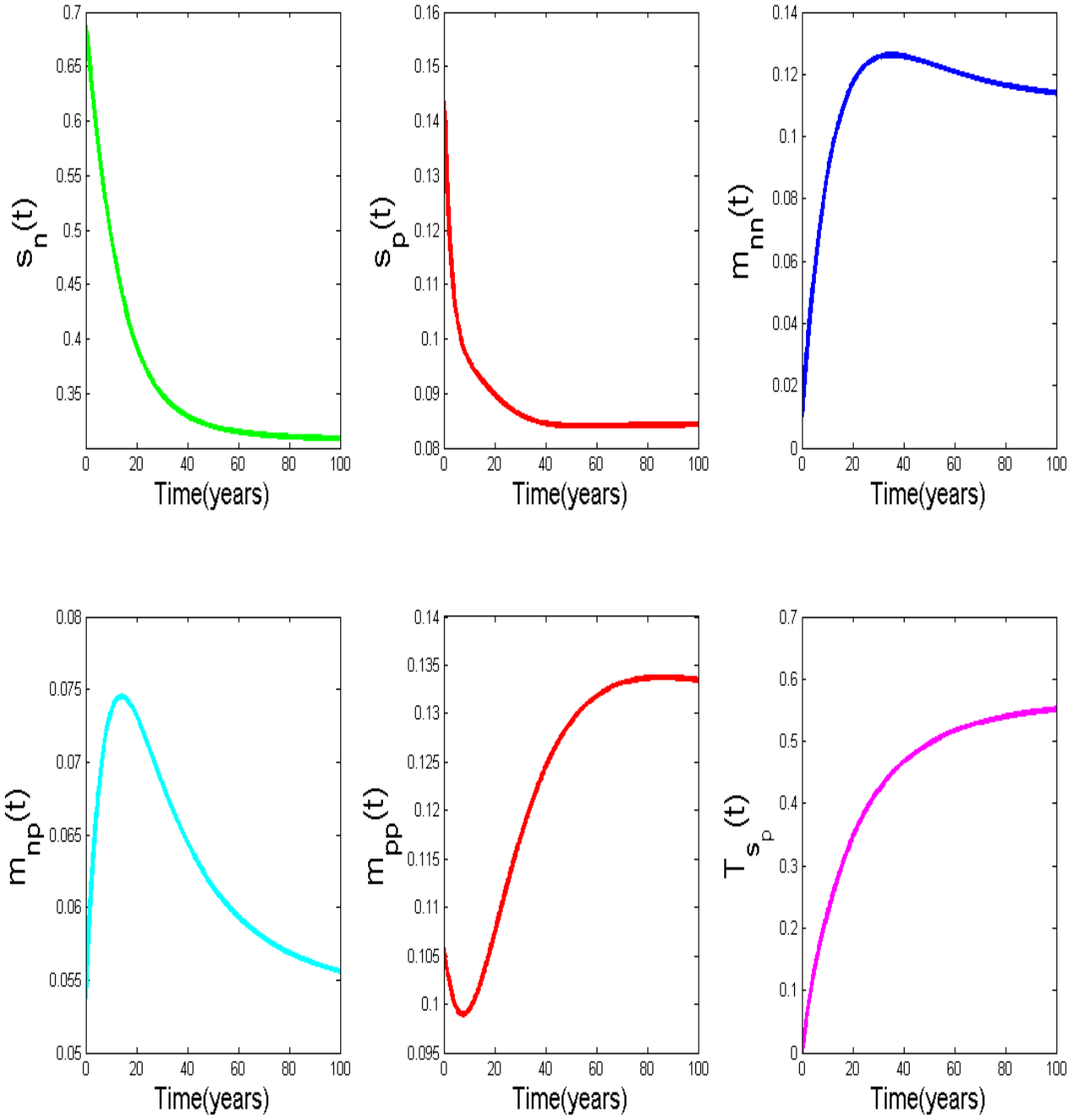

Figure 4.3: Profiles presenting the scenario where only s_p is treated in the entire population.

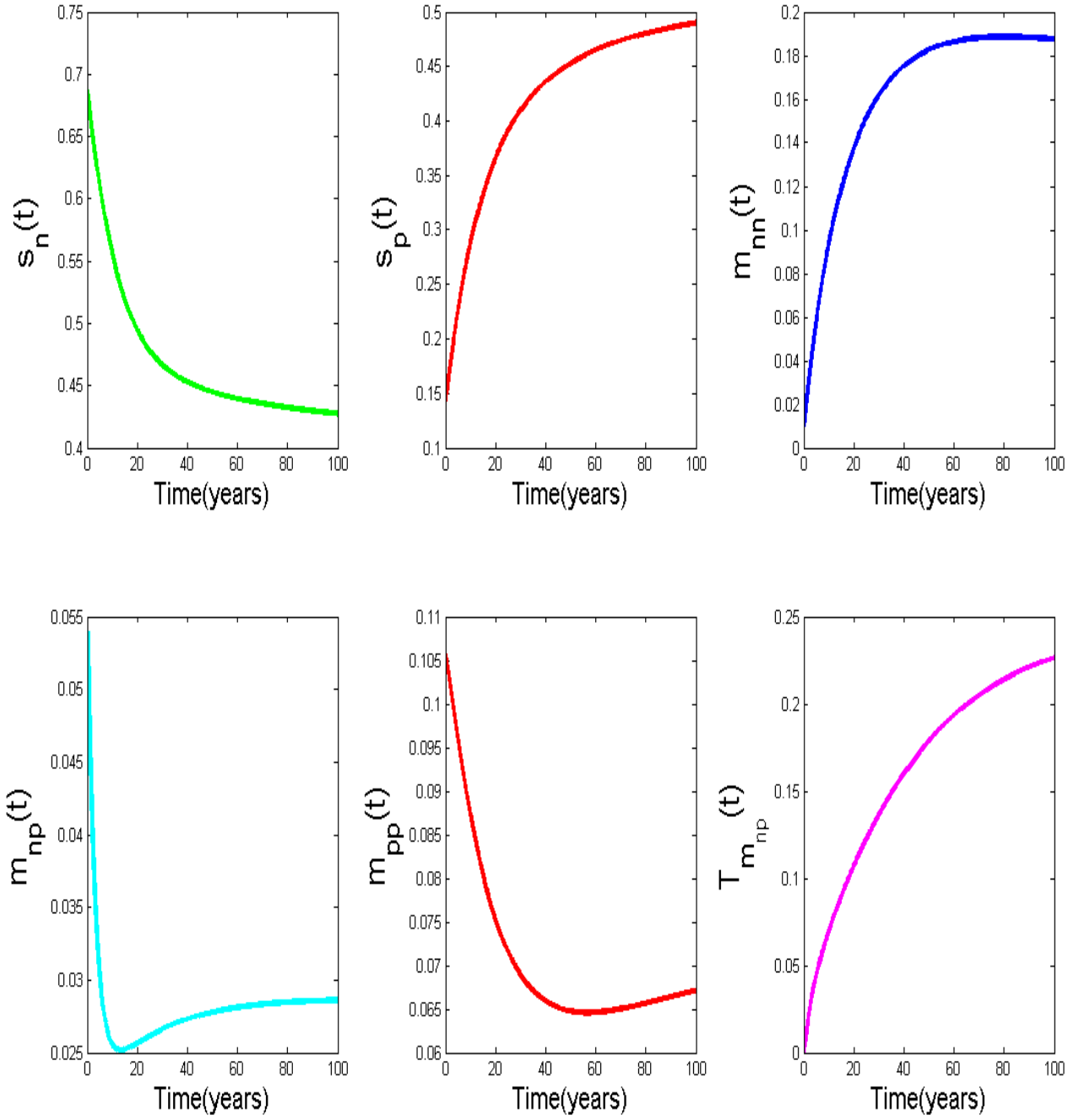

Figure 4.4: Profiles presenting the scenario where only m_{np} is treated in the entire population.

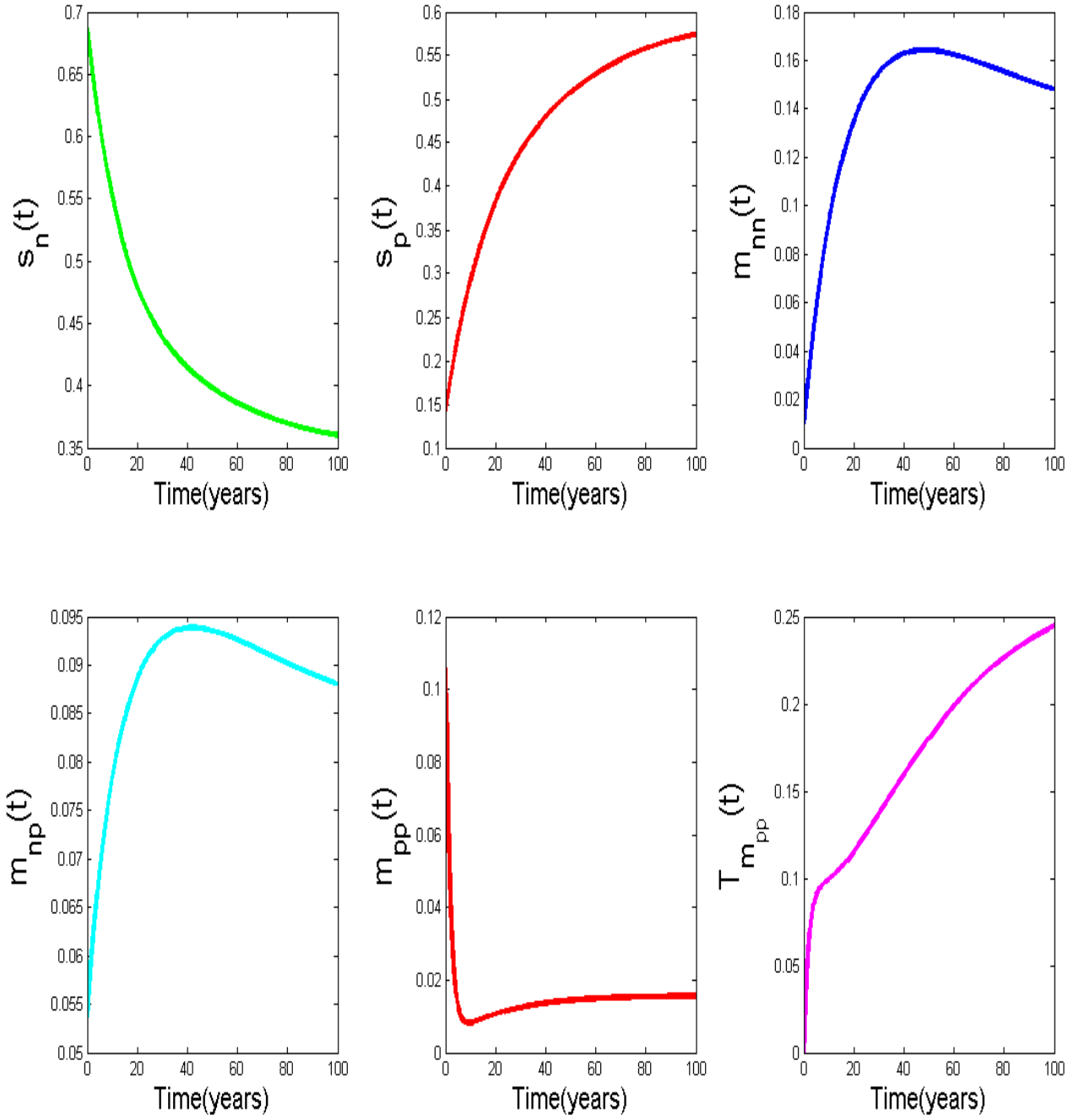

Figure 4.5: Profiles presenting the scenario where only m_{pp} is treated in the entire population.

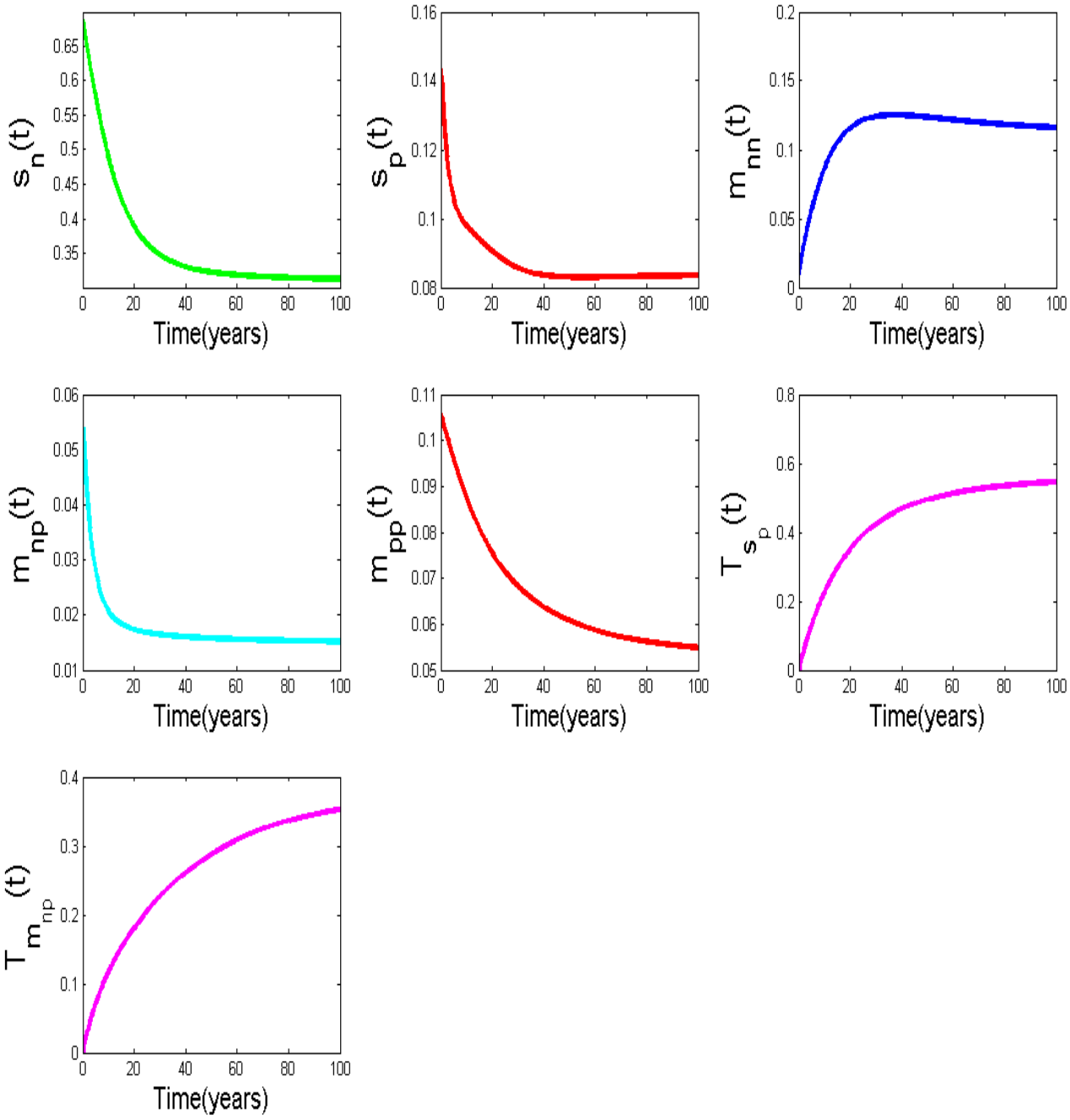

Figure 4.6: Profiles presenting the scenario where only s_p and m_{np} is treated in the entire population.

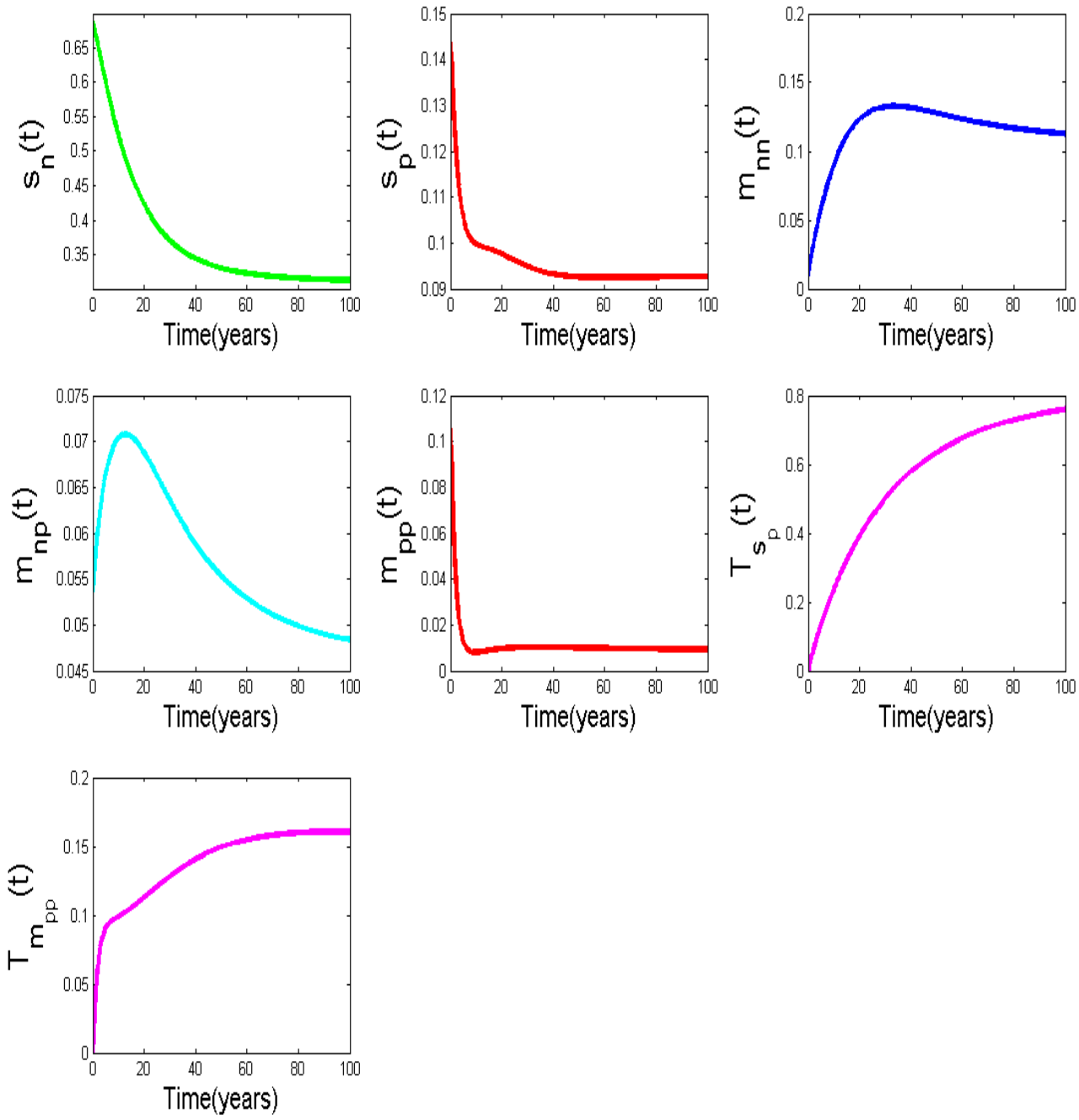

Figure 4.7: Profiles presenting the scenario where only s_p and m_{pp} is treated in the entire population.

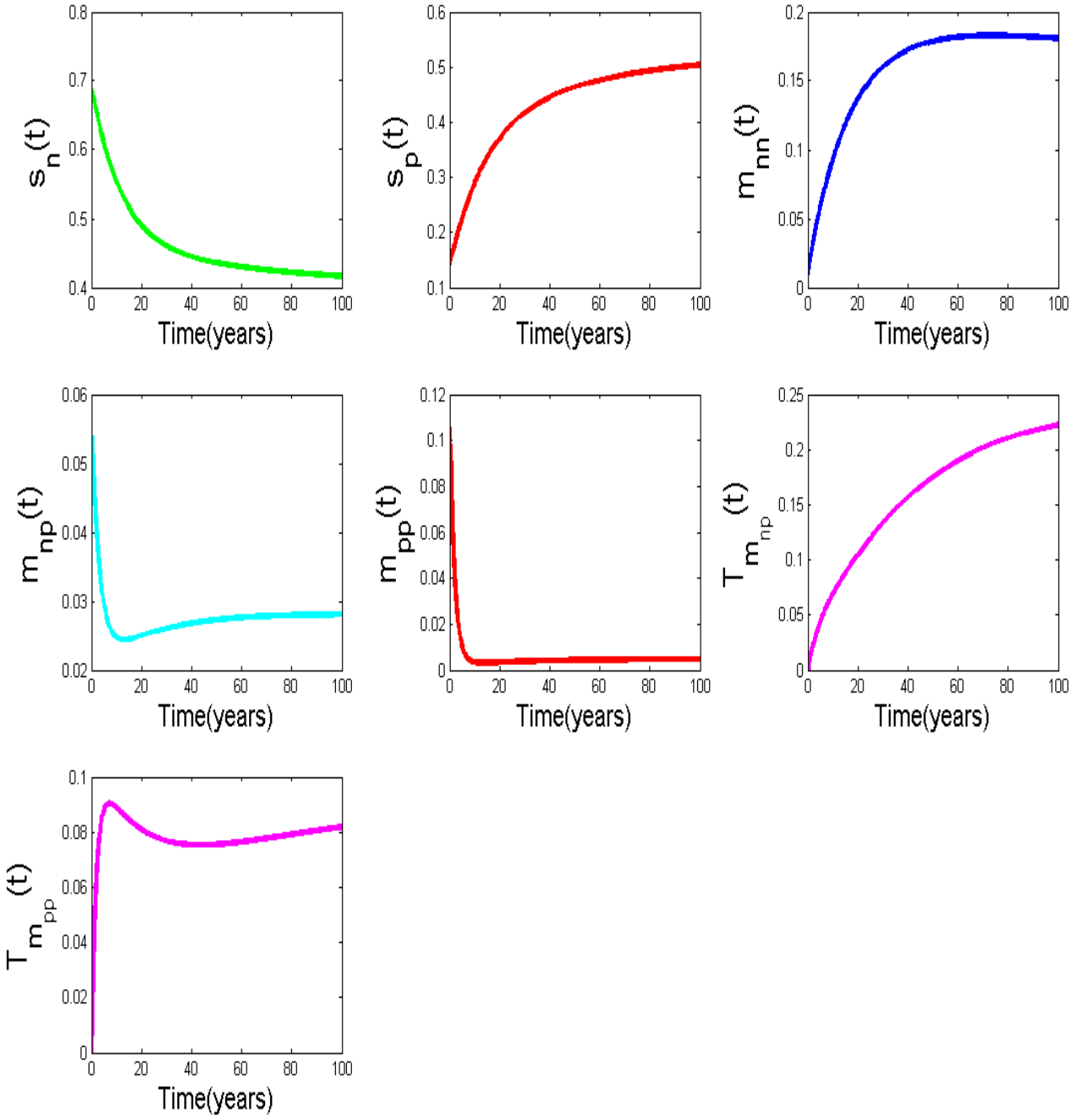

Figure 4.8: Profiles presenting the scenario where only m_{np} and m_{pp} is treated in the entire population.

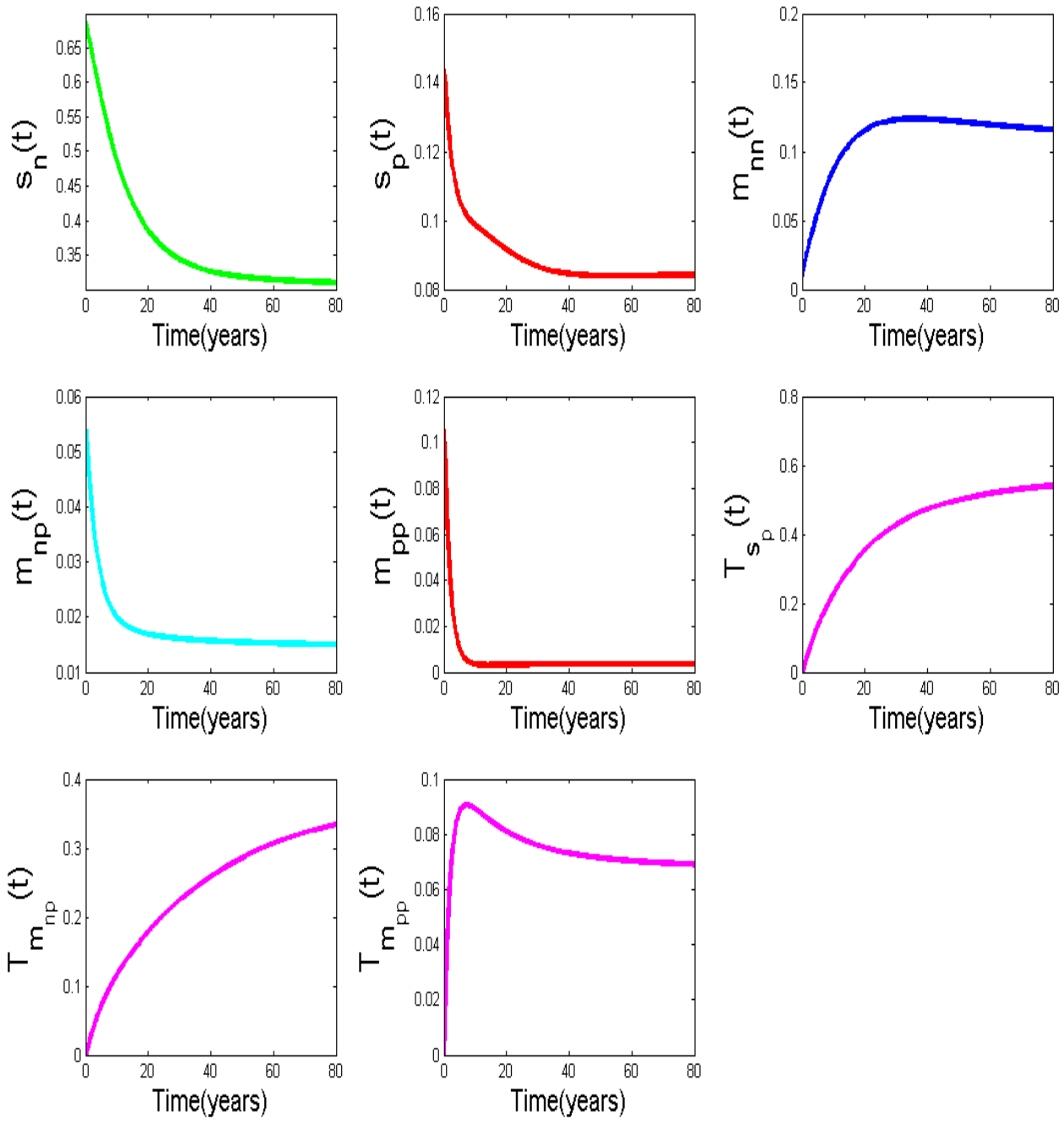

Figure 4.9: Profiles presenting population with treatment in every infected compartment and the state variables are dimensionalized.

4.3 Influence of α and β in the population

The marriage rate, α, and the transmission rate, β, play a significant role in the behavior of the population. We investigate the effect of various marriage rate and the transmission rate under the scenarios where there is no treatment rate and where there is a treatment rate.

Figure 4.10 shows the behavior of the populations for various marriage rate values while other variables are fixed and there is no treatment. For lower values of , α, the single's compartments, s_n and s_p, increase indicating that few individuals are removed through marriage. Consequently, the married couples compartments, m_{nn}, m_{np} and m_{pp}, decrease since there is less recruitment from the single's compartments. For larger values of, α, the single's compartments decrease drastically indicating a large number of individuals removed from this compartment through marriage. While the larger values of, α, leads to an increase in the married couples compartments. Figure 4.11 shows the behavior of the population compartments for various transmission rate values while other variables are fixed and there is no treatment. Lower, β, values have less effect in decreasing population compartments. Larger, β, values have a greater effect on reducing the compartments, s_n, m_{nn} and m_{np}, and that effect is reflected on the increase in the compartments, s_p, and , m_{pp}.

Figure 4.12 shows the behavior of the population compartments for various marriage rate values with treatment and all other variables are fixed. Low values of, α, have less effect on removing the single individuals from their respective compartments, s_n, s_p and T_{s_p}. This means less recruitment for the married couples compartments, m_{nn}, m_{np}, m_{pp}, $T_{m_{np}}$ and $T_{m_{pp}}$. For lager values of, α, the single's compartments decrease significantly and the effect of marriage is reflected on, m_{np} and $T_{m_{np}}$. The presence of treatment in the population causes the compartments, m_{np} and m_{pp}, to decrease even if there is a huge inflow of married couples coming into these compartments due to high marriage rates.

Figure 4.13 shows the behavior of the population compartments for various transmission rate values with treatment and all other variables are fixed. For low values of, β, the susceptible compartments, s_n and m_{nn}, are least affected and they experience an increase. While the infective compartments experience a decrease. The presence of treatment causes serodiscordant compartments, m_{np} and $T_{m_{np}}$, to experience a slight decrease than the other married couples compartments at low, β, values. For larger ,β, values the susceptible and the serodiscordant married couples compartments decrease sharply regardless of the introduction of treatment in the population. While all other infective compartments increase drastically at lager values of, β.

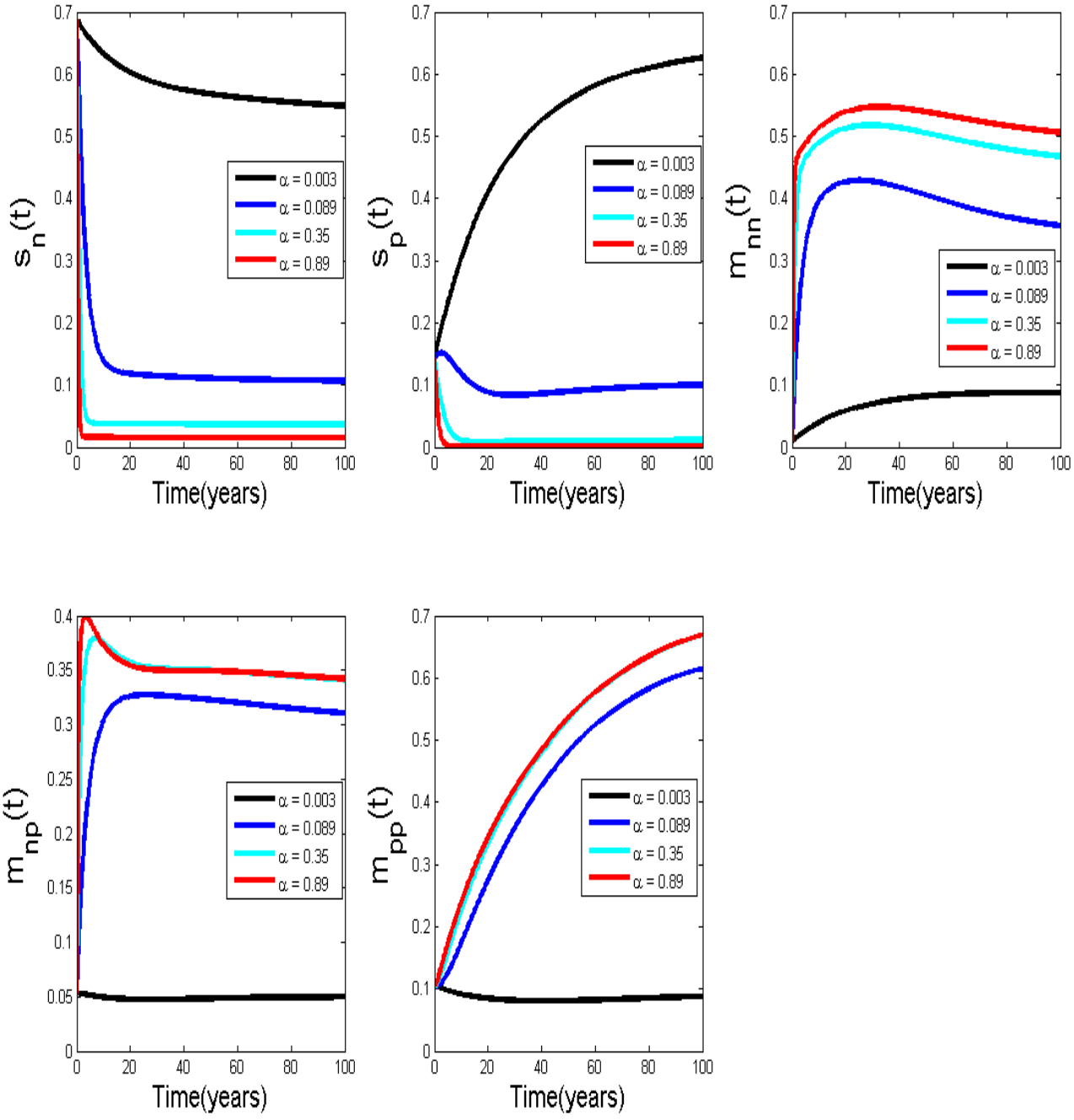

Figure 4.10: Profiles presenting the behavior of the state variables for various values of the marriage rate, α, while other variables are fixed and the treatment rate function is zero.

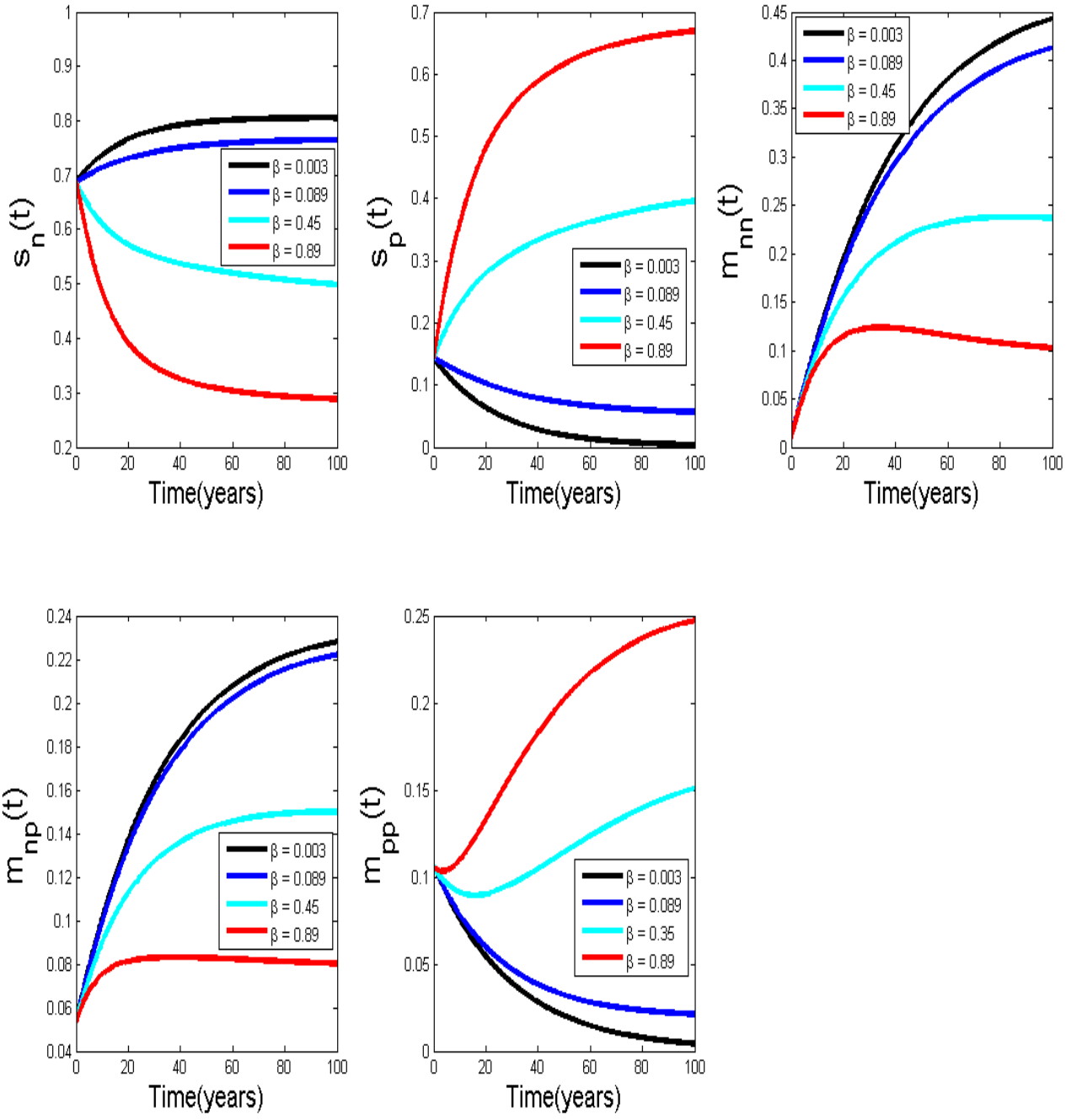

Figure 4.11: Profiles presenting the behavior of the state variables for various values of the transmission rate, β, while other variables are fixed and the treatment rate function is zero.

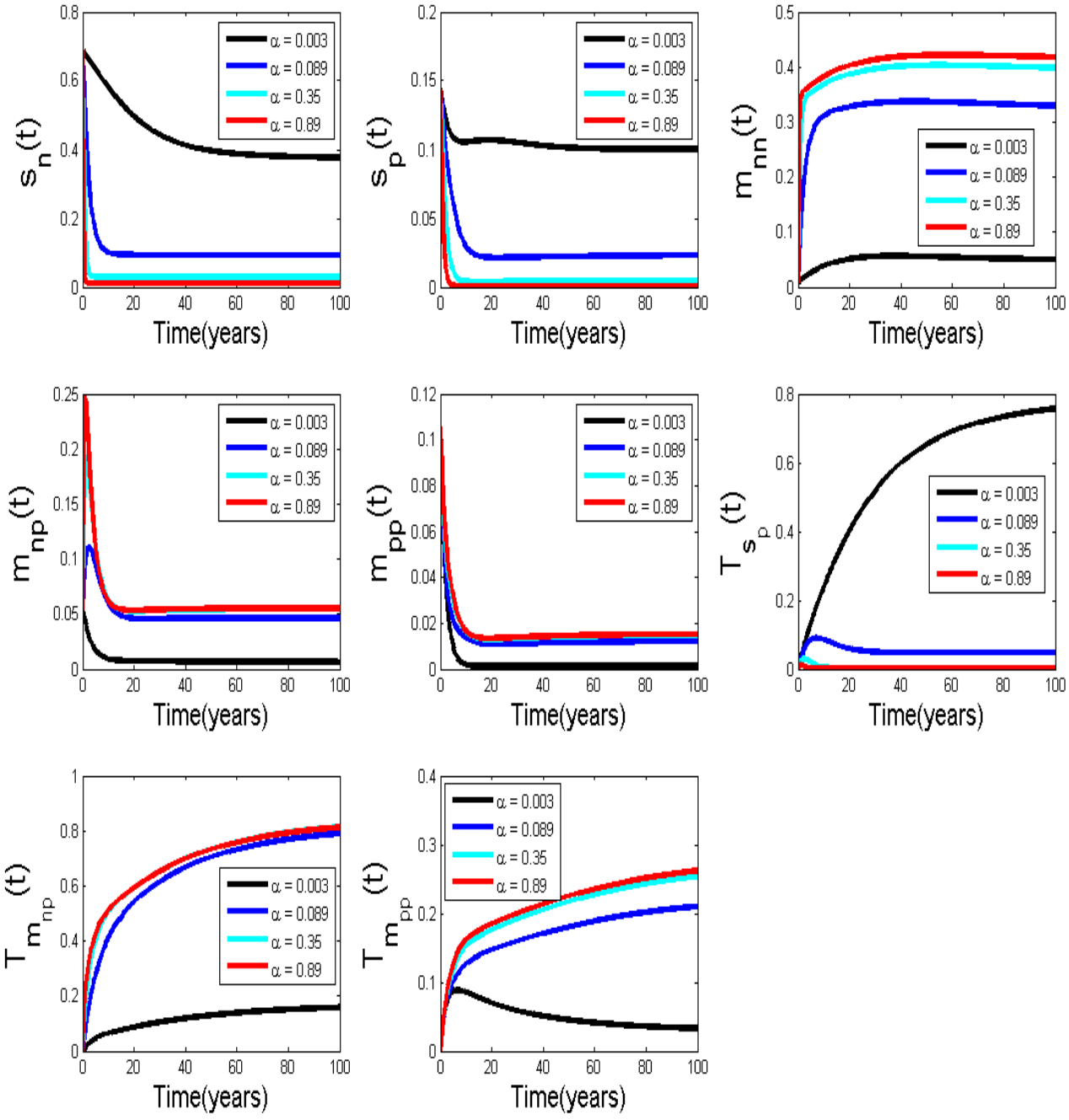

Figure 4.12: Profiles presenting the behavior of the state variables for various values of the marriage rate, α, while other variables are fixed and the treatment rate varies.

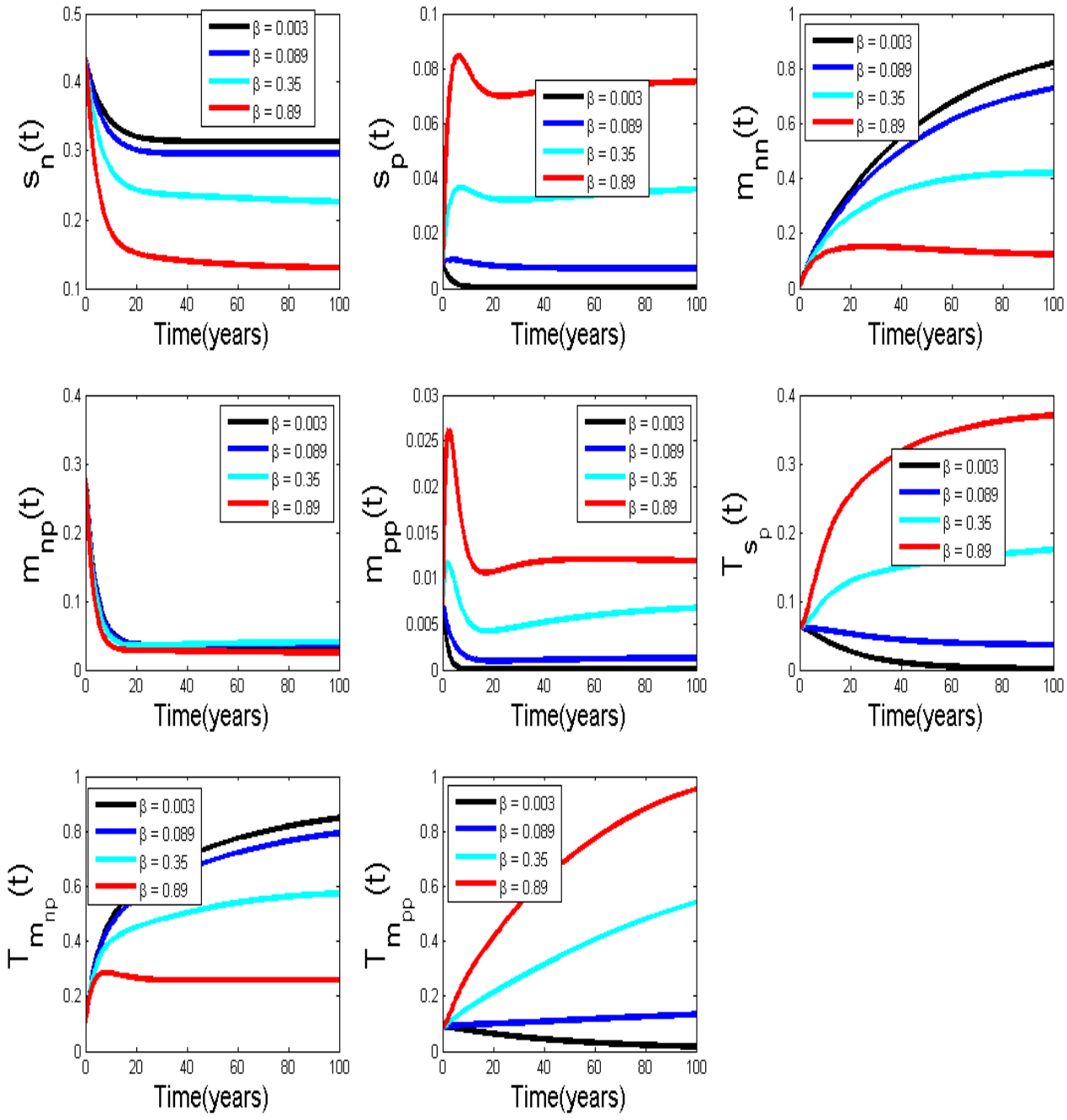

Figure 4.13: Profiles presenting the behavior of the state variables for various values of the transmission rate, β, while other variables are fixed and the treatment rate varies

Chapter 5

Conclusion

This study was motivated by a concern of the high HIV transmission rate amongst the serodiscordant married couples in the sub-Saharan African region. We used concepts from the fields of mathematical and economic epidemiology to investigate and analyze the mathematical models of HIV formulated in this work. In chapter 1 we gave a detailed explanation of infectious diseases and their causes and examples. We looked at the history and importance of mathematical and economic modelling in epidemiology. In chapter 2 a literature was reviewed on mathematical and economic models for different infectious diseases and also the preliminary concepts were looked at. In chapter 3 explored the first objective of the study which was to formulate two sub-models and analyze them analytically in order to gain insight to the dynamics of the formation of the serodiscordant married couples through marriage and through infection. We then combined the two sub-models to form a more complex model with some economic aspects incorporated.

The first sub-model involved the dynamics of marriage of HIV negative single individuals and HIV positive single individuals to form the serodiscordant married couples. We carried out the model analysis, where we proved boundedness and positivity of solutions. We also found that this sub-model does not have a disease free equilibrium point but only has an endemic equilibrium point. This means there is always a disease in this subpopulation because there are always serodiscordant couples present. Hence, we determined the invasion reproduction number, R_{inv}, using the next generation matrix method for discrete systems [31]. Using the Descartes rule of signs we showed that there is at least one positive real root and we required that the spectral radius be less than one to

ensure the stability of the endemic equilibrium point.

The second sub-model involved the dynamics of only the married couples to form the serodiscordant married couples through HIV infection. We analyzed the model and concluded that it has a feasible region. We found that this model has the diseases free and the endemic equilibrium points. We used the fixed point theory on three forces of infections to investigate the existence of the endemic equilibrium points. Stability analysis revealed that the disease free equilibrium point is locally asymptotically stable if $R_0 < 1$. This condition indicates that the disease is controllable.

The sub-models helped us understand the dynamics of the formation of the serodiscordant married couples in the sub-population involving single individuals and in the sub-population involving married couples with different HIV status. We then combined the dynamics of the two sub-model to formulate a complex model of single individuals and married couples. In this model we incorporated the treatment rate that is dependent on price and prevalence rather than the constant treatment rate as in the sub-models. We solved this model using numerical techniques. We also investigated the relationship between R_0, R_{inv} and the transmission rate, β, and the constant treatment rate ϵ. The change in the basic reproduction number and the invasion reproduction number, with respect to the transmission rate indicated the positive relationship. This means that in order to reduce the basic reproduction number and the invasion reproduction number intervention strategies should target to decrease the transmission rate in these sub-populations. We also found that the change in, R_0, and, R_{inv}, with respect to the treatment rate must be less than zero for the treatment rate to be effective in the sub-populations. We also explored the different types of price-dependent deterministic models in order to find the type that is applicable to our model set up. We assumed the treatment rate to be the logit demand function that depends on time.

In chapter 4 we explored the second objective of the study which was to analyze the main model numerically to obtain the best intervention strategies in terms of reducing HIV transmission amongst serodiscordant married couples and by other infected individuals. We performed numerical simulations on the main model to investigate the best strategies that could reduce the HIV transmission rate amongst the serodiscordant married couples and by other infected single individuals and married couples which may contribute to an increase in the transmission rate in the population. In this study

our only intervention strategy was the treatment. We had eight intervention strategies with which we wanted to explore the effects of treatment implementation into the population. These strategies were, no treatment implemented, treat HIV positive single individuals, treat serodiscordant married couples, treat concordant positive married couples, treat HIV positive single individuals and serodiscordant married couples, treat HIV positive single individuals and HIV concordant positive married couples, treat serodiscordant married couples and HIV positive concordant married couples and treat every infected individuals in the population.

We found that six out of the eight strategies were capable of reducing the transmission rate amongst the serodiscordant married couples. However, the most effective strategy was treating the serodiscordant couples directly. This strategy is not only effective in reducing the HIV transmission rate amongst the serodiscordant married couples only but also amongst the HIV concordant positive married couples. The HIV concordant positive married couples are the most important couples that influence the rate at which seronegative partners contract the disease. In this strategy at least one infected individual out of four is treated and the positive effects reflect on three individuals. Hence, the demand for treatment in this case is low since only a small proportion of the total prevalence demands treatment. The price for treatment in the market is also expected to be low in this strategic scenario.

Based on our findings, we recommend that poor resource setting health authorities strive to implement one or more of the above best intervention strategies. However, the 2013/2014 data indicates that the treatment coverage in the sub-Saharan region was approximately 41% and only 16% in the world infected class, and this region highly depends on foreign aids [11, 12]. We therefore recommend that one of the strategies, which is to treat the serodiscordant married couples be implemented in the sub-Saharan region. This strategy is more effective in reducing the HIV transmission rate amongst the serodiscordant married couples and affordable to implement in poor resource setting regions since there are limited resources. It is evidenced in [49, 50], that treating the seropositive partner in the serodiscordant relationship has a positive effect in reducing the rate of HIV transmission amongst the serodiscordant couples. Nevertheless, the strategy of treating the HIV positive single individuals could be very effective in poor resource setting regions like the sub-Saharan Africa that is dominated by the youth population, and the marriage rate in this region is high. Therefore, reducing the rate of HIV transmission by HIV positive single individuals will increase the number of newly recruited serodiscordant couples with low rate of HIV transmission.

In reality, it is important to note that treatment as the only intervention strategy is not enough. The health authorities may need to use it in combination with other intervention strategies in order obtain even better results [51]. The models we formulated do not present the entire reality since its based on assumptions. In our models we restricted marriage interactions to only the possibilities that led to the formation of serodiscordant married couples and that they only die of natural death, which is not entirely true in reality. We also assumed that there is no immigration and emigration, no marriage dissolution and no HIV re-infection, and these aspects play a vital role in the rate of HIV transmission in poor resource setting regions where having multiple sexual partners is deemed normal. The strategies could help in reducing rate of HIV transmission but it is not easy or possible for health authorities to allow treatment access to only a class of certain individuals or married couples in the communities. However, the models gave us a picture of the real problem in the poor resource setting region and the findings could be very useful.

5.1 Future work

In future study, we could bring our model closer to reality by allowing recruitment through immigration of single individuals and married couples with different HIV status. We could also allow marriage dissolution since marriage is one of the focal aspect in HIV transmissions in the poor resource setting region. We could also consider to improve our results by including other forms of intervention strategies in the model.

Bibliography

[1] Leigh Johnson. An introduction to the mathematics of hiv/aids modeling. Technical report, 2004.

[2] Nega Jibat, Berihanu Nigussie, and Selamawit Tesfaye. Original article dilemmas, risks and familial implications of living in hiv serodiscordant relationships, jimma town/oromia. *European Scientific Journal*, 10(27), 2014.

[3] J. D. Murray. *Mathematical Biology: An Introduction*, volume 17. Springer-Verlag Berlin Heidelberg, 3 edition, 2002.

[4] Lawrence Perko. *Differential equations and dynamical systems*, volume 7. Springer Science & Business Media, 2013.

[5] F. Brauer and C. Castillo-Chavez. *Evidence-Based Relapse Prevention*. Springer-Verlag New York, Inc., 2001.

[6] Mauricio L Barreto, Maria Glória Teixeira, and Eduardo Hage Carmo. Infectious diseases epidemiology. *Journal of epidemiology and community health*, 60(3):192–195, 2006.

[7] Eili Klein, Ramanan Laxminarayan, David L Smith, and Christopher A Gilligan. Economic incentives and mathematical models of disease. *Environment and development economics*, 12(05):707–732, 2007.

[8] Fred Brauer et al. Mathematical models for communicable diseases. 84, 2012.

[9] José A Tapia Granados. Response: on economic growth, business fluctuations, and health progress. *International Journal of Epidemiology*, 34(6):1226–1233, 2005.

[10] Fred S Roberts. Greedy algorithms in economic epidemiology. *Modeling Paradigms and Analysis of Disease Transmission Models*, 75:249, 2010.

[11] UNAIDS. Fact sheet. Technical report, United Nations Programme on HIV/AIDS (UNAIDS), 2014.

[12] Michel Sidib. How africa turned aids around. Technical report, United Nations Programme on HIV/AIDS (UNAIDS), May 2013.

[13] Michel Garenne. Trends in marriage and contraception in sub-saharan africa: a longitudinal perspective on factors of fertility decline. 2014.

[14] Hiam Chemaitelly, Susanne F Awad, James D Shelton, and Laith J Abu-Raddad. Sources of hiv incidence among stable couples in sub-saharan africa. *Journal of the International AIDS Society*, 17(1), 2014.

[15] Thomas Pullum and Sarah Staveteig. Hiv status and cohabitation in sub-saharan africa. Technical Report 35, USAID, December 2013.

[16] Fred Brauer. Compartmental models in epidemiology. pages 19–79, 2008.

[17] Daniel Bernoulli and Sally Blower. An attempt at a new analysis of the mortality caused by smallpox and of the advantages of inoculation to prevent it. *Reviews in medical virology*, 14(5):275–288, 2004.

[18] L.M . Walker and M. Jucker. Koch's postulates and infectious proteins. *Acta Neuropathologica*, pages 1–4.

[19] Eili Klein, Ramanan Laxminarayan, David L Smith, and Christopher A Gilligan. Economic incentives and mathematical models of disease. *Environment and development economics*, 12(05):707–732, 2007.

[20] Elsje Pienaar, Aaron M Fluitt, Scott E Whitney, Alison G Freifeld, and Hendrik J Viljoen. A model of tuberculosis transmission and intervention strategies in an urban residential area. *Computational biology and chemistry*, 34(2):86–96, 2010.

[21] Samuel Bowong and AM Aziz Alaoui. Optimal intervention strategies for tuberculosis. *Communications in Nonlinear Science and Numerical Simulation*, 18(6):1441–1453, 2013.

[22] Catherine Heffernan and Jacob A Dunningham. Simplifying mathematical modelling to test intervention strategies for chlamydia. *Journal of Public Health and Epidemiology*, 1(1):022–030, 2009.

[23] Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, and Brian G Williams. Universal voluntary hiv testing with immediate antiretroviral therapy as a strategy for elimination of hiv transmission: a mathematical model. *The Lancet*, 373(9657):48–57, 2009.

[24] Sabine C de Greeff, Anna K Lugnér, Danielle M van den Heuvel, Frits R Mooi, and Hester E de Melker. Economic analysis of pertussis illness in the dutch population: implications for current and future vaccination strategies. *Vaccine*, 27(13):1932–1937, 2009.

[25] Mark Jit and Marc Brisson. Modelling the epidemiology of infectious diseases for decision analysis. *Pharmacoeconomics*, 29(5):371–386, 2011.

[26] David Aadland, David C Finnoff, and Kevin XD Huang. Syphilis cycles. *The BE Journal of Economic Analysis & Policy*, 13(1):297–348, 2013.

[27] Geoff P Garnett. An introduction to mathematical models in sexually transmitted disease epidemiology. *Sexually transmitted infections*, 78(1):7–12, 2002.

[28] J. P. Trapman. *On Stochastic models for the spread of infections*. PhD thesis, de Vrije Universiteit Amsterdam, September 2006.

[29] Stephen Wiggins. *Introduction to applied nonlinear dynamical systems and chaos*, volume 2. Springer Science & Business Media, 2003.

[30] Herbert W Hethcote. The mathematics of infectious diseases. *SIAM review*, 42(4):599–653, 2000.

[31] Linda JS Allen and P Van Den Driessche. The basic reproduction number in some discrete-time epidemic models. *Journal of Difference Equations and Applications*, 14(10-11):1127–1147, 2008.

[32] K. Curran, J. M. Baeten, T.J. Coates, A. Kurth, N.R. Mungo, and C. Celum. Hiv-1 prevention for hiv-1 serodiscordant couples. *National Institute of Health*, 9(2):160–170, June 2012.

[33] Seth C Kalichman, David Rompa, Webster Luke, and James Austin. Hiv transmission risk behaviours among hiv-positive persons in serodiscordant relationships. *International journal of STD & AIDS*, 13(10):677–682, 2002.

[34] Nafiu Hussaini. *Mathematical modelling and analysis of HIV transmission dynamics*. PhD thesis, Brunel University, School of Information Systems, Computing and Mathematics, 2010.

[35] Thomas Pullum and Sarah Staveteig. Hiv status and cohabitation in sub-saharan africa. 2013.

[36] F. Barayarama, J. Y. T. Mugisha, and L. S. Luboobi. An hiv model with variable forces of infection and its application to the epidemic in uganda. *American Journal of Applied Sciences*, 2(9):1274–1278, 2005.

[37] National Collaborating Centre for Infection. Intervention to prevent hiv in serodiscordant couples. Technical report, NCC, January 2010.

[38] CP Bhunu, W Garira, Z Mukandavire, and M Zimba. Tuberculosis transmission model with chemoprophylaxis and treatment. *Bulletin of Mathematical Biology*, 70(4):1163–1191, 2008.

[39] Carlos Castillo-Chavez and Baojun Song. Dynamical models of tuberculosis and their applications. *Mathematical biosciences and engineering*, 1(2):361–404, 2004.

[40] David Murillo, Susan A Holechek, Anarina L Murillo, Fabio Sanchez, and Carlos Castillo-Chavez. Vertical transmission in a two-strain model of dengue fever. *Letters in Biomathematics*, 1(2):249–271, 2014.

[41]

[42] Donath Emusu, Nataliya Ivankova, Pauline Jolly, Russell Kirby, Herman Foushee, Fred Wabwire-Mangen, Drake Katongole, and John Ehiri. Experience of sexual violence among women in hiv discordant unions after voluntary hiv counselling and testing: a qualitative critical incident study in uganda. *AIDS care*, 21(11):1363–1370, 2009.

[43] Uganda Ministry Of Public Health. National couples hiv counseling and testing community strategy. Technical report, Public Health, 2009.

[44] Jian Huang, Mingming Leng, and Mahmut Parlar. Demand functions in decision modeling: A comprehensive survey and research directions. *Decision Sciences*, 44(3):557–609, 2013.

[45] Ron Michener. Notes on logarithms, January 2003.

[46] Guillermo Gallego and Ruxian Wang. Multiproduct price optimization and competition under the nested logit model with product-differentiated price sensitivities. *Operations Research*, 62(2):450–461, 2014.

[47] Abdulaziz Mukhtar et al. Mathematical modeling of population dynamics of hiv with antiretroviral treatment and herbal medicine. Master's thesis, University of Western Cape, 2014.

[48] Abdulaziz Mukhtar et al. *Mathematical modeling of population dynamics of HIV with antiretroviral treatment and herbal medicine*. PhD thesis, University of Western Cape, 2014.

[49] IAS 2011 Conference:. summary, hiv and aids treatment in practice. Technical report, aidsmap, 2011.

[50] Rachelle J Chadwick, Joanne E Mantell, Jennifer Moodley, Jane Harries, Virginia Zweigenthal, and Diane Cooper. Safer conception interventions for hiv-affected couples: implications for resource-constrained settings. *Top Antivir Med*, 19(4):148–155, 2011.

[51] Thomas J Coates, Linda Richter, and Carlos Caceres. Behavioural strategies to reduce hiv transmission: how to make them work better. *The Lancet*, 372(9639):669–684, 2008.