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Modelling the Dynamics of Methamphetamine Abuse in the Western Cape

by

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Declaration

I, the undersigned, hereby declare that the work contained in this thesis is my own original work and has not previously, in its entirety or in part, been submitted at any university for a degree.

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Abstract

The production and abuse of methamphetamine has increased dramatically in South Africa, especially in the Western Cape province. A typical methamphetamine use cycle consists of concealed use after initiation, addiction, treatment and recovery. The model by Nyabadza and Musekwa in [32], is extended to include a core group, fast and slow progression to addiction. The model is analysed analytically and numerically using mass action incidence function and non-linear incidence function. The analysis of the model with mass action incidence is presented in terms of the methamphetamine epidemic threshold R_0 . The analysis shows that the drug free equilibrium is locally asymptotically stable when $R_0 < 1$ and drug persistent equilibrium is locally asymptotically stable when $R_0 > 1$. The model also exhibits a backward bifurcation. Sensitivity analysis of the model on R_0 is performed. The most sensitive parameters are transmission rate and recruitment rate of individuals into the core group. The non-linear incidence incorporates innovators and behaviour change. Analytically, the model is analysed in the absence of behaviour change. With behaviour change two cases were considered. Firstly without innovators and secondly with innovators. In the absence of innovators the non-linear incidence reduced to standard incidence and similar results to the ones in the first model were obtained. With the presence of innovators there is no drug free equilibrium. Numerically we fit the model to data on the number of patients who enter into treatment centers for rehabilitation. Using the fitted model, we determine the prevalence and incidence of methamphetamine abuse. We investigate the impact of behaviour change, ‘reinfection’ rate as well as uptake rate into treatment on prevalence. Our results suggest that intervention and prevention programs focusing on behaviour change and uptake rate into treatment would reduce the prevalence. Projections are made to determine the possible long term trends of the prevalence of methamphetamine abuse in the Western Cape. We give suggestions related to data that should be collected from a modelling perspective.

Opsomming

Die vervaardiging en misbruik van metamfetamien het dramaties in Suid-Afrika toegeneem, veral in die Wes-Kaap provinsie. 'n Tipiese metamfetamien gebruiksiklus bestaan uit heimlike gebruik na aanvang, verslawing, behandeling en herstel. Die model deur Nyabadza en Musekwa in [32], is uitgebrei om 'n kerngroep in te sluit, vinnige en stadige verloop tot verslawing. Die model is analities en numeries ontleed deur van massa-aksie insidensie funksie en 'n nie-liniêre insidensie funksie gebruik te maak. Die ontleding van die model met massa-aksie insidensie word voorgestel in terme van die metamfetamien epidemiese drempel R_0 . Die ontleding toon dat die dwelmvrye ewewig lokaal asimptoties stabiel is as $R_0 < 1$ en die dwelmblydende ewewig is lokaal asimptoties stabiel as $R_0 > 1$. Die model beeld ook 'n terugwaartse bifurkasie uit. Sensitiwiteitsontleding van die model ten opsigte van R_0 is uitgevoer. Die mees sensitiewe parameters is die oordraagbaarheidskoers en die rekrute koers van individue in die kerngroep in. Die nuweling en gedragsverandering word deur die nie-liniêre insidensie opgeneem. Analities, is die model ontleed in die afwesigheid van gedragsverandering. Met gedragsverandering is twee gevalle beskou. Eerstens sonder nuweling en tweedens met nuweling. In die afwesigheid van nuweling is die nie-liniêre insidensie herlei tot standaard insidensie en soortgelyke resultate is verkry, as dié wat in die eerste model verkry is. Met die aanwesigheid van nuweling is daar geen dwelmvrye ewewig nie. Numeries pas ons die model aan die data wat betrekking het met die aantal pasiënte wat in rehabilitasie sentra opgeneem word vir behandeling. Deur die gepaste model te gebruik, het ons die voorkoms en insidensie van metamfetamien misbruik bepaal. Ons ondersoek die impak van gedragsverandering, “re-infeksie” koers sowel as die koers van opname in behandeling op voorkoms. Ons resultate toon dat intervensie- en voorkomingsprogramme sal voorkoms verlaag, wat op die gedragsverandering en die koers van opname in behandeling konsentreer. Die model is ook gebruik om die aantal metamfetamien gebruikers te projekteer. Ons maak voorstelle verwant aan die data, wat vanuit 'n modellerings-oogpunt ingesamel moet word.

Dedication

This thesis is dedicated to my parents Mr and Mrs. Saidi Kalula and to my fiance Mr. Geoffrey.W. Sikazwe. I have been able to reach this far because of your sacrifices.

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Chapter 1

Introduction

1.1 Methamphetamine

Methamphetamine (MA) is a powerful addictive stimulant that affects many areas of the central nervous system. It is a white, orderless, bitter-tasting crystalline powder that readily dissolves in water or alcohol. The drug can easily be made in clandestine laboratories from relatively inexpensive over-the counter ingredients and can be purchased at a relatively low cost [39]. Production and abuse of methamphetamine has increased dramatically in South Africa. Similar trends have been observed in United States, Australia, Japan, New Zealand and Thailand, see for instance [26, 40], and the references cited there in.

Methamphetamine has variety of forms and street names. It is commonly known as ‘tik’ in South Africa [29] and was introduced through gang culture in affected communities. The common effects of intoxication are: increased energy and self confidence, heightened sense of sexuality, tremors, appetite suppression and weight loss. The prolonged use of it is usually characterized by severe weight loss, higher risk of seizures, violent behaviour, confusion, impaired concentration and memory and mood disturbances. Also, long term use increases the risk of contracting HIV and other infectious diseases due to injection drug use and sexual risky behaviour. Risky sexual behaviour has been observed among methamphetamine users. For example, it has been found that methamphetamine users were more likely to have, exchanged sex for money or drugs, multiple sex partners and unsafe sex [34, 29, 49, 53, 56].

1.2 Reasons for using methamphetamine

As in any activity, people get involved for different reasons or motivations. For the case of methamphetamine, some people's reasons to use methamphetamine include aphrodisia, others for weight loss, job performance or to enhance sexual pleasure [17]. These have been observed in different studies in [21, 50]. In [21], it has been stated that many women start using methamphetamine so that they can be slimmer and improve their sex drive. Some use methamphetamine so that it will give them extra energy. It has been observed in [50], that due to methamphetamine's ability to increase sense of well-being and a feeling of mastery and power reinforces methamphetamine users to escalate in using it more frequently. This shows that some of methamphetamine's effects such as weight loss, increased energy and self confidence, and heightened sense of sexuality properties act as a motivating factor for some individuals to use it.

1.3 Motivation

In South Africa, there has been dramatic increase in treatment demand for drugs such as dagga, mandrax, cocaine, heroin and methamphetamine, especially in the Western Cape province. Increased treatment demand may be a sign that drug use has increased. It is thus important to understand the dynamics of drug use in order to design meaningful control strategies. It is under this background and the implications of methamphetamine abuse to public health, that we modify the model presented in [32]. This is done in three ways, firstly by having individuals who progress fast into hard drug use. Secondly, by having individuals who move from hard drug use to light drug use, as well as individuals who move from treatment class going back into hard drug use class. Finally, we consider a core group model in which self initiation is a contributing factor to drug use.

1.4 Objectives

The main objective of this thesis is to model the dynamics of methamphetamine.

Specific objectives:

- To extend the model in [32] and apply it to data on individuals on treatment in the Western Cape.
- To investigate the impact of behaviour change in methamphetamine abuse.
- To investigate the possibility of backward bifurcation in the developed model and its implications to public health.
- To investigate conditions under which methamphetamine abuse will persist or die out of the population.
- To project the number of methamphetamine users based on the fit to data of individuals under treatment.
- To determine the incidence of methamphetamine abuse, that is estimating the number of individuals who are recruited annually into using methamphetamine.

1.5 Mathematical concepts and tools

In this section, we describe some of the mathematical concepts and tools which we used in the qualitative analysis of the mathematical models developed in this thesis.

1.5.1 Linearization

Linearization refers to finding the linear approximation to a function at a given point. In the study of dynamical systems, linearization is a method for assessing the local stability of an equilibrium point of a system of non-linear differential equations [55]. Linearization makes it possible to use tools for studying linear systems to analyse the behaviour of a non-linear system near a given point. The linearization of a function involves the first

order term of its Taylor expansion around the point of interest. We briefly describe the linearization process:

Let $x_1(t)$, $x_2(t)$, \dots , $x_n(t)$ be the population sizes of n compartments where t is an independent variable, then the system is modeled by autonomous system of n first order differential equations given by,

$$\begin{aligned} x_1' &= F_1(x_1, x_2, \dots, x_n), \\ x_2' &= F_2(x_1, x_2, \dots, x_n), \\ &\vdots \\ x_n' &= F_n(x_1, x_2, \dots, x_n). \end{aligned} \tag{1.1}$$

We define the steady state of the system (1.1) as a solution $(x_1^*, x_2^*, \dots, x_n^*)$ of the system of equations,

$$\begin{aligned} F_1(x_1^*, x_2^*, \dots, x_n^*) &= 0, \\ F_2(x_1^*, x_2^*, \dots, x_n^*) &= 0, \\ &\vdots \\ F_n(x_1^*, x_2^*, \dots, x_n^*) &= 0. \end{aligned} \tag{1.2}$$

Considering a small perturbation ϵ from the steady state $(x_1^*, x_2^*, \dots, x_n^*)$ gives

$$\begin{aligned} x_1(t) &= x_1^* + \epsilon \bar{x}_1(t), \\ x_2(t) &= x_2^* + \epsilon \bar{x}_2(t), \\ &\vdots \\ x_n(t) &= x_n^* + \epsilon \bar{x}_n(t). \end{aligned} \tag{1.3}$$

Then substituting (1.3) into (1.1), the differential equations becomes

$$\begin{aligned} x_1'(t) &= F_1(x_1^* + \epsilon \bar{x}_1, x_2^* + \epsilon \bar{x}_2, \dots, x_n^* + \epsilon \bar{x}_n), \\ x_2'(t) &= F_2(x_1^* + \epsilon \bar{x}_1, x_2^* + \epsilon \bar{x}_2, \dots, x_n^* + \epsilon \bar{x}_n), \\ &\vdots \\ x_n'(t) &= F_n(x_1^* + \epsilon \bar{x}_1, x_2^* + \epsilon \bar{x}_2, \dots, x_n^* + \epsilon \bar{x}_n). \end{aligned} \tag{1.4}$$

Using a Taylor's expansion for several variables we have

$$\begin{aligned}
\epsilon \frac{d\bar{x}_1}{dt} &= F_1(x_1^*, x_2^*, \dots, x_n^*) + \epsilon \left. \frac{\partial F_1}{\partial x_1} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_1 + \epsilon \left. \frac{\partial F_1}{\partial x_2} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_2 + \\
&\quad + \epsilon \left. \frac{\partial F_1}{\partial x_n} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_n + O(x, t) \\
\epsilon \frac{d\bar{x}_2}{dt} &= F_2(x_1^*, x_2^*, \dots, x_n^*) + \epsilon \left. \frac{\partial F_2}{\partial x_1} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_1 + \epsilon \left. \frac{\partial F_2}{\partial x_2} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_2 + \dots \\
&\quad + \epsilon \left. \frac{\partial F_2}{\partial x_n} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_n + O(x, t) \\
&\quad \vdots \\
\epsilon \frac{d\bar{x}_n}{dt} &= F_n(x_1^*, x_2^*, \dots, x_n^*) + \epsilon \left. \frac{\partial F_n}{\partial x_1} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_1 + \epsilon \left. \frac{\partial F_n}{\partial x_2} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_2 + \dots \\
&\quad + \epsilon \left. \frac{\partial F_n}{\partial x_n} \right|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_n + O(\|\bar{x}_1, \bar{x}_2, \dots, \bar{x}_n\|)
\end{aligned} \tag{1.5}$$

where $O(\|\bar{x}_1, \bar{x}_2, \dots, \bar{x}_n\|)$ represents the higher order terms of the expression. Since $(x_1^*, x_2^*, \dots, x_n^*)$ is a steady state, then

$$F_1(x_1^*, x_2^*, \dots, x_n^*) = F_2(x_1^*, x_2^*, \dots, x_n^*) = \dots = F_n(x_1^*, x_2^*, \dots, x_n^*) = 0.$$

Neglecting higher order terms of (1.5), the linearization of the system is given by

$$\begin{aligned}
\epsilon \frac{d\bar{x}_1}{dt} &= \epsilon \frac{\partial F_1}{\partial x_1} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_1 + \epsilon \frac{\partial F_1}{\partial x_2} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_2 + \dots \\
&\quad + \epsilon \frac{\partial F_1}{\partial x_n} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_n \\
\epsilon \frac{d\bar{x}_2}{dt} &= \epsilon \frac{\partial F_2}{\partial x_1} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_1 + \epsilon \frac{\partial F_2}{\partial x_2} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_2 + \dots \\
&\quad + \epsilon \frac{\partial F_2}{\partial x_n} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_n \\
&\quad \vdots \\
&\quad \vdots
\end{aligned} \tag{1.6}$$

$$\begin{aligned}
\epsilon \frac{d\bar{x}_n}{dt} &= \epsilon \frac{\partial F_n}{\partial x_1} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_1 + \epsilon \frac{\partial F_n}{\partial x_2} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_2 + \dots \\
&\quad + \epsilon \frac{\partial F_n}{\partial x_n} \Big|_{(x_1^*, x_2^*, \dots, x_n^*)} \bar{x}_n.
\end{aligned}$$

which can be written as

$$\begin{pmatrix} \bar{x}'_1 \\ \bar{x}'_2 \\ \vdots \\ \bar{x}'_n \end{pmatrix} = \begin{pmatrix} \frac{\partial F_1}{\partial x_1} & \frac{\partial F_1}{\partial x_2} & \dots & \frac{\partial F_1}{\partial x_n} \\ \frac{\partial F_2}{\partial x_1} & \frac{\partial F_2}{\partial x_2} & \dots & \frac{\partial F_2}{\partial x_n} \\ \vdots & \vdots & \vdots & \vdots \\ \frac{\partial F_n}{\partial x_1} & \frac{\partial F_n}{\partial x_2} & \dots & \frac{\partial F_n}{\partial x_n} \end{pmatrix} \begin{pmatrix} \bar{x}_1 \\ \bar{x}_2 \\ \vdots \\ \bar{x}_n \end{pmatrix} \tag{1.7}$$

in matrix form, where

$$\begin{pmatrix} \frac{\partial F_1}{\partial x_1} & \frac{\partial F_1}{\partial x_2} & \dots & \frac{\partial F_1}{\partial x_n} \\ \frac{\partial F_2}{\partial x_1} & \frac{\partial F_2}{\partial x_2} & \dots & \frac{\partial F_2}{\partial x_n} \\ \vdots & \vdots & \vdots & \vdots \\ \frac{\partial F_n}{\partial x_1} & \frac{\partial F_n}{\partial x_2} & \dots & \frac{\partial F_n}{\partial x_n} \end{pmatrix}$$

is the Jacobian matrix of the system (1.1) evaluated at steady state $(x_1^*, x_2^*, \dots, x_n^*)$. The stability analysis can be done using the eigenvalues of the Jacobian matrix. If all the eigenvalues have negative real parts then the steady state is locally asymptotically stable. If all at least one of the eigenvalues have a positive real part then the steady state is unstable.

1.5.2 Descartes' rule of signs

Descartes' rule of signs is a method for determining the number of positive or negative real roots of a polynomial. Suppose that $P(x)$ is a polynomial written in descending powers of x such that

$$P(x) = a_n x^n + a_{n-1} x^{n-1} + a_{n-2} x^{n-2} + \cdots + a_0 \quad (1.8)$$

with coefficients $a_n, a_{n-1}, a_{n-2}, \dots, a_0$ all real. Let \bar{N} be the number of sign change between consecutive non zero coefficients $a_n, a_{n-1}, a_{n-2}, \dots, a_0$. Then Descartes' rule of signs says that the number of positive real zeros of P does not exceed the number of sign changes \bar{N} of (1.8). For example consider a polynomial

$$a_3 x^3 + a_2 x^2 - a_1 x + a_0 = 0, \quad (1.9)$$

where a_i s are positive. There are two sign changes in the sequence of coefficients which shows that polynomial (1.9) has at most two positive real roots. The number of negative roots is the number of changes after substituting the negation of the variable for the variable itself. So for our example, the polynomial becomes

$$-a_3 x^3 + a_2 x^2 + a_1 x^1 + a_0 = 0. \quad (1.10)$$

Since there is one change of sign then there is one negative root. The rule gives us an upper bound number of positive or negative roots of a polynomial but does not tell the exact number of positive or negative real roots. For example if the polynomial has three change of signs, then it has one or three positive roots. This means that one may not be sure of how many positive root the polynomial exactly has, that is whether it has one or three.

1.5.3 Sensitivity analysis

Sensitivity analysis is the study of how the uncertainty in the output of a model can be allocated to different sources of uncertainty in the model input. It is a technique for systematically changing parameters in a model to determine the effects of such changes. Sensitivity analysis as the assessment of the impact of changes input values on a model

output has the following advantages:

- Sensitivity analysis helps to build confidence in the model by studying the uncertainty associated with parameters in the model. This is because many parameters in the system dynamics models represent quantities that are very difficult or even impossible to measure accurately in the real world.
- It helps to determine what level of accuracy is necessary for a parameter to make the model sufficiently useful and valid.
- It also indicates which parameter values are reasonable to use in the model. That is if the model behaves as expected from real world observations, it gives some indication that the parameter value reflects at least the real world.
- Sensitivity tests help the modeller to understand dynamics of the system under study.
- Sensitivity analysis of model input parameters can serve as a guide to any further use of the model.
- Sensitivity analysis can also be used as an aid in identifying the important uncertainties for the purpose of prioritizing additional data collection or research.
- It can also be used to provide insight into the robustness of model results when making decisions.

In general, modellers perform sensitivity analysis so as to determine which input parameters contribute the most to output variability. It also facilitates model development, verification and validation.

1.6 Project outline

The organization of the work is as follows; Chapter 1 gives a general introduction on methamphetamine abuse and rationale for methamphetamine abuse. It also includes the motivation, objectives and mathematical tools used in this thesis. Chapter two reviews some literature on drug abuse in the Western Cape, illicit drug models and effects of methamphetamine abuse. Chapter two also includes some reviews on core and non-core group models, bifurcation analysis, model fitting and a methamphetamine model. In Chapter 3 we present a mathematical model for methamphetamine abuse with a mass action force of recruitment and we perform qualitative, sensitivity and numerical analysis of the model. In Chapter 4 the model for methamphetamine abuse with non linear incidence function which incorporates innovators and behavioural change is presented. Mathematical analysis, sensitivity and simulation results of the model including model fitting to the data are presented. We conclude in Chapter 5 by discussion.

Chapter 2

Literature Review

2.1 Drug abuse in the Western Cape

The range of drugs abused and the burden of drug use is generally greater in the Western Cape than in other provinces of South Africa. From the review of treatment demand data collected via South Africa Community Epidemiology Network on Drug Use (SACENDU) project from over twenty specialists treatment centers since 1996, it has been shown that there is dramatic increase in treatment demand for drugs like dagga, mandrax, cocaine and heroin. There has also been a sudden increase in the number of patients having methamphetamine as a primary or secondary drug of abuse. In the second half of 2003, the percentage of individuals having methamphetamine and other drug of abuse seeking treatment was 7.3 percent. This increased to 19 percent in the first half of 2004 [39]. The percentage in 2004 was thus twice more than in 2003 and more than half of these patients were under 20 years of age [33]. Similar results were observed in 2008 where by the average age reported in the first half of 2008 for patients with methamphetamine as their primary substance of abuse was 23 years, among which 30 percent were younger than 20 years of age. Apart from this increase, the increase in multiple-drug use has been observed with 10 percent of patients in treatment in Cape Town during the second half of 2003 reporting four or more substances of abuse. The studies highlighted also that methamphetamine abuse is often used in conjunction with other substances. For example Clare Kapp reports that methamphetamine has been used in conjunction with heroin where methamphetamine ‘takes’ them up and heroin is used to ‘calm’ them down [21].

A decrease in methamphetamine abuse was noted in 2007 from 1451 individuals in the second half of 2006 to 1413 individuals in the first half of 2007 and then to 1356 individuals in the second half of 2007.

In the Western Cape the most primary substances of abuse reported by 29 specialist treatment centers or programmes participating in the SACENDU project between January to June 2008 were methamphetamine, alcohol, heroin and cannabis which all together comprised 90 percent of all admissions [37]. A rise in methamphetamine abuse was observed in the same report for the first half of 2009.

2.2 Drug abuse models

Illicit drug use and related crime have imposed significant costs in different countries. This has been observed in United States, Australia, Japan, New Zealand, Thailand and South Africa just to mention few.

Mathematical models have been used in the understanding of drug abuse. For example in [54], heroin use in Ireland was modeled in a similar way to the modelling of disease. A compartmental model having susceptibles (individuals not on drug use but at risk of becoming drug users), drug users not in treatment and drug users in treatment was used as shown in FIG. 2.1. The results show that prevention of drug initiation is better than treatment. We refer the reader to [54], for detailed explanations on the variables, parameters, assumptions and the model analysis. Behrens et al. [4], used a model with a feedback

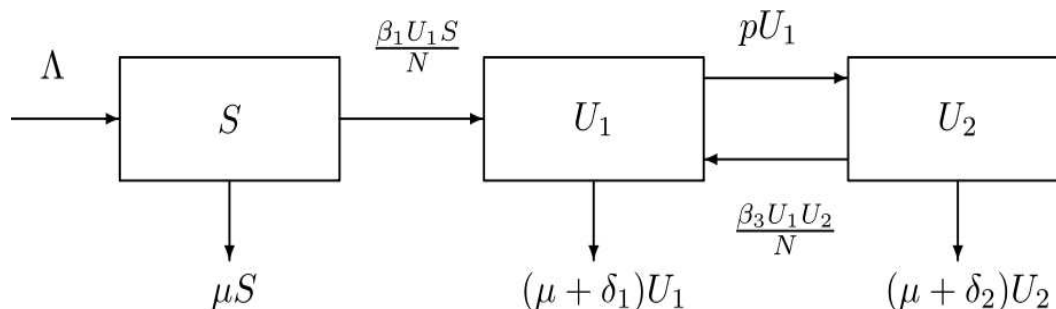


FIG. 2.1. A model for heroin use. The figure is taken from [54]

effect of the prevalence on initiation to model cocaine use in US. Their results suggested

that drug prevention can temper with drug prevalence and consumption, but treatment effectiveness depends critically on the stage in the epidemic in which it is employed. In [5], the same model used in [4] was used, and drug prevention and treatment were studied. The insights obtained were that the effectiveness of prevention and treatment depend critically on the stage in the epidemic in which they are employed. They also found that prevention is most appropriate at the beginning of an epidemic (i.e, when there are relatively few heavy users) and treatment is more effective later. Furthermore, it was concluded that the total social costs increase dramatically if control is delayed.

Everingham et al. [14], used a markov model of population recruitments in and out of light and heavy cocaine use. Their results suggest that reducing initiation is necessary but not sufficient to control drug use and hence measures that directly address consumption by the heavy users should be seriously considered.

2.3 Methamphetamine abuse and infectious diseases

Methamphetamine abuse has many effects on the users. The consequences include mental disorders, involvement in risky sexual behaviour and violence behaviour. There are several studies which have been done with regard to risky sexual behaviour among methamphetamine users. This has drawn more research due to the fact that risky sexual behaviour is related to the transmission and spread of the most problematic epidemic in the world, HIV/AIDS. In the study by Simbayi et al. in [49], it was found that methamphetamine abuse is strongly associated with risky sexual behaviour. Their results showed that, methamphetamine users were more likely to exchange sex for drugs. They were also more likely to have multiple sex partners and have unsafe sex.

Also, the relationship between methamphetamine use and risky sexual behaviour in adolescents was examined among school students in Cape Town. The results indicate significant association between methamphetamine use and engagement in unprotected sex [38]. This has not been observed in Cape Town only but also in Taiwan in the study by Yen [56], in which risky sexual behaviour was compared not only between methamphetamine users and non-users, but also between high-frequency and low-frequency methamphetamine users. The result was that previous sexual experience was more likely in methamphetamine users

than non users which indicates that methamphetamine users are more sexually active than non-users. It also showed that methamphetamine users were also more likely to have had a greater number of sexual partners. Furthermore, they found that high-frequency methamphetamine use was associated with increased tendencies to engage in unprotected sex. Generally, it was observed that the chance of having had sexual intercourse increased in proportion to the frequency of methamphetamine use.

The relationship between drug use and risky sexual behaviour has also been observed among commercial sex workers who have sex with their drug dealers or are usually forced to have unprotected sex by their partners who need money for drugs [35]. It has also been observed among men who have sex with men [28, 35, 36]. In [36], a study on the attitudes about condoms and sexual risky was done among HIV- positive men who have sex with men who are methamphetamine users. The analysis showed that the correlation between methamphetamine frequency and unprotected sex was significant for methamphetamine users who had more negative attitudes towards condoms. Furthermore, a similar correlation was observed in heterosexual methamphetamine users in [44]. In [3], the findings suggest that methamphetamine use heightens multiple sexual partner and unprotected sexual intercourse.

Other findings that relate to methamphetamine use suggest that a history of a psychiatric disorder was a risk factor in methamphetamine users [43]. Another study showed that drug use and mental illness were very common among methamphetamine users [52].

Violent behaviour has been observed among methamphetamine users as methamphetamine use heightens the risk for violence. Also it has been observed that methamphetamine users engaged in a wide range of criminal activities [50].

2.4 Core and non-core group model

Core and non-core group models have been used to model HIV/AIDS and sexually transmitted infections STI's in general [2, 18, 19, 22]. The models have been used in the modelling of gonorrhoea in [19] where the core group is defined as the group of individuals who are very sexually active and are efficient transmitters of the infection. They showed

that a small core group can be very important in the spread of a disease. Haderler and Castillo-Chavez in [18] also used the idea of core and non-core group where a demographic-epidemiological model was formulated in which the total population comprising of core and non-core group was constant. They concluded that partially effective vaccination or education programs may increase the total number of cases while decreasing the relative frequency of cases in the core group. In [22], the core group recruitment effects in SIS models with constant total populations were studied. In this study, the interaction between core and non-core members was considered, whereas for other core-non core group models, interaction was considered within the members of the core group itself and the non-core group being considered completely inactive. In their study it was seen that discouraging recruitment into a core group by promoting fear of infection can cause undesirable effects. Also they found that reduction of the rate at which potentially infectious contacts occur, by lowering sexual activity or using safe sex methods appear to be more safely desirable than preventing people from joining the more active core.

Furthermore, in [30], two core group models for the sexually transmitted disease were studied. In the first model, the susceptible population was divided into two subpopulations S_1 and S_2 where S_1 was the regular susceptible population and S_2 the core group. In the second model, infective individuals are divided into similar groupings. The core and non-core groups were thus within the susceptible and infective populations. The results showed that the transmission dynamics of the epidemic were critically dependent on the effects of small subpopulations with varying levels of sexual activity and hence the core group can play an important role in the spread of disease.

2.5 Bifurcation analysis

The appearance of qualitatively different behaviour of a system as a parameter in an equation is varied is called a bifurcation. A bifurcation could occur when an equilibrium or a fixed point of the system being considered changes its stability.

In epidemiology, bifurcation phenomena are associated with the threshold parameters, the most commonly used is the basic reproduction number, R_0 . The basic reproduction number is a dimensionless quantity which represents the average number of secondary infections

caused by an infective individual introduced into a purely susceptible population. If $R_0 > 1$ the number of infections after an initial introduction grows creating an epidemic while if $R_0 < 1$, small introductions are not sufficient to cause an epidemic and hence an endemic disease will fade out [41].

The most common types of bifurcation are forward and backward bifurcation. Forward bifurcation brings about an exchange in stability between the disease-free equilibrium and endemic equilibrium. The disease-free equilibrium will exist for all values of R_0 while the endemic equilibrium will exist only when $R_0 > 1$. For a system with backward bifurcation, the endemic equilibrium exist for $R_0 < 1$ and hence under certain initial conditions it is possible for the disease to invade or persist in the population. FIG. 2.2, taken from [23], is included here to illustrate forward and backward bifurcations. However among the

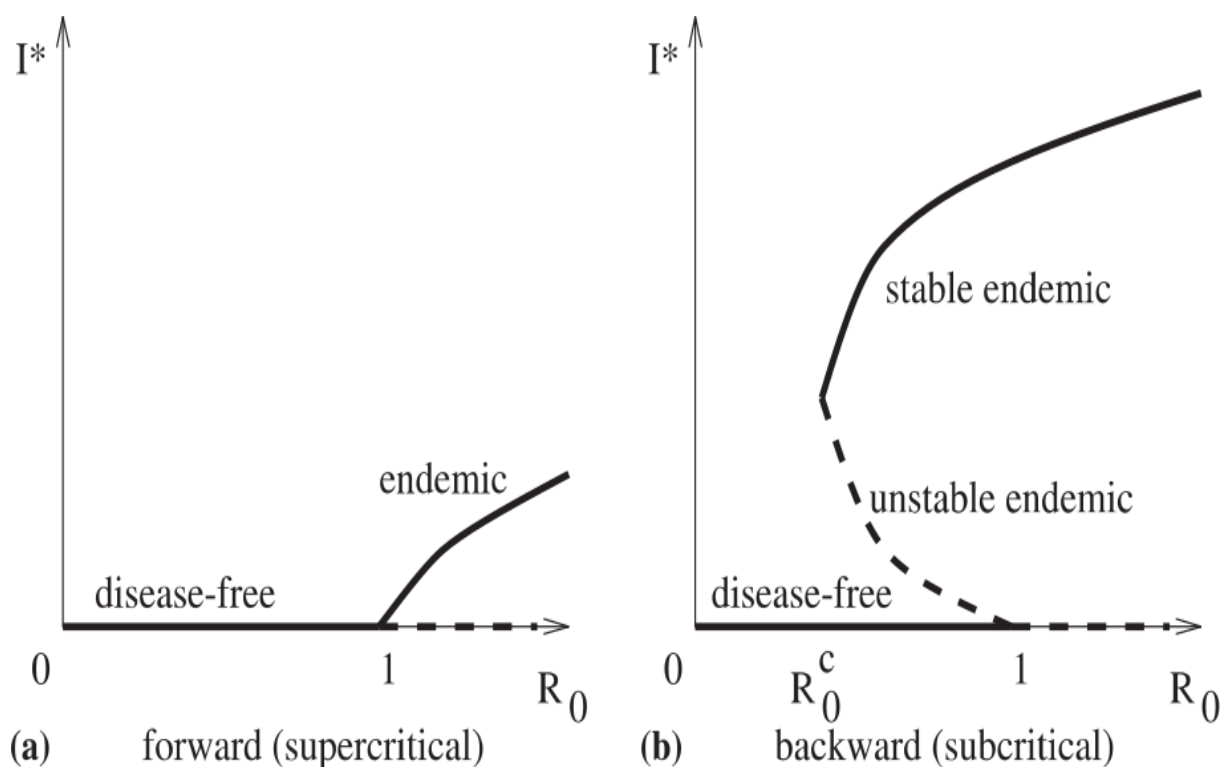


FIG. 2.2. Shows the comparison between forward and backward bifurcation. The figure is taken from [23]

two types of bifurcations, backward bifurcation has been of interest to epidemiological modelling due to its important consequences in the dynamics of infectious diseases. One of these consequences is that, in order to eradicate the disease, R_0 must be reduced to

below critical reproduction number R_0^c . This means that it is not sufficient to have $R_0 < 1$ for the eradication of a disease. This is because for systems with backward bifurcation, there are usually two thresholds $R_0 = R_0^c$ and $R_0 = 1$ where by the model has two endemic equilibrium if $R_0^c < R_0 < 1$, no endemic equilibria when $R_0 < R_0^c$ and a unique endemic equilibrium if $R_0 > 1$. In this section we review some literature with models that exhibit backward bifurcation.

Backward bifurcation has been studied in models of infectious diseases such as dengue transmission dynamics in [16], HIV/AIDS models [20, 48] and transmission dynamics of chlamydia trachomatis [46]. It has also been studied in TB models in [8, 15, 11, 23, 24, 41]. In [16], it was observed that the backward bifurcation was caused by the use of standard incidence and hence it can be removed by replacing standard incidence with mass action incidence. The same phenomena been observed in HIV models discussed in [46], but since standard incidence is realistic in dengue disease as compared to mass action, then backward bifurcation has direct impact on the control of dengue disease whereas for other infectious disease and HIV in particular, questions still remain as to which incidence function is realistic. The choice of the incidence function is usually determined by the assumptions made on the mixing patterns of the population.

Furthermore backward bifurcation has been observed to be associated with re-infection. For example in [46], it has been shown that backward bifurcation phenomena is caused by re-infection of individuals who recovered from the disease. Similar observation were made in [8, 15, 47]. Apart from the models with re-infection, backward bifurcation also has been observed in multi-group models [45]. Backward bifurcation is thus expected in the model developed in this thesis due to relapse into hard drug use caused by interaction with other drug users.

2.6 Model fitting

Curve fitting is a process of constructing a curve or mathematical function that has the best fit to a series of data points. There are different methods used in model fitting which includes least squares, maximum likelihood and the method of moments. In the least squares method, the unknown parameters are estimated by minimizing the sum of the

squared deviations between the data and the model. The best fit in the least squares minimizes the sum of squared distances between the observed values from the data and the value provided by the model. On the other hand the maximum likelihood chooses values of the model parameters that maximize the likelihood function. The least squares can be derived as the maximum likelihood estimator under the assumption that the errors are normally distributed. Both least squares and maximum likelihood use residual square estimation. The results of fitting process can be used to estimate the model parameters. Apart from the model parameters estimation, model fitting helps in the validation of the model.

This will be of particular importance in this thesis as we try to fit the model to data on the number of individuals seeking treatment. The questions we seek to answer include; if the model is fitted to the data available, can we estimate the number of drug users in a given community based on the fit (which will be for those individuals on treatment)? Can we estimate the prevalence and the incidence of methamphetamine abuse? Can we obtain reasonable estimates to the parameter values of the model?

2.7 Methamphetamine models

In spite of the usefulness of mathematical models in the understanding of different diseases and even illicit drugs abuse, not much has been done with regard to methamphetamine abuse. Recently a mathematical model was used to model the dynamics of methamphetamine abuse in [32]. The model used in [32] was an extension of the work in [54] applied to methamphetamine abuse epidemics in South Africa. In [54], the mathematical model was presented to model heroin use in Ireland as shown in FIG. 2.1. The compartment of drug users not in treatment was divided into two compartments in [32], of light methamphetamine users and hard methamphetamine users. A recovery class was also added see FIG. 2.3. The data for the methamphetamine users on treatment from South African Community Epidemiology Network on Drugs and Alcohol (SACENDU) was fitted into the model. The results showed that there is indication of persistence of methamphetamine users in community. For a detailed analysis and description of the model we refer the reader to [32].

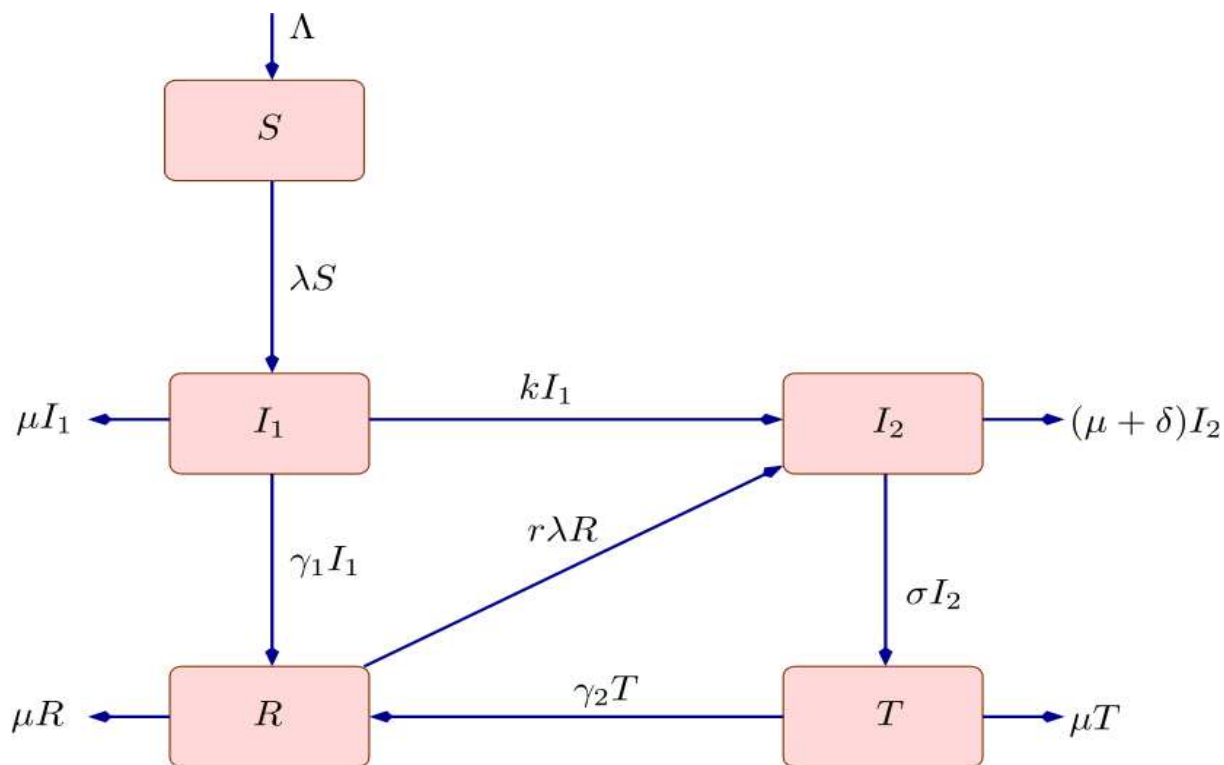


FIG. 2.3. A model for Methamphetamine abuse. The figure is taken from [32]

2.8 Summary

In this chapter the review of some research related to illicit drug and methamphetamine abuse was done. The review includes some trends in drug abuse and methamphetamine particularly in the Western Cape. The trends of substance abuse in the province, gives raise to a need for prevention and treatment. These trends also show the need to focus on multiple-substance use rather than focusing on a single substance. Some findings on the effects or consequences of methamphetamine abuse are presented. These include risky sexual behaviour, mental problems and violent behaviour among methamphetamine users. Methamphetamine abuse being associated with risky sexual behaviour, risk for mental health problems and violence behaviour has implications to both public health as well as criminal justice sector. All these are important and they should be considered when developing interventions. We also reviewed some literature on core and non-core group as well as bifurcation analysis. Generally we have seen that the idea of core and non-core group in modelling, plays an important role in studying transmission and spread of diseases.

Due to the role of the core group, control, prevention and management strategies should be directed at the core group. With regard to backward bifurcation, we have seen that the understanding of backward bifurcation is necessary in the control of disease as the classical idea of reducing R_0 to less than unit is necessary but not sufficient for disease eradication. Rather R_0 needs to be reduced to less than R_0^c where endemic equilibrium does not exist. We also reviewed existing methamphetamine models to get better understanding of the dynamics of the methamphetamine in a given population.

Chapter 3

Methamphetamine Abuse Model

3.1 General introduction

A mathematical model is a description of a system using a mathematical language. It is defined by a series of equations, input factors, parameters and variable aimed at characterizing the process being investigated. Mathematical models have been developed over years and they have been used extensively in many fields such as physics, engineering, statistics, operational research, economic as well as in epidemiology. In this chapter we formulate and analyse a mathematical model for methamphetamine abuse in the Western Cape. The model helps us to understand the dynamics of methamphetamine abuse.

Our model is an extension of the model presented in [32]. The following differentiates our model to the one presented in [32].

(i) We allow fast progression, from being susceptible to being a hard drug users, see [42]. This is also due to the possibility of individuals starting to use methamphetamine in large quantities or at a higher frequency after initiation. These individuals might be the ones who change from other illicit drugs to methamphetamine.

(ii) We allow reversion from hard drug use to light drug use. We also allow for a relapse for those individuals in treatment so that they revert to hard drug use.

(iii) We also include the removal from the treatment class that include drug related death rate, unlike in [32].

(iv) In [32], initiation into drug use was due to interactions with a standard incidence function. In our model we include innovators. Innovators are the individuals who start

drug or methamphetamine use on their own, not due to the influence of individuals who are already methamphetamine users. This is realistic as for some individuals, the desire may be due to curiosity or any other internal motivations. The idea of innovators has also been used for cocaine users in [4].

(v) Lastly the population is divided into core and non-core so as to take into account the active population or high risk population who are more important in the spread of the methamphetamine epidemic.

3.2 Model formulation

The total population $N(t)$ is divided into two groups, the core group N_C and non-core group N_P . The core group is a subgroup of the population whose members are more prone to becoming drug users and cause others to become drug users i.e. the active group. The non-core group is the non active subgroup of the population. The idea of core and non core groups has also been used in the modelling of sexual transmitted diseases by Hadelor and Castillo-Chavez in [18] and references cited there in. The use of the terms core and non-core helps in the disease management strategies. Prevention strategies should be aimed at the core group. Members of the core group are recruited from the non active group. The core group is further subdivided into five different sub-groups of namely, susceptibles $S(t)$, light drug users $U_L(t)$, hard drug users $U_H(t)$, drug users in treatment $U_T(t)$ and permanent quitters $Q(t)$ at any time t so that

$$N(t) = N_P(t) + N_C(t),$$

and

$$N_C(t) = S(t) + U_L(t) + U_H(t) + U_T(t) + Q(t).$$

We assume that there is no removal or death related to drug use for light users. We also assume that the removal or death related to drug use is different between hard drug users and drug users in treatment. Furthermore, the probability for hard drug users to generate new drug users is given by η so that $0 < \eta < 1$. This is because hard drug users manifest ill effects of drug use and some may have been using drugs for a long time and may be older and socially distant from youths. Light drug users generally do not manifest obvious

adverse effects of drug use and are therefore more accepted to a non user [4]. A description of the parameters used in the model are given in TABLE. 3.1.

TABLE. 3.1. Description of parameters

Parameter	Description
β	Transmission rate
σ	A rate of becoming a hard user
γ	Uptake rate into treatment
ψ	A rate of reversion to light drug use
r	'Reinfection' rate to being a hard drug user
ρ_1, ρ_2	Permanent recovery rate
δ_1, δ_2	Removal rates related to drug use
π	Recruitment rate
θ	Proportions of individuals who progress fast into hard drug use
μ	Natural mortality rate
η	Relative infectivity of U_H when compared to U_L

Note that, 'reinfection' in this case depicts the reversion to drug use for those in treatment. The flow of individuals between compartment is shown in FIG. 3.1.

3.2.1 Model's equations

Based on the model diagram and the model parameters described in TABLE. 3.1, we now describe the movement of individuals in and out of each class.

Susceptible (S):

Susceptibles are increased by the recruitment of individuals from the non core class (N_P) at a constant rate πN_P . We assume that the susceptibles can become drug users (in classes U_L or U_H) through contact with drug users at a rate β and they suffer natural death at a rate μ . A proportion θ becomes hard drug users while the remainder becomes light drug users. So the rate of change of the population of susceptibles is given by,

$$\frac{dS}{dt} = \pi N_P - (\mu + \lambda)S, \quad (3.1)$$

where

$$\lambda = \beta(U_L + \eta U_H), \quad (3.2)$$

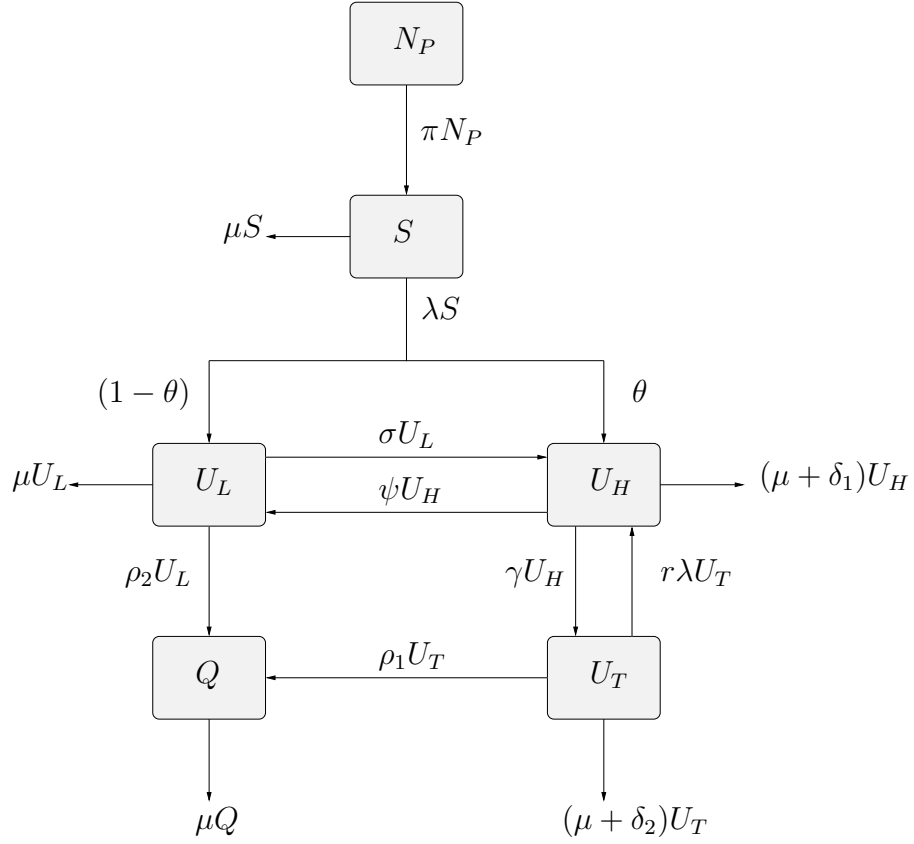


FIG. 3.1. Flow diagram for the Methamphetamine abuse model

is a force of infection.

Light drug users (U_L):

The population of light drug users is increased by a proportion $(1 - \theta)$ of those who are recruited into drug use, is also increased by hard users who revert to light drug use at a rate ψ . The population is decreased when; light drug users become hard drug users at a rate σ , quit using drugs at rate ρ_2 or die from natural causes at a rate μ , giving

$$\frac{dU_L}{dt} = \lambda S(1 - \theta) + \psi U_H - (\rho_2 + \sigma + \mu)U_L. \quad (3.3)$$

Hard drug users (U_H):

The population of hard drug users is generated by a proportion θ of susceptibles upon recruitment into drug use, when light drug users become hard drug users at a rate σ and

when individuals in treatment revert to hard drug use at a rate $r\lambda$. It is decreased by natural death at a rate μ , removal rate δ_1 and when hard drug users moves into treatment class at a rate γ . The removal rate that models deaths related to drug use in hard drug users class is given by δ_1 . Thus

$$\frac{dU_H}{dt} = \lambda S\theta + \sigma U_L + r\lambda U_T - (\gamma + \psi + \mu + \delta_1)U_H. \quad (3.4)$$

Drug users in treatment (U_T):

Drug users in treatment are generated by hard drug users who start treatment at a rate γ . They are decreased by natural death at the rate μ , removal due to death related to drug use at rate δ_2 , when they become hard drug users at a rate r and when they permanently quit using drugs at a rate ρ_1 , so that

$$\frac{dU_T}{dt} = \gamma U_H - (\rho_1 + \mu + \delta_2 + r\lambda)U_T. \quad (3.5)$$

Permanent quitters (Q):

The population of permanent quitters is increased when light drug users permanently quit using drugs at a rate ρ_2 as well as when drug users in treatment quit using drugs permanently at a rate ρ_1 . It is decreased by natural death at the rate μ . So we have

$$\frac{dQ}{dt} = \rho_2 U_L + \rho_1 U_T - \mu Q. \quad (3.6)$$

The model equations are thus given by

$$\left. \begin{aligned}
\frac{dS}{dt} &= \pi N_P - (\mu + \lambda)S, \\
\frac{dU_L}{dt} &= \lambda(1 - \theta)S + \psi U_H - (\rho_2 + \sigma + \mu)U_L, \\
\frac{dU_H}{dt} &= \lambda\theta S + \sigma U_L + r\lambda U_T - (\gamma + \psi + \mu + \delta_1)U_H, \\
\frac{dU_T}{dt} &= \gamma U_H - (\rho_1 + \mu + \delta_2 + r\lambda)U_T, \\
\frac{dQ}{dt} &= \rho_2 U_L + \rho_1 U_T - \mu Q,
\end{aligned} \right\} \quad (3.7)$$

with initial conditions $S(0) = S_0$, $U_L(0) = U_{L0}$, $U_H(0) = U_{H0}$, $U_T(0) = U_{T0}$, $Q(0) = Q_0$.

3.3 Analysis of the model

3.3.1 Basic properties

System (3.7) will be analyzed in a suitable feasible region G of biological interest.

Lemma 1 *The feasible region G defined by*

$$G = \{(S(t), U_L(t), U_H(t), U_T(t), Q(t)) \in \mathbb{R}_+^5 : S + U_L + U_H + U_T + Q \leq \frac{\pi N_P}{\mu}\}$$

is positively invariant and attracting with respect to model system for all $t > 0$.

Proof:

Adding the equations of the system (3.7) we obtain

$$\begin{aligned}
\frac{dN_C}{dt} &= \pi N_P - \mu N_C - \delta_1 U_H - \delta_2 U_T, \\
&\leq \pi N_P - \mu N_C,
\end{aligned}$$

whose analytic solution is

$$N_C(t) \leq N_C(0)e^{-\mu t} + \frac{\pi N_P}{\mu}[1 - e^{-\mu t}].$$

If $N_C(0) \leq \frac{\pi N_P}{\mu}$, then $N_C(t) \leq \frac{\pi N_P}{\mu}$, $\forall t > 0$.

Further, if $N_C(0) > \frac{\pi N_P}{\mu}$, then the solutions $(S(t), U_L(t), U_H(t), U_T(t), Q(t))$ enter G or approach it asymptotically and hence G is positively-invariant. Therefore in G , the basic model (3.7) is well-posed epidemiologically and mathematically. Hence, it is sufficient to study the dynamics of the basic model in G .

3.3.2 Positivity of solutions

For system (3.7), it is important to prove that all the state variables remain non-negative for all $t > 0$. In other words, the solutions of the system (3.7) with positive initial conditions will remain positive for all $t > 0$.

Lemma 2 *The initial conditions be $S(0) > 0$, $U_L(0) > 0$, $U_H(0) > 0$, $U_T(0) > 0$ and $Q(0) > 0$. Then, the solutions $S(t)$, $U_L(t)$, $U_H(t)$, $U_T(t)$ and $Q(t)$ of system (3.7) are non-negative for all $t > 0$.*

Proof:

Assume that $\bar{t} = \sup\{t > 0 : S > 0, U_L > 0, U_H > 0, U_T > 0, Q > 0\} \in [0, t]$. Thus $\bar{t} > 0$ and it follows from the first equation of the system (3.7) that

$$\frac{dS}{dt} = \pi N_P - (\mu + \lambda)S,$$

which can be written as

$$\frac{d}{dt} \left[S(t) \exp \left\{ \mu t + \int_0^t \lambda(s) ds \right\} \right] \geq \pi N_P \exp \left[\mu t + \int_0^t \lambda(s) ds \right].$$

Hence

$$S(\bar{t}) \exp \left[\mu \bar{t} + \int_0^{\bar{t}} \lambda(s) ds \right] - S(0) \geq \int_0^{\bar{t}} \pi N_P \exp \left[\mu \hat{t} + \int_0^{\hat{t}} \lambda(w) dw \right] d\hat{t},$$

so that

$$S(\bar{t}) \geq S(0) \exp \left[- \left\{ \mu \bar{t} + \int_0^{\bar{t}} \lambda(s) ds \right\} \right] \\ + \exp \left[- \left\{ \mu \bar{t} + \int_0^{\bar{t}} \lambda(s) ds \right\} \right] \left(\int_0^{\bar{t}} \pi N_P \exp \left[\mu \hat{t} + \int_0^{\hat{t}} \lambda(w) dw \right] d\hat{t} \right) > 0.$$

Then, from the second equation of (3.7),

$$\frac{dU_L}{dt} \geq -(\mu + \sigma + \rho_2)U_L, \\ U_L(t) \geq U_L(0) \exp -(\mu + \sigma + \rho_2)t > 0.$$

Similarly, it can be shown that $U_H(t) > 0$, $U_T(t) > 0$ and $Q(t) > 0$ for all $t > 0$. This completes the proof.

3.3.3 Steady states

Considering the first four equations of the system (3.7), we analyse the model by first looking at the equilibrium points. Equating the equations of the system (3.7) equal to zero as follows

$$0 = \pi N_P^* - (\mu + \lambda^*)S^*, \quad (3.8)$$

$$0 = \lambda^*S^*(1 - \theta) + \psi U_H^* - (\rho_2 + \sigma + \mu)U_L^*, \quad (3.9)$$

$$0 = \lambda^*S^*\theta + \sigma U_L^* + r\lambda^*U_T^* - (\gamma + \psi + \mu + \delta_1)U_H^*, \quad (3.10)$$

$$0 = \gamma U_H^* - (\rho_1 + \mu + \delta_2 + r\lambda^*)U_T^*, \quad (3.11)$$

$$0 = \rho_2 U_L^* + \rho_1 U_T^* - \mu Q^*. \quad (3.12)$$

we compute the state variables of the model (3.7) in terms of the force of infection λ^* . Solving for S^* from equation (3.8) we obtain

$$S^* = \frac{\pi N_P^*}{\lambda^* + \mu}.$$

Substituting it into equation(3.9), and solving for U_L^* we have

$$U_L^* = \frac{\pi N_P^* \lambda^* (1 - \theta) + \psi U_H^* (\lambda^* + \mu)}{(\lambda^* + \mu) b_1},$$

where $b_1 = (\mu + \sigma + \rho_2)$. Then from equation (3.11), we obtain

$$U_T^* = \frac{\gamma U_H^*}{r\lambda^* + b_3},$$

where $b_3 = (\rho_1 + \mu + \delta_2)$. Substituting U_L^* and U_T^* in equation (3.10) and solving for U_H^* gives

$$U_H^* = \pi N_P^* \lambda^* (r\lambda^* + b_3) \frac{[\sigma(1 - \theta) + \theta b_1]}{b_1 b_2 (r\lambda^* + b_3)(1 - q_1) - b_1 r \lambda^* \gamma},$$

where $b_2 = \gamma + \psi + \mu + \delta_1$ and $q_1 = \frac{\sigma\psi}{b_1 b_2}$.

Then by substituting back U_H^* into U_L^* and U_T^* , we have

$$U_L^* = \frac{\pi \lambda^* N_P^* \{r\lambda^* [\theta\psi - \gamma(1 - \theta)] + \theta\psi b_3 + b_2(1 - \theta)(r\lambda^* + b_3)\}}{b_1 b_2 (\lambda^* + \mu)(r\lambda^* + b_3)(1 - q_1) - b_1 r \lambda^* \gamma (\lambda^* + \mu)},$$

$$U_T^* = \frac{\pi \gamma \lambda^* N_P^* [\sigma(1 - \theta) + \theta b_1]}{b_1 b_2 (\lambda^* + \mu)(r\lambda^* + b_3)(1 - q_1) - b_1 r \lambda^* \gamma (\lambda^* + \mu)}.$$

So, we can write S^* , U_L^* , U_H^* , U_T^* and Q^* in terms of λ^* as follows

$$S^* = \frac{\pi N_P^*}{\lambda^* + \mu},$$

$$U_L^* = \frac{\pi \lambda^* N_P^* \{r\lambda^* [\theta\psi - \gamma(1 - \theta)] + \theta\psi b_3 + b_2(1 - \theta)(r\lambda^* + b_3)\}}{b_1 b_2 (\lambda^* + \mu)(r\lambda^* + b_3)(1 - q_1) - b_1 r \lambda^* \gamma (\lambda^* + \mu)},$$

$$U_H^* = \pi N_P^* \lambda^* (r\lambda^* + b_3) \frac{[\sigma(1 - \theta) + \theta b_1]}{(\lambda^* + \mu) \{b_1 b_2 (r\lambda^* + b_3)(1 - q_1) - r \lambda^* b_1 \gamma\}},$$

$$U_T^* = \frac{\pi \gamma \lambda^* N_P^* [\sigma(1 - \theta) + \theta b_1]}{b_1 b_2 (\lambda^* + \mu)(r\lambda^* + b_3)(1 - q_1) - b_1 r \lambda^* \gamma (\lambda^* + \mu)},$$

$$Q^* = \pi \lambda^* N_P^* \left\{ \frac{\rho_1 \{r\lambda^* [\theta\psi - \gamma(1 - \theta)] + \theta\psi b_3 + b_2(1 - \theta)(r\lambda^* + b_3)\} + \gamma \rho_2 [\sigma(1 - \theta) + \theta b_1]}{\mu b_1 b_2 (\lambda^* + \mu)(r\lambda^* + b_3)(1 - q_1) - b_1 r \lambda^* \gamma (\lambda^* + \mu)} \right\}.$$

Substituting back b_1 , b_2 , b_3 and q_1 , we obtain

$$\begin{aligned}
S^* &= \frac{\pi N_P^*}{\lambda^* + \mu}, \\
U_L^* &= \frac{\pi N_P^* \lambda^* \{r\lambda^* \theta \psi + [\theta \psi + \gamma(1 - \theta)] \{\mu + \delta_2 + \rho_1\} + (1 - \theta)(\mu + \psi + \delta_1)(r\lambda^* + \mu + \delta_2 + \rho_1)\}}{K}, \\
U_H^* &= \frac{\pi N_P^* \lambda^* (r\lambda^* + \mu + \delta_2 + \rho_1) [\sigma(1 - \theta) + \theta(\mu + \sigma + \rho_2)]}{K}, \\
U_T^* &= \frac{\pi \gamma \lambda^* N_P^* [\theta \mu + \sigma + \theta \rho_2]}{K}, \\
Q^* &= \frac{\pi \lambda^* N_P^* \{r\lambda^* + \mu + \delta_2 + \rho_1\} \rho_2 + \gamma \rho_1 [\sigma(1 - \theta) + \theta(\mu + \sigma + \rho_2)]}{\mu K},
\end{aligned}$$

where $\lambda^* = \beta(U_L^* + \eta U_H^*)$

and $K = (\lambda^* + \mu)(\mu + \sigma + \rho_2) \{ (r\lambda^* + \mu + \delta_2 + \rho_1) [\mu + \psi(\mu + \rho_2) + \delta_1] + \gamma(\mu + \delta_2 + \rho_1) \}$.

Substituting the expressions of U_L^* and U_H^* into the expression of λ^* , we obtain a polynomial

$$\lambda^* [A\lambda^{*2} + B\lambda^* + C] = 0 \quad (3.13)$$

where

$$\begin{aligned}
A &= -r[b_1(\mu + \delta_1) + \psi(\mu + \rho_2)], \\
B &= r\gamma\mu b_1 - r\mu b_1 b_2(1 - q_1) - b_1 b_2 b_3(1 - q_1) - \pi r \beta \gamma N_P(1 - \theta) + \pi r \beta \theta \psi N_P \\
&\quad + \pi r \beta b_2 N_P(1 - \theta) + \pi r \beta \sigma N_P \eta(1 - \theta) + \pi r \beta \theta b_1 N_P \eta, \\
C &= \mu b_1 b_2 b_3(1 - q_1) \left\{ \frac{\pi \beta N_P}{\mu(1 - q_1)} \left[\frac{\theta \psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} + \eta \left\{ \frac{\sigma(1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right\} \right] - 1 \right\}.
\end{aligned}$$

From equation (3.13), we thus have $\lambda^* = 0$ or

$$A\lambda^{*2} + B\lambda^* + C = 0. \quad (3.14)$$

The case $\lambda^* = 0$, gives the drug free equilibrium (DFE) so that

$$E_0 = (S^*, U_L^*, U_H^*, U_T^*, Q^*) = \left(\frac{\pi N_P}{\mu}, 0, 0, 0, 0 \right)$$

and the drug persistent equilibrium can be obtained from the quadratic equation (3.14).

Before proceeding with the analysis of the quadratic equation (3.14), we compute the basic reproduction number R_0 of the system (3.7) using E_0 above.

3.3.4 R_0 and local stability of the drug free equilibrium (E_0)

R_0 is the basic reproduction number of the model. It represents the average number of secondary cases that one drug user can generate during his duration of drug use in a population of potential drug users. There are several methods that are used in the calculation of basic reproduction number such as the next generation matrix, the survival function and many others. For our model, we use next generation matrix as presented in [51]. The system (3.7) can be written as

$$x' = \mathcal{F}(x) - \mathcal{V}(x)$$

where

$$\mathcal{F}(x) = \begin{pmatrix} 0 \\ \beta S(1 - \theta)(U_L + \eta U_H) \\ \beta S\theta(U_L + \eta U_H) \\ 0 \\ 0 \end{pmatrix},$$

and

$$\mathcal{V}(x) = \begin{pmatrix} (\mu + \lambda)S - \pi N_P \\ b_1 U_L - \psi U_H \\ b_2 U_H - \sigma U_L - r\lambda U_T \\ (b_3 + r\lambda)U_T - \gamma U_H \\ \mu Q - \rho_1 U_T - \rho_2 U_L \end{pmatrix}.$$

The matrices for new infection terms (F) and the transfer terms (V) at the DFE are as follows;

$$F = \begin{pmatrix} \frac{\beta(1 - \theta)\pi N_P}{\mu} & \frac{\beta(1 - \theta)\eta\pi N_P}{\mu} \\ \frac{\beta\theta\pi N_P}{\mu} & \frac{\beta\theta\eta\pi N_P}{\mu} \end{pmatrix}$$

and

$$V = \begin{pmatrix} b_1 & -\psi \\ -\sigma & b_2 \end{pmatrix}.$$

According to [51], the basic reproduction number is the spectra radius of the FV^{-1} , given

by

$$R_0 = \frac{\pi\beta N_P}{\mu(1-q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1-\theta)}{b_1} + \eta \left\{ \frac{\sigma(1-\theta)}{b_1 b_2} + \frac{\theta}{b_2} \right\} \right]. \quad (3.15)$$

The expression of R_0 is the sum of two terms representing the contribution of light drug users and hard drug users respectively. It can be interpreted as follows:

- $\frac{1}{b_1}$ refers to the duration methamphetamine users spends in light drug use stage,
- $\frac{1}{b_2}$ is the duration methamphetamine users spends in hard drug use stage,
- $\frac{\theta\psi}{b_1 b_2} + \frac{(1-\theta)}{b_1}$ is the contribution of light drug users to the MA epidemics,
- $\eta \left(\frac{\sigma(1-\theta)}{b_1 b_2} + \frac{\theta}{b_2} \right)$ is the contribution of hard drug users to the MA epidemics.

A reproduction number obtained by this method determines the local stability of the drug free equilibrium with local asymptotic stability for $R_0 < 1$ and instability for $R_0 > 1$. We thus summarise our results in the following theorem.

Theorem 3.3.1 *The drug free equilibrium point, E_0 , is locally asymptotically stable if $R_0 < 1$ and unstable otherwise.*

3.3.5 Existence of drug persistent equilibriums

Existence of drug persistent equilibrium depends on the quadratic equation (3.14), that is, if it has positive roots. The sign of the roots depends on the sign of B and C since $A < 0$. We present the quadratic equation again here for the convenience of reading.

$$A\lambda^{*2} + B\lambda^* + C = 0, \quad (3.16)$$

with

$$\begin{aligned}
A &= -r[b_1(\mu + \delta_1) + \psi(\mu + \rho_2)], \\
B &= r\gamma\mu b_1 - r\mu b_1 b_2(1 - q_1) - b_1 b_2 b_3(1 - q_1) - \pi r\beta\gamma N_P(1 - \theta) + \pi r\beta\theta\psi N_P + \pi r\beta b_2 N_P(1 - \theta) \\
&\quad + \pi r\beta\sigma N_P\eta(1 - \theta) + \pi r\beta\theta b_1 N_P\eta, \\
C &= \mu b_1 b_2 b_3(1 - q_1) \left\{ \frac{\pi\beta N_P}{\mu(1 - q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} + \eta \left\{ \frac{\sigma(1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right\} \right] - 1 \right\}.
\end{aligned}$$

We solve for λ^* using the general quadratic formula

$$\lambda_{1,2}^* = \frac{-B \pm \sqrt{B^2 - 4AC}}{2A}. \quad (3.17)$$

Now expressing C in terms of R_0 , gives

$$C = -\mu b_1 b_2 b_3(1 - q_1)[1 - R_0].$$

Therefore from the general formula (3.17), if $R_0 > 1$ then $C > 0$ and if $B < 0$, then the quadratic (3.16) has two distinct roots of opposite signs. The same result is obtained if $B > 0$ with $R_0 > 1$. So irrespective of the sign of B as long as $R_0 > 1$, we have a unique drug persistent equilibrium.

If $R_0 < 1$ then $C < 0$ and if $B < 0$, then the quadratic (3.16) has two distinct negative roots. If $B > 0$ and $R_0 < 1$ then it has two distinct positive roots.

So if $R_0 < 1$ and $B > 0$, then two positive roots do exist. This result is of particular interest, as two positive roots exist when $R_0 < 1$. We thus have the following result.

Theorem 3.3.2 *The model (3.7) has;*

- (i) *a unique drug persistent equilibrium if $R_0 > 1$,*
- (ii) *a unique drug persistent equilibrium if $B > 0$, and $C = 0$ or $B^2 - 4AC = 0$,*
- (iii) *two drug persistent equilibria if $B > 0$ and $R_0 < 1$,*
- (iv) *no drug persistent equilibrium otherwise.*

It is clear from Theorem (3.3.2) case (i) that the model has a unique drug persistent equilibrium whenever $R_0 > 1$. Further, case (iii) indicates the possibility of backward

bifurcation. To check for this, we set the discriminant zero and the result solved for the critical value of R_0 , giving

$$R_0^c = 1 + \frac{B^2}{4A\mu b_1 b_2 b_3 (1 - q_1)}, \quad (3.18)$$

where R_0^c is a critical value of R_0 , below which no drug persistent equilibrium exist:

Remark 1 *For an effective drug control, the reproduction number should be brought below R_0^c . The condition $R_0 < 1$ is not sufficient.*

From Theorem (3.3.2) assertions (ii) and (iii), (3.18), it can be shown that backward bifurcation occurs and for values of R_0 such that $R_0^c < R_0 < 1$, the model has two positive equilibria coexisting with the drug free equilibrium. This is illustrated by simulating the model equation (3.7) with parameter values in TABLE. 3.2.

TABLE. 3.2. Parameter values used in the simulations for the bifurcation diagram

Parameter	Value	Source
π	0.0301	Estimated
σ	0.0126	Estimated
r	19	Estimated
ψ	0.0307	Estimated
η	0.95	Estimated
γ	0.057	Estimated
θ	0.03	Estimated
β	$(1.35 \times 10^{-7}, 1.598 \times 10^{-7})$	Estimated
δ_1	0.0046	Estimated
δ_2	0.0002	Estimated
μ	0.0246	[32]
ρ_1	0.002	Estimated
ρ_2	0.9394	Estimated

These parameter values are chosen for illustrative purposes only and may not necessarily be realistic. FIG. 3.2 with the corresponding numerical values in TABLE. 3.3 where $R_0^c = 0.961$ shows backward bifurcation.

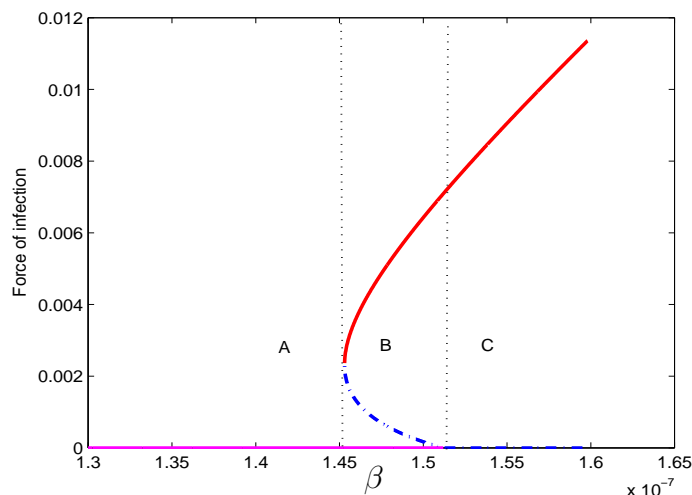


FIG. 3.2. Shows a backward bifurcation as β varied from 1.3×10^{-7} to 1.65×10^{-7} for parameter values in TABLE. 3.2. Region A, B and C as described in TABLE. 3.3. The dash-dot blue curve depicts unstable equilibria and the continuous curve depicts stable equilibria. The value for $r = 19$.

The simulation results depicted in FIG. 3.2, show that the model (3.7) has only drug free equilibrium when $R_0 < R_0^c$, has two drug persistent equilibria when $R_0^c < R_0 < 1$ and has one drug persistent equilibrium when $R_0 > 1$ as shown by regions A, B and C respectively. In region A, the drug free equilibrium is locally asymptotically stable, while in region B one of the drug persistent equilibrium is stable and the other is unstable. This clearly shows co-existence of two stable equilibria when $R_c < R_0 < 1$, confirming that the model (3.7) exhibits backward bifurcation. In region C, the drug persistent equilibrium is stable as shown in TABLE. 3.3.

TABLE. 3.3. A numerical summary of FIG. 3.2 with the corresponding reproduction number (R_0) and local stability of equilibria for each region A, B and C.

Region	β	R_0	Type of steady states	Stability of steady state
A	$< 1.453 \times 10^{-7}$	< 0.961	Drug free equilibrium	Stable
B	$(1.453 \times 10^{-7}, 1.512 \times 10^{-7})$	$(0.961, 1)$	Drug free and two drug persistent equilibria	Stable drug free and one drug persistent equilibria while the other drug persistent equilibrium is unstable
C	$> 1.512 \times 10^{-7}$	> 1	Drug free and one drug persistent equilibria	The drug free equilibrium is unstable while drug persistent equilibrium is stable

The simulation also agrees with the Theorem (3.3.1). To further illustrate this phenomenon, we include a time series plot FIG. 3.3, using different initial conditions and the parameter values in TABLE. 3.2 with β values within each of the regions A, B and C. We observe that irrespective of initial conditions, the graphs stabilize to, drug free equilibrium in region A, one drug persistent and drug free equilibria in region B and in region C to the drug persistent equilibrium.

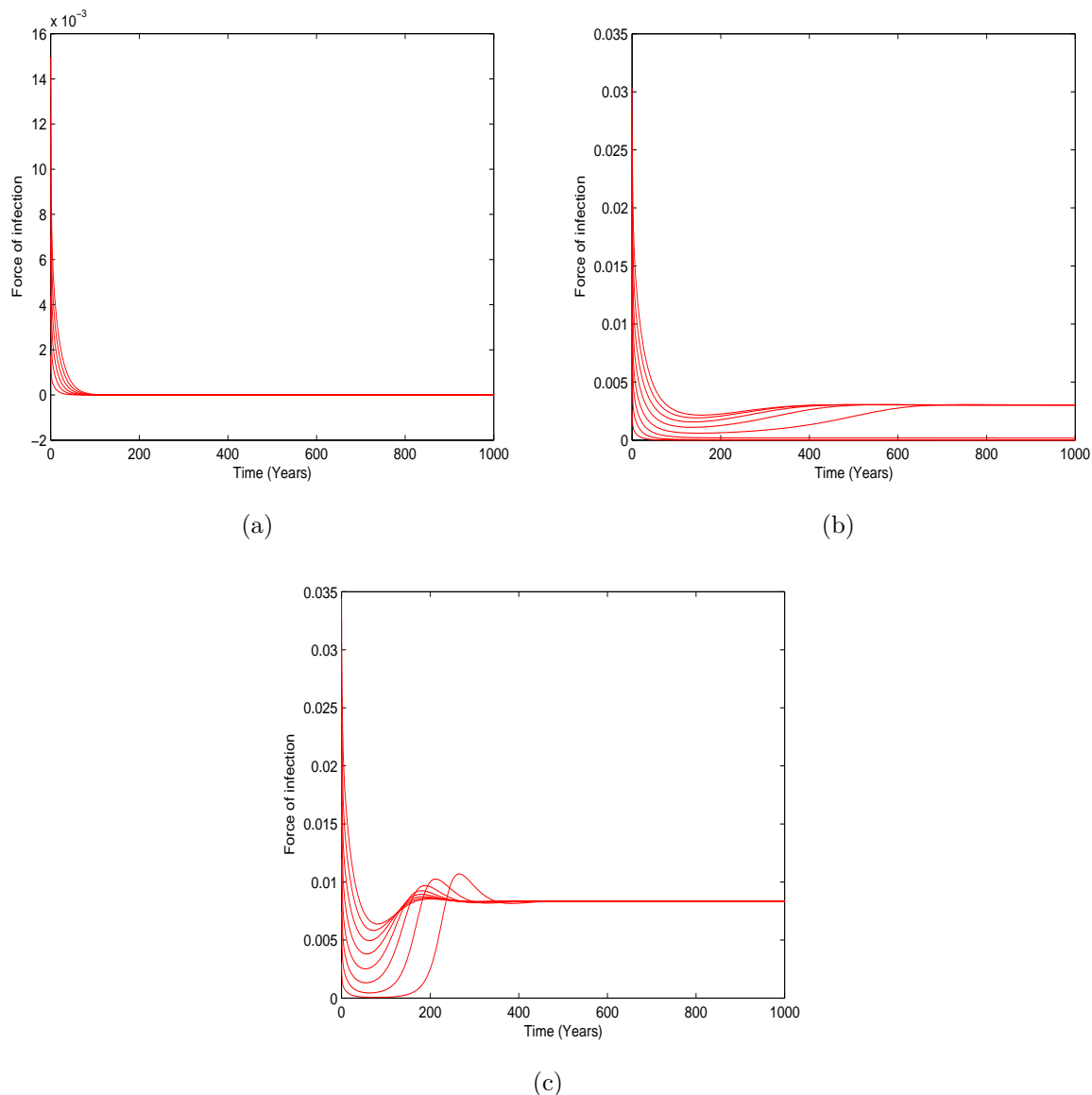


FIG. 3.3. Time series plot using different initial conditions of the model (3.7) and parameter values in TABLE. 3.2. (a) shows that in region A of FIG. 3.2 the drug free equilibrium is stable with $\beta = 1 \times 10^{-7}$. (b) shows that the drug free equilibrium and one drug persistent equilibrium are stable in region B for $\beta = 1.499 \times 10^{-7}$ and (c) shows that there is a stable drug persistent equilibrium in region C with $\beta = 1.7 \times 10^{-7}$. For $r = 19$.

3.3.6 Stability of drug persistent equilibria

In this subsection, we determine the stability of drug persistent equilibrium and further investigate the possibility of backward bifurcation due to existence of multiple equilibria as

indicated in Theorem (3.3.2) case(iii). The stability analysis of drug persistent equilibrium point require us to determine the eigenvalues of the Jacobian matrix evaluated at drug persistent equilibrium. Since expressing drug persistent equilibria explicitly is complicated for the system (3.7), calculation of eigenvalues is mathematically cumbersome. So we use the center manifold theory as presented in [8]. To apply this method we first change the variables of the model equations (3.7) so that

$$S = x_1, U_L = x_2, U_H = x_3, U_T = x_4, \text{ and } Q = x_5 \text{ with } \frac{dx_1}{dt} = f_1, \frac{dx_2}{dt} = f_2, \frac{dx_3}{dt} = f_3, \frac{dx_4}{dt} = f_4, \frac{dx_5}{dt} = f_5.$$

System (3.7) becomes

$$\left. \begin{aligned} f_1 &= \pi N_P - \mu x_1 - \beta x_1(x_2 + \eta x_3), \\ f_2 &= \beta x_1(1 - \theta)(x_2 + \eta x_3) + \psi x_3 - b_1 x_2, \\ f_3 &= \beta x_1 \theta(x_2 + \eta x_3) + \sigma x_2 + \beta r x_4(x_2 + \eta x_3) - b_2 x_3, \\ f_4 &= \gamma x_3 - b_3 x_4 - \beta r x_4(x_2 + \eta x_3), \\ f_5 &= \rho_2 x_2 + \rho_1 x_4 - \mu x_5. \end{aligned} \right\} \quad (3.19)$$

We choose $\phi = \beta$ as the bifurcation parameter. We thus equate $R_0 = 1$, we obtain

$$\phi = \frac{\mu b_1 b_2 (1 - q_1)}{\pi N_P \{ \eta \sigma (1 - \theta) + \theta \psi + \eta \theta b_1 + b_2 (1 - \theta) \}}. \quad (3.20)$$

The Jacobian of the system (3.19) at DFE, E_0 when $\phi = \beta$ is given as

$$J(\phi) = \begin{pmatrix} -\mu & -\phi & -\frac{\phi \eta \pi N_P}{\mu} & 0 & 0 \\ 0 & \frac{\phi(1-\theta)\pi N_P}{\mu} - b_1 & \frac{\eta \phi(1-\theta)\pi N_P}{\mu} + \psi & 0 & 0 \\ 0 & \frac{\phi \theta \pi N_P}{\mu} + \sigma & \frac{\phi \theta \eta \pi N_P}{\mu} - b_2 & 0 & 0 \\ 0 & 0 & \gamma & -b_3 & 0 \\ 0 & \rho_2 & 0 & \rho_1 & -\mu \end{pmatrix}.$$

The Jacobian $J(\phi)$ of the linearized system has a simple zero eigenvalue. We can thus use the center manifold theory to analyse the dynamics of (3.19). The right eigenvector

associated with zero eigenvalue are given by $w = [w_1, w_2, w_3, w_4, w_5]^T$, where

$$\begin{aligned} w_1 &= \frac{-(\eta\sigma + b_2)(1 - q_1)b_1b_2b_3}{\mu\{\theta[(1 - q_1)b_1b_2 + \sigma\{\eta\sigma(1 - \theta) + \theta\psi + \eta\theta b_1 + b_2(1 - \theta)\}]\}}w_4, \\ w_2 &= \frac{b_3[\eta\theta\sigma\psi + b_2\{\eta\sigma(1 - \theta) + \theta\psi + b_2(1 - \theta)\}]}{\theta(1 - q_1)b_1b_2 + \gamma\sigma[\eta\sigma(1 - \theta) + \theta\psi + \eta\theta b_1 + b_2(1 - \theta)]}w_4, \\ w_3 &= b_3w_4, \\ w_4 &= \gamma w_4 > 0, \\ w_5 &= \frac{(b_2 + \eta\sigma)(\theta\psi b_3\rho_2 + \theta\gamma\rho_1 b_1) + [\eta\sigma(1 - \theta) + b_2(1 - \theta)](\gamma\sigma\rho_1 + \rho_2 b_2 b_3)}{\mu\{\theta(1 - q_1)b_1b_2 + \sigma[\eta\sigma(1 - \theta) + \theta\psi + \eta\theta b_1 + b_2(1 - \theta)]\}}w_4. \end{aligned}$$

Further, $J(\phi)$ has a corresponding left eigenvector $v = [v_1, v_2, v_3, v_4, v_5]^T$, where

$$\begin{aligned} v_1 &= 0, \\ v_2 &= \alpha v_2 > 0, \\ v_3 &= \frac{\alpha b_1\{\sigma\psi(1 - \theta) + b_1[\eta\sigma(1 - \theta) + \theta\psi]\}}{\theta b_1 b_2(1 - q_1) + \sigma[\eta\sigma(1 - \theta) + \theta\psi + \eta\theta b_1 + b_2(1 - \theta)]}v_2 \\ v_4 &= 0, \\ v_5 &= 0, \end{aligned}$$

where

$$\alpha = \frac{\gamma\{\theta b_1 b_2(1 - q_1) + \sigma[\eta\sigma(1 - \theta) + \theta\psi + \eta\theta b_1 + b_2(1 - \theta)]\}}{b_3\{\sigma\psi[\eta\theta + (1 - \theta)] + (b_1 + b_2)\{\eta\sigma(1 - \theta) + \theta\psi\} + \eta\theta b_1^2 + b_2^2(1 - \theta)\}}.$$

We note that all the eigenvectors are positive except for w_1 and the value of α is chosen so that $v \cdot w = 1$. Following [8], we restate the following Theorem and use it to prove local stability of drug persistent equilibrium near $R_0 = 1$.

Theorem 3.3.3 : Consider the following general system of ordinary differential equations with a parameter ϕ :

$$\frac{dx}{dt} = f(x, \phi), \quad f : \mathbb{R}^n \times \mathbb{R} \rightarrow \mathbb{R} \quad \text{and} \quad f \in \mathcal{C}(\mathbb{R}^n \times \mathbb{R}),$$

where 0 is an equilibrium point of the system (i.e., $f(0, \phi) \equiv 0$ for all ϕ) and assume $A1$: $A = D_x f(0, 0) = \left(\frac{\partial f}{\partial x_j}(0, 0)\right)$ is the linealization matrix of the system around the equilibrium 0 with ϕ evaluated at 0 . Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts;

$A2$: Matrix A has a non zero right eigenvectors w and a left eigenvector v corresponding to the zero eigenvalue. Let f_k be the k th component of f and

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

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

The local dynamics of the system around 0 depends on the sign of \mathbf{a} and \mathbf{b} .

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

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

iii. $\mathbf{a} > 0, \mathbf{b} < 0$. When $\phi < 0$ with $|\phi| \ll 1$, 0 is unstable and there exists a locally asymptotically stable negative equilibrium; when $0 < \phi \ll 1$, 0 is stable and a positive unstable equilibrium appears;

iv. $\mathbf{a} < 0, \mathbf{b} > 0$. When ϕ changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.

In particular, since $v_1 = v_4 = v_5 = 0$

$$\mathbf{a} = v_2 \sum_{i,j=1}^5 w_i w_j \frac{\partial^2 f_2}{\partial x_i \partial x_j}(0,0) + v_3 \sum_{i,j=1}^5 w_i w_j \frac{\partial^2 f_3}{\partial x_i \partial x_j}(0,0),$$

and

$$\mathbf{b} = v_2 \sum_{i=1}^5 w_i \frac{\partial^2 f_2}{\partial x_i \partial \phi}(0,0) + v_3 \sum_{i=1}^5 w_i \frac{\partial^2 f_3}{\partial x_i \partial \phi}(0,0).$$

To compute the value of \mathbf{a} and \mathbf{b} , we first compute the non zero second order partial derivatives of the system (3.19) at drug free equilibrium as follows

$$\frac{\partial^2 f_2}{\partial x_1 \partial x_2} = \frac{\partial^2 f_2}{\partial x_2 \partial x_1} = \phi(1-\theta), \quad \frac{\partial^2 f_2}{\partial x_1 \partial x_3} = \frac{\partial^2 f_2}{\partial x_3 \partial x_1} = \phi(1-\theta)\eta, \quad \frac{\partial^2 f_3}{\partial x_1 \partial x_2} = \frac{\partial^2 f_3}{\partial x_2 \partial x_1} = \phi\theta,$$

$$\frac{\partial^2 f_3}{\partial x_1 \partial x_3} = \frac{\partial^2 f_3}{\partial x_3 \partial x_1} = \phi\theta\eta, \quad \frac{\partial^2 f_3}{\partial x_2 \partial x_4} = \frac{\partial^2 f_3}{\partial x_4 \partial x_2} = r\phi, \quad \frac{\partial^2 f_3}{\partial x_3 \partial x_4} = \frac{\partial^2 f_3}{\partial x_4 \partial x_3} = r\phi\eta,$$

$$\frac{\partial^2 f_2}{\partial x_2 \partial \phi} = \frac{\pi(1-\theta)N_P}{\mu}, \quad \frac{\partial^2 f_2}{\partial x_3 \partial \phi} = \frac{\pi(1-\theta)\eta N_P}{\mu}, \quad \frac{\partial^2 f_3}{\partial x_2 \partial \phi} = \frac{\pi\theta N_P}{\mu}, \quad \frac{\partial^2 f_3}{\partial x_3 \partial \phi} = \frac{\pi\theta\eta N_P}{\mu}.$$

It thus follows that

$$\mathbf{a} = \frac{2\phi w_4(w_2 + w_3\eta)\{\Gamma - X\}}{\gamma\mu(\mu\sigma + \pi\theta\phi N_P)},$$

where

$$\begin{aligned}\Gamma &= r\gamma\mu v_3[(\mu\sigma + \pi\theta\phi N_P)], \\ X &= \pi\phi b_3 N_P(\eta\sigma + b_2)[v_2(1 - \theta) + \theta v_3].\end{aligned}$$

Also

$$\mathbf{b} = \frac{\pi N_P[v_2(1 - \theta) + \theta v_3](w_2 + w_3\eta)}{\mu}.$$

Hence the sign of \mathbf{a} depends on the value of Γ and X , so that if $\Gamma > X$ then $\mathbf{a} > 0$ and if $\Gamma < X$ then $\mathbf{a} < 0$ while $\mathbf{b} > 0$.

We thus have the following result:

Theorem 3.3.4 *If $\Gamma > X$, then the system (3.7) has a backward bifurcation at $R_0 = 1$, otherwise if $\Gamma < X$ then it undergoes forward bifurcation and the drug persistent equilibrium is locally asymptotically stable for $R_0 > 1$ but close to one.*

3.4 Sensitivity analysis

Sensitivity analysis is used to determine how sensitive a model is, to changes in the values of the parameters of the model. It provides information on factors that most contribute to the output variability. In this section we perform sensitivity analysis by calculating the sensitivity indices of the basic reproduction number R_0 , because they determine whether methamphetamine abuse spreads in the population or not. These indices tell us how crucial each parameter is to the spread of methamphetamine abuse. Sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values because there are usually errors in data collection and presumed parameter values [10].

We apply the method presented in [10] to investigate which parameters in our model have a high impact on R_0 . These parameters have to be taken into consideration in intervention strategies. According to [10], the normalized forward sensitivity index of a variable to

a parameter, is a ratio of the relative change in the variable to the relative change in parameter. When the variable is a differentiable function of the parameter, the sensitivity index may alternatively be defined using partial derivatives. We use the following definition;

Definition 3.4.1 : *The normalized forward sensitivity index of a variable, ϑ , that depends on a differentiable parameter ξ is defined as:*

$$\Upsilon_{\xi}^{\vartheta} = \frac{\partial \vartheta}{\partial \xi} \times \frac{\xi}{\vartheta}.$$

3.4.1 Sensitivity indices of R_0

We compute the sensitivity indices of R_0 to each of the methamphetamine abuse model parameters. We use the parameter values displayed in TABLE. 4.3 and the results are shown in TABLE. 3.4. For example, the sensitivity indices of R_0 with respect to β and π are

$$\Upsilon_{\beta}^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1$$

and

$$\Upsilon_{\pi}^{R_0} = \frac{\partial R_0}{\partial \pi} \times \frac{\pi}{R_0} = 1$$

which do not depend on any parameter values. This shows that R_0 is an increasing function of β and π . This also indicates that transmission and recruitment rates have a high impact on the spread of methamphetamine abuse. For the parameter η we have the following expression

$$\Upsilon_{\eta}^{R_0} = \frac{\partial R_0}{\partial \eta} \times \frac{\eta}{R_0} = \frac{\eta(\theta\mu + \sigma + \theta\rho_2)}{\varepsilon} > 0,$$

where

$$\varepsilon = \theta\psi + (1 - \theta)(\mu + \gamma + \psi + \delta_1) + \eta(\theta\mu + \sigma + \theta\rho_2).$$

This shows that increasing (or decreasing) the relative infectivity, increases (or decreases) the number of drug users who will be initiated by hard drug users. Therefore we will have an increase (or decrease) in the spread of methamphetamine abuse. We also obtain that

$$\frac{\partial R_0}{\partial \rho_2} \times \frac{\rho_2}{R_0} = \frac{-[(1-\theta)(\gamma+\mu)+\psi+(1-\theta)\delta_1](\mu+\gamma+\psi+\delta_1+\sigma\eta)\rho_2}{\Lambda} < 0,$$

with

$$\begin{aligned} \Lambda = & [(\gamma+\mu)(\mu+\sigma)+\mu\psi+(\mu+\gamma+\psi)\rho_2+\delta_1(\mu+\sigma+\rho_2)] \\ & \{(1-\theta)(\gamma+\mu)+\psi+(1-\theta)\delta_1+(\theta\mu+\sigma+\theta\rho_2)\}. \end{aligned}$$

This shows that R_0 is a decreasing function of ρ_2 . Therefore increasing ρ_2 reduces R_0 . Other expressions for the sensitivity indices are not obvious to tell whether they are positive or negative. We, therefore evaluate the sensitivity indices using the estimated parameter values given in the TABLE. 4.3 of Chapter 4. These parameter values were obtained after fitting the model to data in Chapter 4. The results are given in TABLE. 3.4.

TABLE. 3.4. Sensitivity indices of R_0

Parameter	Sensitivity index
μ	-1.59079
β	+1.0000
π	+1.0000
ρ_2	-0.221652
σ	-0.180165
γ	-0.126156
ψ	+0.118761
η	+0.0148894
θ	-0.000047493
δ_1	$-3.03373 * 10^{-6}$

The sensitivity indices are arranged in the order of magnitude from the highest to the lowest. The table contains positive and negative sensitivity indices. The indices with positive signs increase the value of R_0 when they are increased and those having negative signs decrease the value of R_0 when they are increased.

The most sensitive parameters are the transmission and recruitment rate β and π respectively. This is because $\Upsilon_{\beta}^{R_0} = +1.0$ and $\Upsilon_{\pi}^{R_0} = 1.0$ which means increasing (or decrease) β and π by 10%, increases (or decreases) R_0 by 10%. Also increasing (or decreasing) relative infectivity η and reversion rate ψ will increase (or decrease) R_0 . These results suggest that intervention strategies should be targeted to transmission, recruitment, reversion rate as well as relative infectivity so as to reduce them. We also observe that R_0 is most sensitive to μ in an inversely proportional way. This is to say R_0 is a decreasing function of μ , where by increasing μ will decrease R_0 and decreasing μ will increase R_0 . Recalling that μ is the natural death rate of population, increasing it is neither ethical nor practical. Furthermore R_0 is a decreasing function of ρ_2 , θ , γ and σ . This tells us that increasing these parameters reduces R_0 . From these parameters we focus on the uptake rate into treatment γ and the recovery rate ρ_2 which can be controlled by intervention and prevention programs. Increasing γ would mean having affordable and more treatment centers so as to allow more drug users into treatment and hence reduce initiation processes. Also, the spread of methamphetamine abuse can be reduced by increasing ρ_2 . Since ρ_2 is the rate at which light drug users quit drug use, increasing it would reduce the number of light drug users as well as drug initiation. This can be done by having intervention programs which focus on light drug users. We include FIG. 3.4 and FIG. 3.5 for more illustrations of sensitivity analysis.

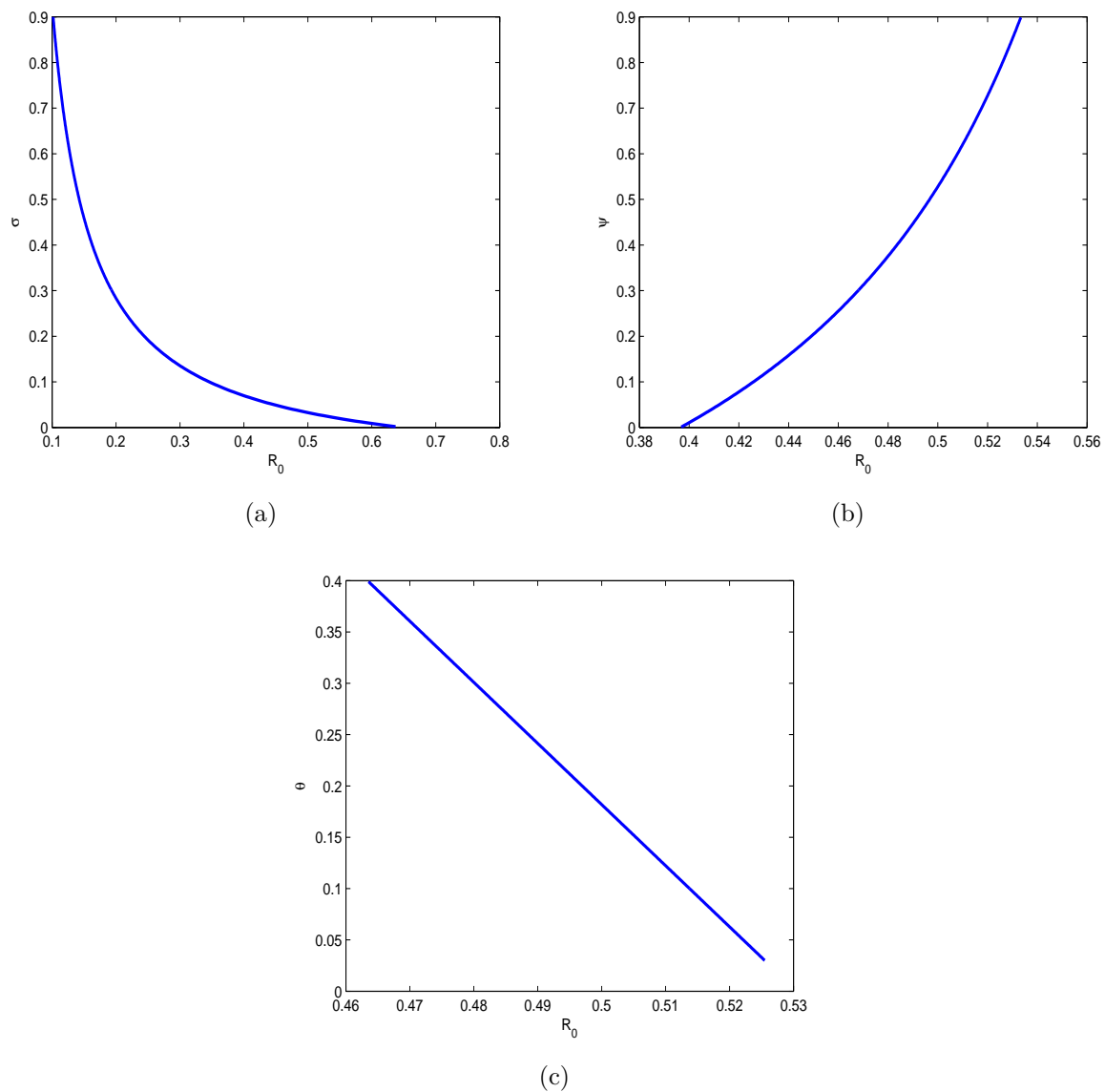


FIG. 3.4. Demonstrates the changes in the R_0 as σ , ψ and θ changes respectively. Graph (a) relates R_0 and σ , (b) relates R_0 and ψ , and (c) shows the relationship between R_0 and θ . Parameter values are given in TABLE. 4.3.

We further investigate the effect of the duration spent in the two drug use classes, U_L and U_H . We observe that as drug users spend more time in U_L , the drug user generation number R_0 increases as shown in FIG. 3.6 (a). In other words R_0 increases for longer duration spent in the light drug use class. On the other hand, R_0 decreases for longer duration spent in the hard drug use class. This is shown in FIG. 3.6 (b).

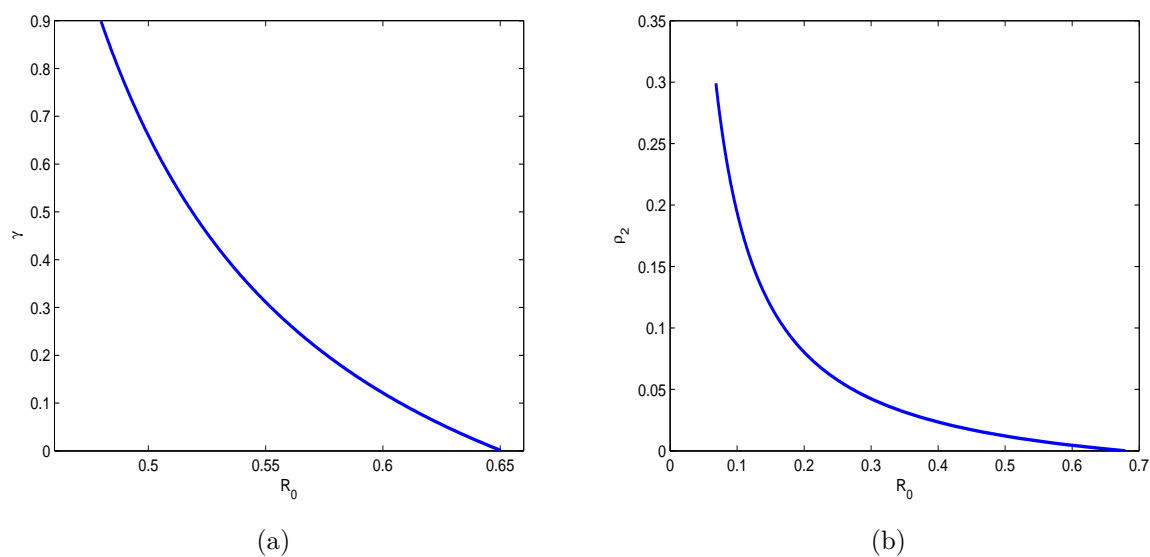


FIG. 3.5. Illustrates how R_0 changes with the change in γ and ρ_2 respectively. Graphs (a) shows the change in R_0 with γ and (b) shows the change in R_0 as a result of change in ρ_2 . Parameter values are given in TABLE. 4.3.

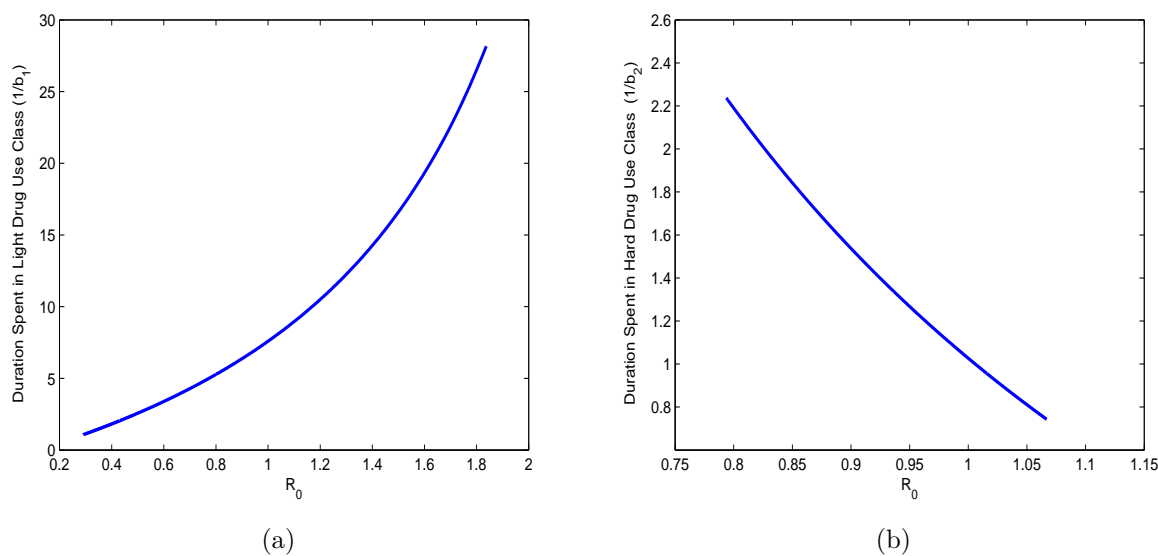


FIG. 3.6. Shows the drug user generation number R_0 as a function of duration drug users spend in light and hard drug use classes respectively. (a) shows how R_0 changes as duration spent in light drug use changes and (b) indicates how R_0 changes with the change of duration spent in hard drug use class. Parameter values are given in TABLE. 4.3.

3.5 Numerical simulations

We carry out numerical simulations using a fourth order Runge Kutta numerical scheme in Matlab. The aim is to verify the analytical results we obtained on the stability of the

system (3.7). We first establish the parameter values to be used in the simulations and initial conditions.

For the purpose of these simulations, we consider the population of one million individuals for the core group and four million for the non core group. The parameter values used in the simulations are given in TABLE. 4.3. These parameter values were obtained from the fitting of the model in Chapter 4.

We now illustrate some of the numerical results we obtained using mass action. We first consider the case when $R_0 < 1$, with $R_0 = 0.5303$. The dynamics of drug users is represented by FIG. 3.7 and FIG. 3.8(a).

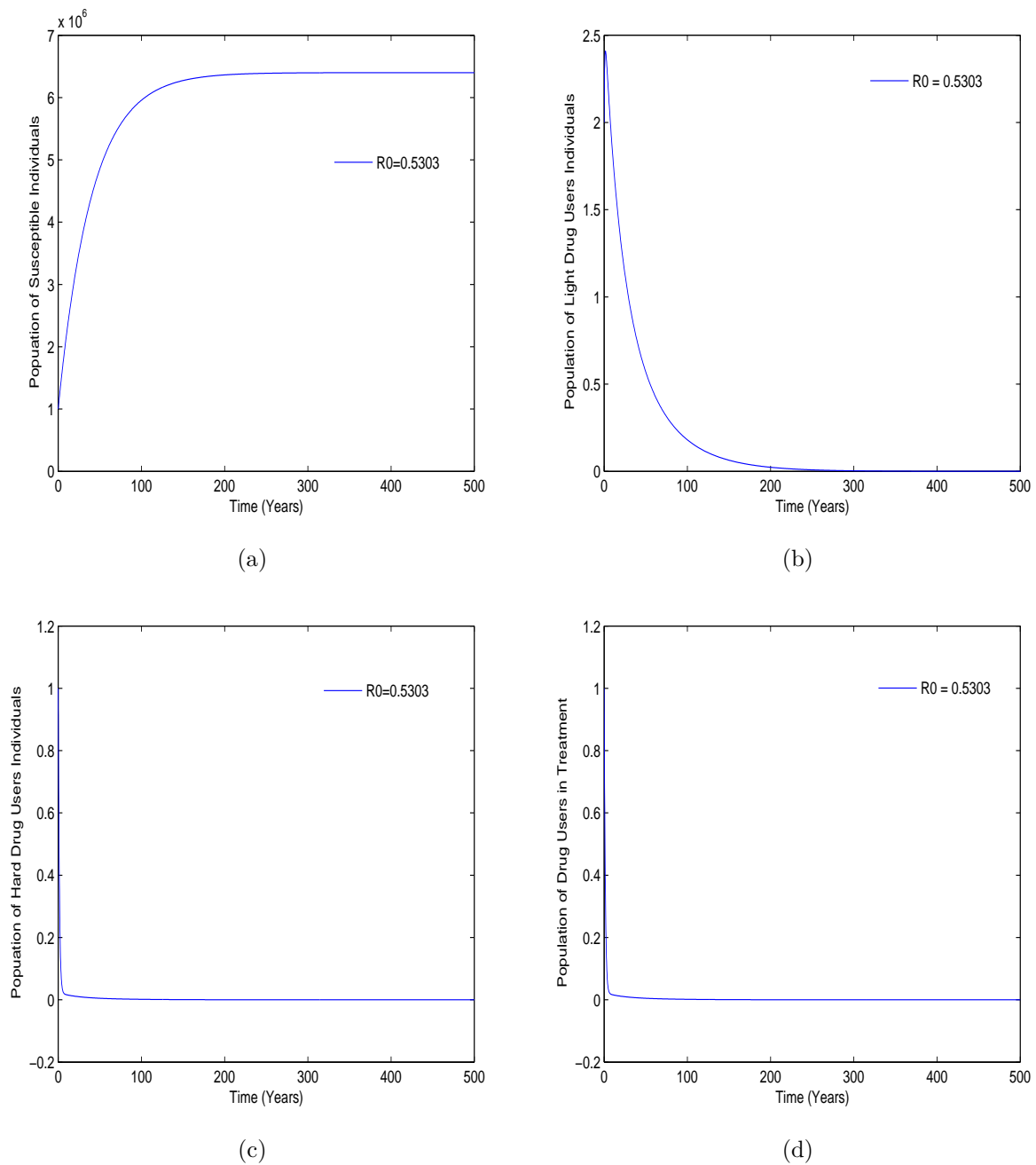


FIG. 3.7. Demonstrates the changes in the state variables of MA model with mass action for $R_0 = 0.5303$. Graphs (a), (b), (c) and (d) show the dynamics of susceptibles, light drug users, hard drug users and drug users in treatment with time, respectively. Parameter values are given in TABLE. 4.3.

The result shows that the system settles at the drug free equilibrium, where all populations except for susceptible vanishes. This result is in agreement with the Theorem (3.3.1) on

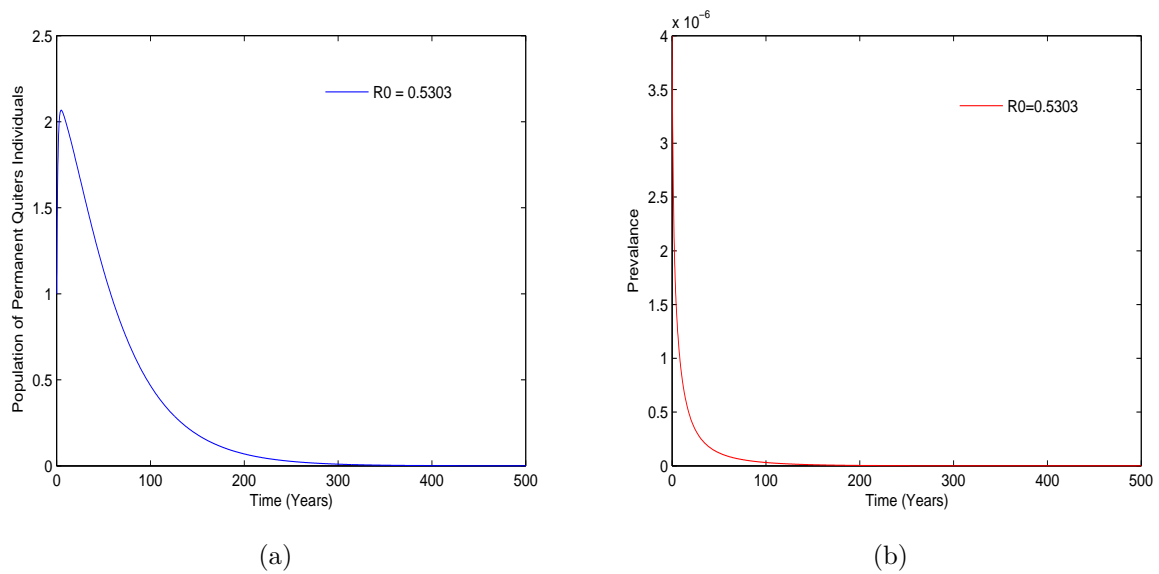


FIG. 3.8. Demonstrates the dynamics of the quitters and prevalence with time, respectively for MA model with mass action for $R_0 = 0.5303$. Graph (a) represents quitters and (b) stands for prevalence. Parameter values are given in TABLE. 4.3.

the local stability of the drug free equilibrium. These results are further supported by the prevalence curve in FIG. 3.8(b). Also, FIG. 3.9 shows that the drug free equilibrium is always stable whenever $R_0 = 0.5303$. This has been simulated using various initial conditions.

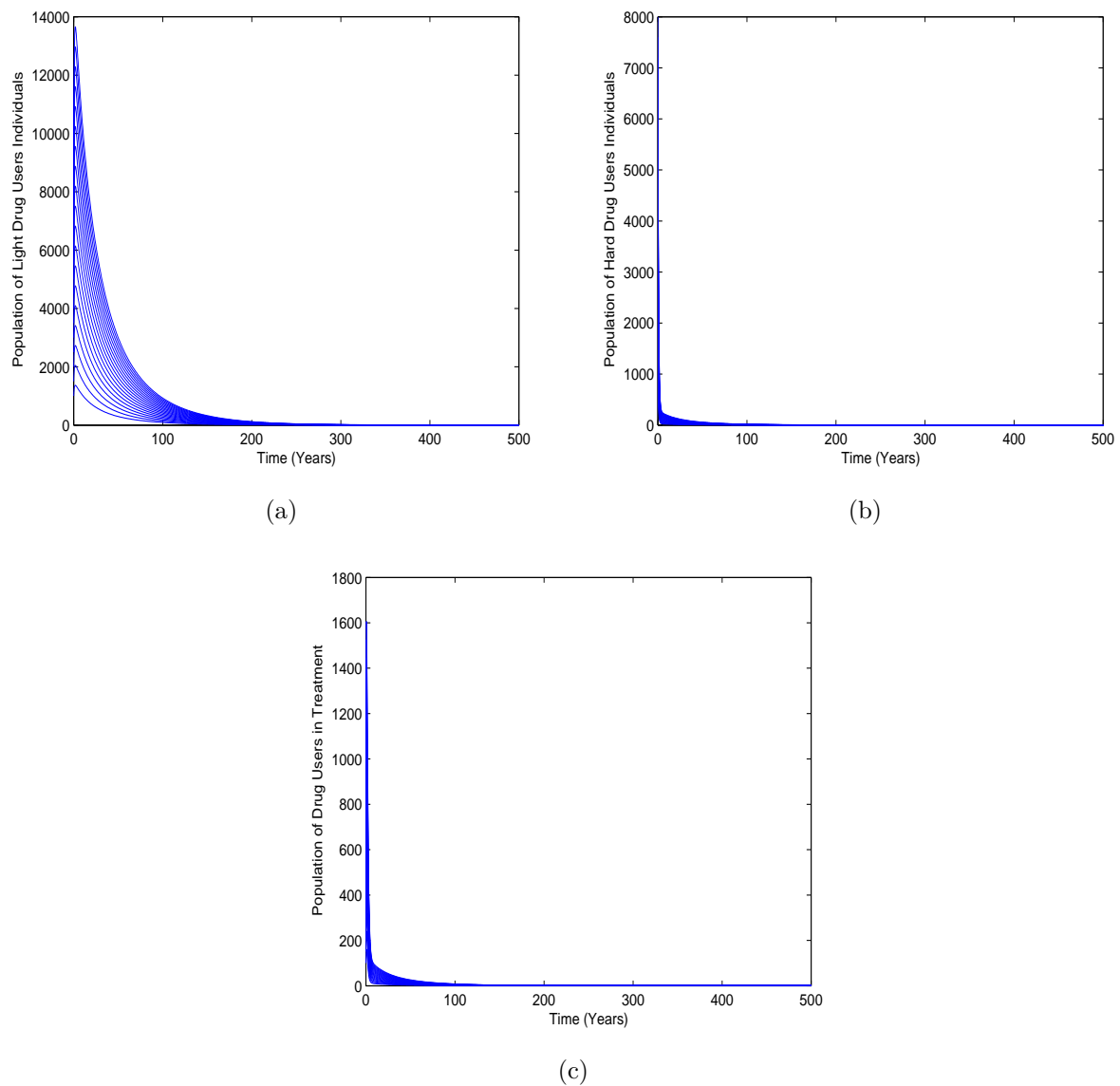


FIG. 3.9. Time series plot of the drug users when $R_0 = 0.5303$ with various initial conditions, parameter values are in TABLE. 4.3.

Further, using the same initial conditions while $R_0 = 1.6666$, all the populations tend to some steady state values as shown in FIG. 3.10 and 3.11(a). This shows that drug abuse persists in population and the system stabilizes at a drug persistent equilibrium. The result supports Theorem (3.3.1) on the stability of drug persistent equilibrium. We also include the prevalence curve in FIG. 3.11(b) which also settles at the drug persistent equilibrium.

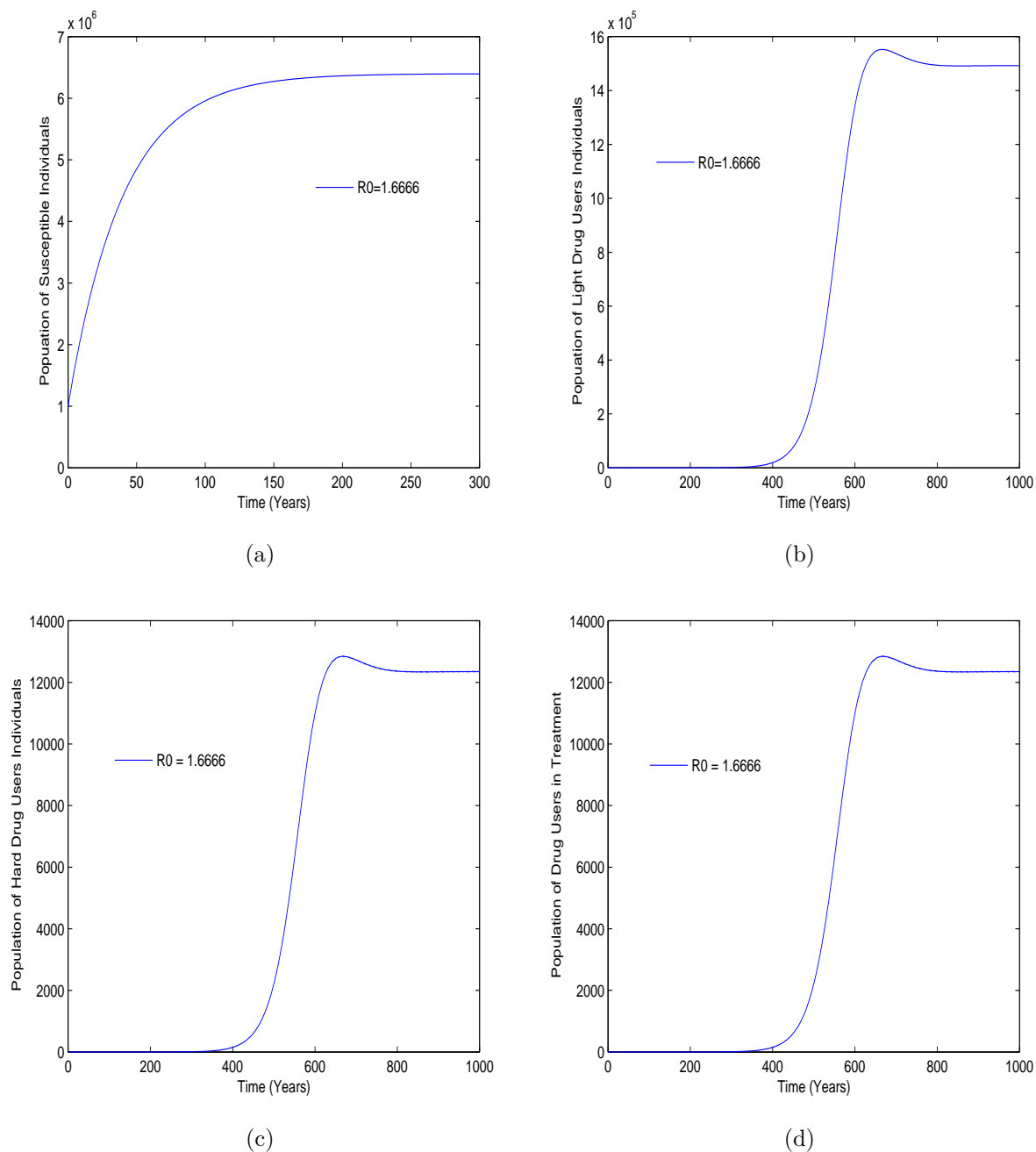


FIG. 3.10. Illustrates the changes in the state variables of MA model with mass action for $R_0 = 1.6666$. Graphs (a), (b), (c) and (d) show the dynamics of susceptible, light drug user, hard drug user and drug user in treatment with time, respectively. Parameter values are given in TABLE. 4.3.

The time series plots for drug users are also included in FIG. 3.12 for varying initial conditions. In these figures all drug populations stabilized at drug persistent equilibrium

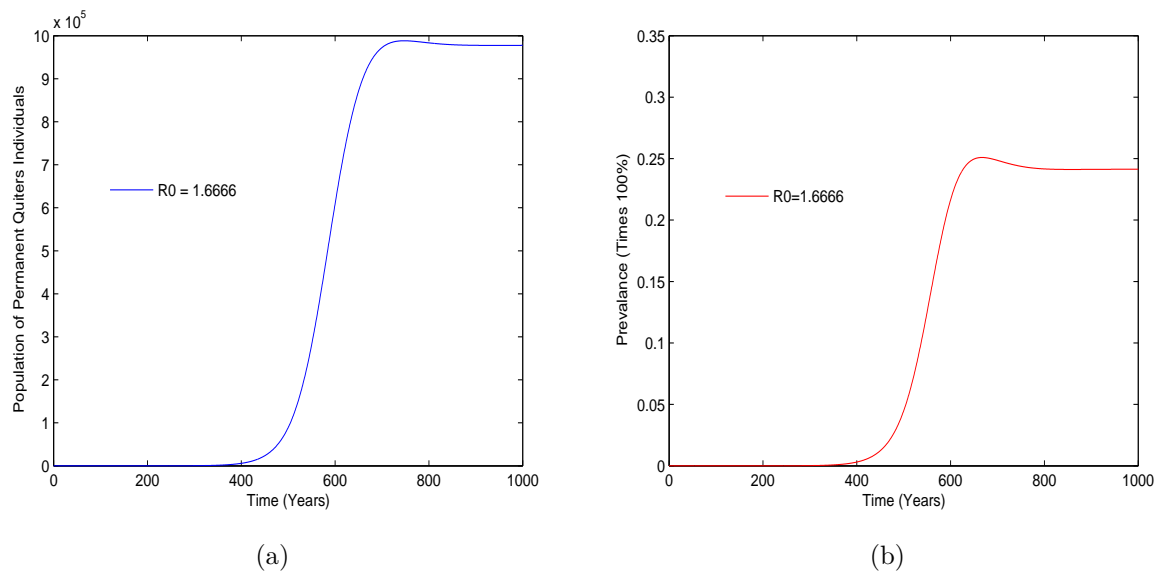


FIG. 3.11. Illustrates the changes in the permanent quitter individuals and prevalence with time, respectively for MA model with mass action for $R_0 = 1.6666$. Graph (a) shows the dynamics of permanent quiter individuals and (b) shows the prevalence. Parameter values are given in TABLE. 4.3.

irrespective of the initial conditions.

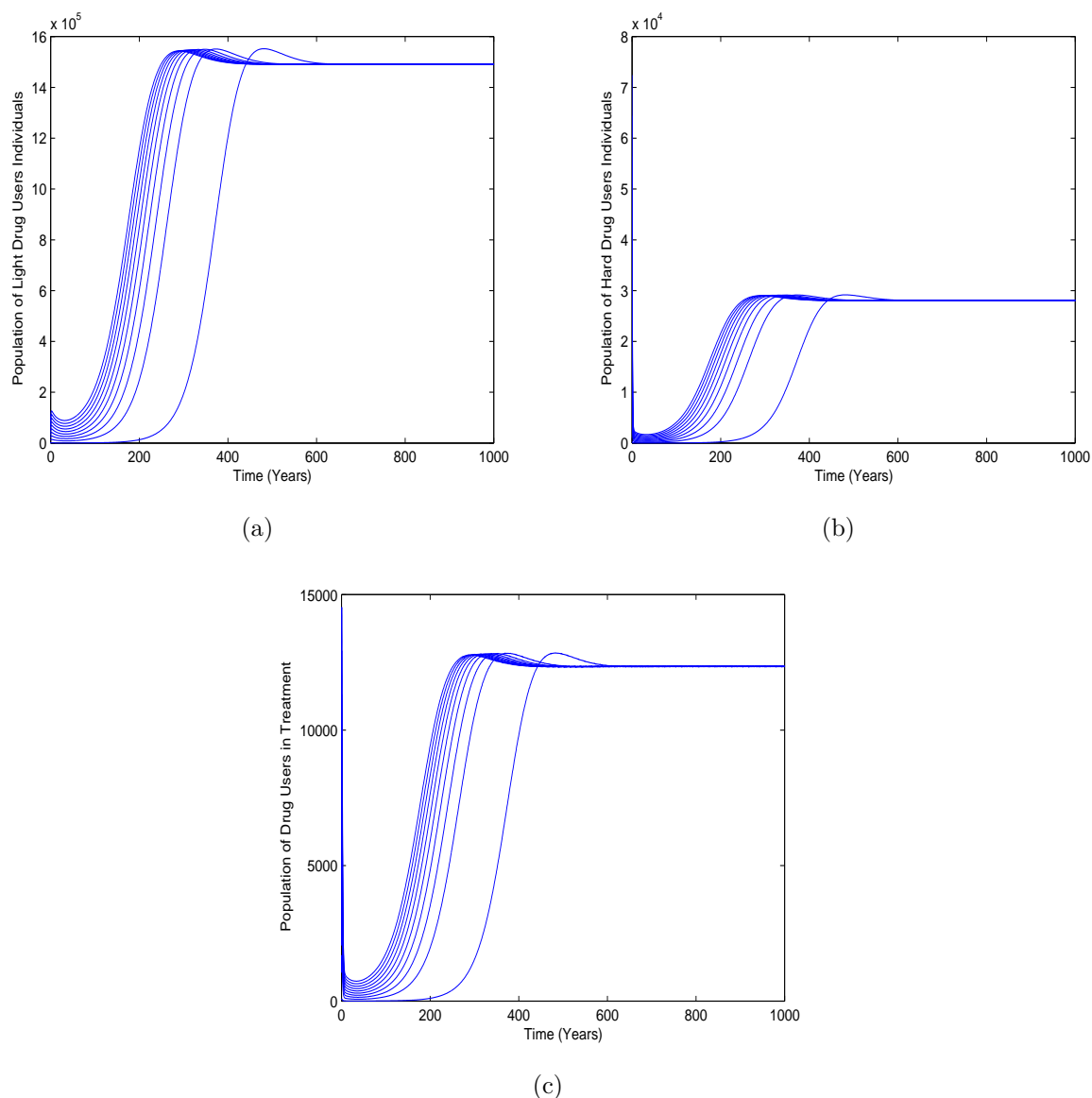


FIG. 3.12. Time series plot of the drug users when $R_0 = 1.6666$ with various initial conditions, parameter values are in TABLE. 4.3.

We then include the phase portrait in FIG. 3.13 for the drug users and susceptible individuals. The result shows that, irrespective of the initial conditions used, the populations will always tends to the steady states. In FIG. 3.13 (a) the populations tends to drug free steady states when $R_0 < 1$ and in FIG. 3.13 (b) the populations tends to the drug persistent steady state when $R_0 > 1$. We also note that, in FIG. 3.13 (a) the susceptible population increase while drug users population decrease and in FIG. 3.13 (b) susceptible

population first increases and then decrease while the drug users population decreases first then increase.

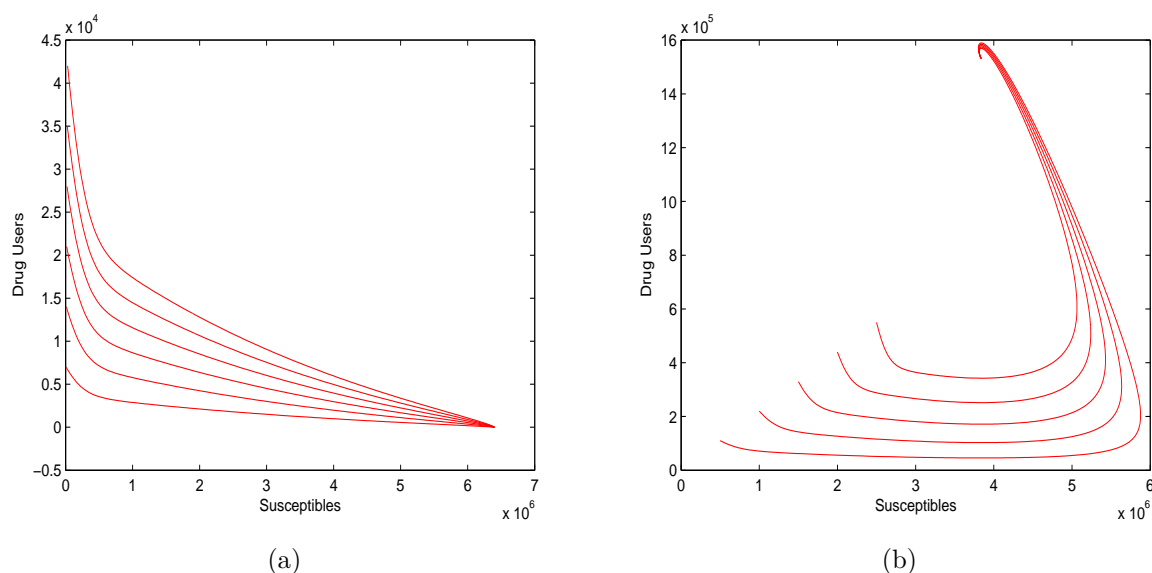


FIG. 3.13. Represents phase portrait for drug users against susceptible individuals. (a), shows that the populations settles at drug free equilibrium for $R_0 = 0.5303$, while in (b) populations settles at drug persistent steady state with $R_0 = 1.6666$. Parameter values are given in TABLE. 4.3.

3.6 Summary

In this chapter we studied the dynamics of methamphetamine abuse. We developed a mathematical model which describes how individuals move from one compartment to another. We analysed the model with a mass action force of infection. This model helps us to understand the dynamics of methamphetamine abuse. Analytical results are presented and numerical simulation were performed to verify analytical results. Sensitivity analysis of the the basic reproduction number to the parameters was done. These results are important as they give an insight of how the dynamics of methamphetamine abuse evolves, and the important parameters which could be targeted for the methamphetamine abuse control strategies. The results also show that for certain conditions, the system exhibits backward bifurcation. With mass action incidence we assume that drug initiation is due to contact between drug users and susceptibles and that all individuals have the same chance

of becoming methamphetamine users. This is because most people who start using drugs do so through contact with a friend who could be a drug user. The reality is that not all individuals start using drug (methamphetamine) through contact with someone who is already a user. For this reason in the next chapter we develop another model with a nonlinear incidence function which includes innovators and considers behavioural change. These additional conditions will make the model more realistic.

Chapter 4

A Methamphetamine Abuse Model with Non Linear Incidence

4.1 Introduction

In this chapter, we relook at the model presented in the previous chapter. As discussed earlier, the notion that initiation into drug abuse is only by interaction with individuals using drugs is not realistic. The initiation was modeled by a mass action incidence function. As an extension to the model with a mass action initiation function, we consider the following two aspects.

- Innovators: Innovators are the individuals who start using drug on their own, which may be due to curiosity, by shifting from other drugs or for some other reasons but not through interactions with those who are already users. The idea of innovators has also been used in the modelling of cocaine use in [4].
- Behaviour change : We also include the possible impact of behaviour change to drug use patterns. The impact of behaviour change has been modeled through mathematical functions. In [1], the function $f(H) = de^{-\lambda H}$ is used to represent the reduced transmission rate of HIV, with d representing the maximum HIV transmission rate, H the HIV prevalence and λ measures of behaviour change in the population. A similar function was used in [12], where the contact rate is a function of the number

of infectives. The function $\beta(I) = \mu e^{-mI}$, where I is the number of infectives, μ a constant and m reflecting the impact of media coverage on the population was used.

4.2 Model formulation

By taking into consideration the two aspects discussed in the previous section, we now reformulate the methamphetamine abuse model taking into consideration innovators and behaviour change. We assume that innovators join the class U_L and U_H at a constant rate τ and the process is proportional to the number of susceptibles. To model behaviour change, we associate behaviour change with removal rates that are associated with drug use. We argue that individuals change their behaviour by seeing individuals dying and being imprisoned for instance due to drug related crimes. We thus propose the use of an exponential function as in [1, 12] for the force of infection. We thus define the force of infection as

$$\lambda = e^{-q(\delta_1 U_H + \delta_2 U_T)} \left[\tau + \beta \left(\frac{U_L + \eta U_H}{N_C} \right) \right], \quad (4.1)$$

where τ is the rate in which individuals start drugs on their own (Innovators), q is the parameter which measures how individuals respond to the increase or decrease in the removal of individuals who use drugs which may be due to committing crime or deaths related to drug use. The remaining parameters are as defined in Chapter 3. We also still have

$$N_C = S + U_L + U_H + U_T + Q.$$

This non linear incidence function is more realistic than the mass action incidence function. Consider the model (3.7) but now with non linear incidence function given by

$$\left. \begin{aligned} \frac{dS}{dt} &= \pi N_P - (\mu + \lambda)S, \\ \frac{dU_L}{dt} &= \lambda S(1 - \theta) + \psi U_H - (\mu + \sigma + \rho_2)U_L, \\ \frac{dU_H}{dt} &= \lambda S\theta + \sigma U_L + r\lambda U_T - (\mu + \gamma + \psi + \delta_1)U_H, \\ \frac{dU_T}{dt} &= \gamma U_H - (\mu + \rho_1 + \delta_2 + r\lambda)U_T, \\ \frac{dQ}{dt} &= \rho_2 U_L + \rho_1 U_T - \mu Q, \end{aligned} \right\} \quad (4.2)$$

where

$$\lambda = e^{-q(\delta_1 U_H + \delta_2 U_T)} \left[\tau + \beta \left(\frac{U_L + \eta U_H}{N_C} \right) \right]. \quad (4.3)$$

4.3 Mathematical analysis of the model

The mathematical analysis of (4.2) is not straightforward due to nonlinearities. We consider the case $q = 0$ and we leave the case $q \neq 0$ for numerical analysis, for simplicity.

4.3.1 Positivity and boundedness of the solutions

We begin our analysis by looking at the positivity and boundedness of solutions. For biological feasibility of the system (4.2), it is important that all variables stay positive at all times and as such we analyse this system in the region Ω as defined in Lemma 3.

Lemma 3 *The feasible region Ω defined by*

$$\Omega = \{(S(t), U_L(t), U_H(t), U_T(t), Q(t)) \in \mathbb{R}_+^5 : S + U_L + U_H + U_T + Q \leq \frac{\pi N_P}{\mu}\}$$

is positively invariant and attracting with respect to model system for all $t > 0$.

Proof:

We want to see that the model is constructed well enough that no population goes negative or unbounded. To do this we integrate equations of the system (4.2) and show that $S(t)$, $U_L(t)$, $U_H(t)$, $U_T(t)$ are always positive for $t > 0$.

From the first equation of (4.2), we have

$$\frac{dS}{dt} \geq -(\mu + \lambda)S,$$

$$\frac{dS}{dt} \geq -[\mu + \tau + \beta(\frac{U_L + \eta U_H}{N_C})],$$

$$\frac{dS}{dt} \geq -[\mu + \tau + \beta(1 + \eta)],$$

$$S(t) \geq S(0)e^{-(\mu + \tau + \beta(1 + \eta))t} \geq 0,$$

given that the variables represent numbers of individuals. Likewise,

$$U_L \geq U_L(0)e^{-(\mu + \rho_2 + \sigma)t} \geq 0,$$

$$U_H \geq U_H(0)e^{-(\mu + \gamma + \psi + \delta_2)t} \geq 0,$$

$$U_T \geq U_T(0)e^{-(\mu + \rho_1 + \delta_2 + r\{\tau + \beta(1 + \eta)\})t} \geq 0.$$

$$Q \geq Q(0)e^{-\mu t} \geq 0.$$

We thus have all the variables remaining positive for all $t \geq 0$. Adding the equations of the system (4.2) we obtain

$$\frac{dN_C}{dt} = \pi N_P - \mu N_C - \delta_1 U_H - \delta_2 U_T,$$

$$\leq \pi N_P - \mu N_C.$$

The solution of the differential equation above is given by

$$0 \leq N_C(t) \leq N_C(0)e^{-\mu t} + \frac{\pi N_P}{\mu}[1 - e^{-\mu t}]$$

where $N_C(0)$ represents the sum of the initial values of the variables. As $t \rightarrow \infty$, $0 \leq N_C \leq \frac{\pi N_P}{\mu}$. So if $N_C(0) \leq \frac{\pi N_P}{\mu}$ then $\lim_{t \rightarrow \infty} N_C(t) = \frac{\pi N_P}{\mu}$. This means that $\frac{\pi N_P}{\mu}$ is the upper bound of N_C . On the other hand if $N_C(0) > \frac{\pi N_P}{\mu}$, then $N_C(0)$ will decrease to $\frac{\pi N_P}{\mu}$. This means that if $N_C(0) > \frac{\pi N_P}{\mu}$, then the solution $(S(t), U_L(t), U_H(t), U_T(t))$ enters Ω or approach it asymptotically. Hence it is positively invariant under the flow induced by system (4.2). Thus in Ω , the model (4.2) is well-posed epidemiologically and mathematically. Hence, it is sufficient to study the dynamics of the model in Ω .

4.3.2 Equilibrium points

These are time-independent states of the system. To find the equilibrium solution, we set derivatives of the model equations of the system (4.2) to zero. Since we are unable to find the equilibrium points explicitly, we express them in terms of the force of infection λ as shown in equations (4.4) to (4.10)

$$S^* = \frac{\pi N_P^*}{\lambda^* + \mu}, \quad (4.4)$$

$$U_L^* = \frac{\pi N_P^* \lambda^* \{r\lambda^* \theta \psi + [\theta \psi + \gamma(1 - \theta)] \{\mu + \delta_2 + \rho_1\}\}}{K} \quad (4.5)$$

$$+ \frac{\pi N_P^* \lambda^* \{(1 - \theta)(\mu + \psi + \delta_1)(r\lambda^* + \mu + \delta_2 + \rho_1)\}}{K}, \quad (4.6)$$

$$U_H^* = \frac{\pi N_P^* \lambda^* (r\lambda^* + \mu + \delta_2 + \rho_1) [\sigma(1 - \theta) + \theta(\mu + \sigma + \rho_2)]}{K}, \quad (4.7)$$

$$U_T^* = \frac{\pi \gamma \lambda^* N_P^* [\theta \mu + \sigma + \theta \rho_2]}{K}, \quad (4.8)$$

$$Q^* = \frac{\pi \lambda^* N_P^* \{r\lambda^* + \mu + \delta_2 + \rho_1\} \rho_2 + \gamma \rho_1 [\sigma(1 - \theta) + \theta(\mu + \sigma + \rho_2)]}{\mu K}, \quad (4.9)$$

$$(4.10)$$

where

$$\lambda^* = e^{-q(\delta_1 U_H^* + \delta_2 U_T^*)} \left[\tau + \beta \left(\frac{U_L^* + \eta U_H^*}{N_C^*} \right) \right],$$

and $K = (\lambda^* + \mu)(\mu + \sigma + \rho_2) \{ (r\lambda^* + \mu + \delta_2 + \rho_1)[\mu + \psi(\mu + \rho_2) + \delta_1] + \gamma(\mu + \delta_2 + \rho_1) \}$.

Substituting U_L^* , U_H^* , U_T^* and $N_C^* = S^* + U_L^* + U_H^* + U_T^* + Q^*$ into (4.3), we obtain

$$G(\lambda) = A\lambda^3 + B\lambda^2 + C\lambda + D = 0, \quad (4.11)$$

when $q = 0$ with

$$\begin{aligned} A &= \pi r \mu N_P (1 - \theta) (\gamma - b_2) - \pi r \mu \sigma N_P (1 - \theta) - \pi r \theta \mu \psi N_P - \pi r \theta \mu b_1 N_P, \\ &\quad + \pi r \rho_2 N_P (1 - \theta) (\gamma - b_2) - \pi r \theta \psi \rho_2 N_P \\ B &= -\pi r \beta \gamma \mu N_P (1 - \theta) - \pi \gamma \mu \sigma N_P (1 - \theta) - \pi r \gamma \mu \tau N_P (1 - \theta) + \pi r \mu \sigma \tau N_P (1 - \theta) \\ &\quad + \pi r \beta \theta \mu \psi N_P + \pi r \mu \sigma \psi N_P + \pi r \theta \mu \tau \psi N_P + \pi r \gamma \mu b_1 N_P - \pi \gamma \theta \mu b_1 N_P + \pi r \theta \mu \tau b_1 N_P \\ &\quad + \pi r \beta \mu b_2 N_P (1 - \theta) + \pi r \mu \tau b_2 N_P (1 - \theta) - \pi r \mu b_1 b_2 N_P - \pi \mu \sigma b_3 N_P (1 - \theta) \\ &\quad - \pi \theta \mu \psi b_3 N_P - \pi \theta \mu b_1 b_3 N_P - \pi \mu b_2 b_3 N_P (1 - \theta) + \pi r \beta \mu \sigma \eta N_P (1 - \theta) \\ &\quad + \pi r \beta \theta \mu b_1 \eta N_P - \pi \gamma \sigma \rho_1 N_P (1 - \theta) - \pi \gamma \theta b_1 \rho_1 N_P - \pi r \gamma \tau \rho_2 N_P (1 - \theta) + \pi r \theta \tau \psi \rho_2 N_P \\ &\quad + \pi r \tau b_2 \rho_2 N_P (1 - \theta) - \pi \theta \psi b_3 \rho_2 N_P - \pi b_2 b_3 N_P (1 - \theta) \rho_2, \\ C &= \pi \gamma \mu \sigma \tau N_P (1 - \theta) - \pi r \mu \sigma \tau \psi N_P - \pi r \gamma \mu \tau b_1 N_P + \pi \gamma \theta \mu \tau b_1 N_P + \pi r \mu \tau b_1 b_2 N_P \\ &\quad + \pi \mu \sigma \tau b_3 N_P (1 - \theta) + \pi \beta \theta \mu \psi b_3 N_P + \pi \mu \sigma \psi b_3 N_P + \pi \theta \mu \tau \psi b_3 N_P + \pi \theta \mu \tau b_1 b_3 N_P \\ &\quad + \pi \beta \mu b_2 b_3 N_P (1 - \theta) + \pi \mu \tau b_2 b_3 N_P (1 - \theta) - \pi \mu b_1 b_2 b_3 N_P + \pi \beta \mu \sigma b_3 \eta N_P (1 - \theta) \\ &\quad + \pi \beta \theta \mu b_1 b_3 \eta N_P + \pi \gamma \sigma \tau \rho_1 N_P (1 - \theta) + \pi \gamma \theta \tau b_1 \rho_1 N_P + \pi \theta \tau \psi b_3 \rho_2 N_P \\ &\quad + \pi \tau b_2 b_3 \rho_2 N_P (1 - \theta), \\ D &= \pi \mu \tau b_1 b_2 b_3 N_P (1 - q_1). \end{aligned}$$

If $\tau = 0$, D becomes zero and the polynomial becomes

$$G(\lambda) = \lambda(A\lambda^2 + B_1\lambda + C_1) = 0, \quad (4.12)$$

where

$$\begin{aligned}
B_1 &= \pi r \beta \theta \mu \psi N_P - \pi r \beta \gamma \mu N_P (1 - \theta) - \pi \gamma \mu \sigma N_P (1 - \theta) + \pi r \mu \sigma \psi N_P + \pi r \gamma \mu b_1 N_P \\
&\quad - \pi \gamma \theta \mu b_1 N_P + \pi r \beta \mu b_2 N_P (1 - \theta) - \pi r \mu b_1 b_2 N_P - \pi \mu \sigma b_3 N_P (1 - \theta) - \pi \theta \mu \psi b_3 N_P \\
&\quad - \pi \theta \mu b_1 b_3 N_P - \pi \mu b_2 b_3 N_P (1 - \theta) + \pi r \beta \mu \sigma N_P \eta (1 - \theta) + \pi r \beta \theta \mu b_1 N_P \eta \\
&\quad - \pi \gamma \sigma N_P \rho_1 (1 - \theta) - \pi \gamma \theta b_1 N_P \rho_1 - \pi \theta \psi b_3 N_P \rho_2 - \pi b_2 b_3 N_P \rho_2 (1 - \theta), \\
C_1 &= \pi \beta \mu b_1 b_2 b_3 N_P \left[\frac{\theta \psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} + \eta \left\{ \frac{\sigma (1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right\} \right] - \pi \mu b_1 b_2 b_3 N_P (1 - q_1).
\end{aligned}$$

So, one root is $\lambda = 0$ and the other roots can be obtained from the quadratic equation

$$A\lambda^2 + B_1\lambda + C_1 = 0. \quad (4.13)$$

The root $\lambda = 0$ corresponds to the drug free equilibrium and the non trivial steady states can be obtained from equation (4.13). Since we can not explicitly solve for the roots of equation (4.13), we opt to determine the sign of the roots. This will help us to determine drug persistent equilibria. We know that $A < 0$, but B_1 and C_1 can be negative or positive, we will consider some cases. Before proceeding with the roots of (4.13), we first determine the basic reproduction number when $\tau = 0$.

4.3.3 Basic reproduction number when $\tau = 0$

We use next generation matrix, where by

$$\mathcal{F}(x) = \begin{pmatrix} 0 \\ \frac{\beta S(1 - \theta)(U_L + \eta U_H)}{S + U_L + U_H + U_T + Q} \\ \frac{\beta S \theta (U_L + \eta U_H)}{S + U_L + U_H + U_T + Q} \\ 0 \\ 0 \end{pmatrix},$$

and

$$\mathcal{V}(x) = \begin{pmatrix} \mu S + \frac{(U_L + \eta U_H)}{S + U_L + U_H + U_T + Q} - \pi N_P \\ b_1 U_L - \psi U_H \\ b_2 U_H - \sigma U_L - r \left(\frac{U_L + \eta U_H}{S + U_L + U_H + U_T + Q} \right) U_T \\ \left\{ b_3 + r \left(\frac{U_L + \eta U_H}{S + U_L + U_H + U_T + Q} \right) \right\} U_T - \gamma U_H \\ \mu Q - \rho_1 U_T - \rho_2 U_L \end{pmatrix}.$$

The matrices of the generation of new infections and transfers for the infected compartments are given by

$$F = \begin{pmatrix} \beta(1 - \theta) & \beta(1 - \theta)\eta \\ \beta\theta & \beta\theta\eta \end{pmatrix},$$

and

$$V = \begin{pmatrix} b_1 & -\psi \\ -\sigma & b_2 \end{pmatrix}.$$

Inverse of V is

$$V^{-1} = \begin{pmatrix} \frac{1}{b_1(1 - q_1)} & \frac{\psi}{b_1 b_2(1 - q_1)} \\ \frac{\sigma}{b_1 b_2(1 - q_1)} & \frac{1}{b_2(1 - q_1)} \end{pmatrix}.$$

The product of FV^{-1} is given by

$$FV^{-1} = \begin{pmatrix} \frac{\beta(1 - \theta)[b_2 + \sigma\eta]}{b_1 b_2(1 - q_1)} & \frac{\beta(1 - \theta)[\psi + b_1\eta]}{b_1 b_2(1 - q_1)} \\ \frac{\beta\theta[b_2 + \sigma\eta]}{b_1 b_2(1 - q_1)} & \frac{\beta\theta[\psi + b_1\eta]}{b_1 b_2(1 - q_1)} \end{pmatrix},$$

R_0 is given by

$$R_0 = \frac{\beta}{(1 - q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} + \eta \left\{ \frac{\sigma(1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right\} \right]$$

The interpretation of R_0 is as follows:

- $\frac{1}{b_1}$ refers to the duration methamphetamine users spends in light drug use stage,
- $\frac{1}{b_2}$ the duration methamphetamine users spends in hard drug use stage,
- $\frac{\theta\psi}{b_1b_2} + \frac{(1-\theta)}{b_1}$ is the contribution of light drug users to the MA epidemics,
- $\eta \left\{ \frac{\sigma(1-\theta)}{b_1b_2} + \frac{\theta}{b_2} \right\}$ is the contribution of hard drug users to the MA epidemics.

Going back to the quadratic equation, we express C_1 in terms of R_0 so that

$$C_1 = -\pi\mu b_1 b_2 b_3 N_P (1 - q_1) [1 - R_0].$$

Therefore $C_1 < 0$ if $R_0 < 1$ and $C_1 > 0$ if $R_0 > 1$. So from the equation (4.13), we have $A < 0$, $C_1 < 0$ if $R_0 < 1$ and $C_1 > 0$ if $R_0 > 1$ and B_1 can be negative or positive. Using the general formula

$$\lambda_{1,2}^* = \frac{-B_1 \pm \sqrt{B_1^2 - 4AC_1}}{2A}, \quad (4.14)$$

by considering

$$B_1^2 - 4AC_1 > 0,$$

we have the following cases from the general formula (4.14),

If $R_0 > 1$ that is $C_1 > 0$ and

$$B_1 \begin{cases} < 0 & \text{then two distinct roots of opposite signs,} \\ > 0 & \text{two distinct roots of opposite signs.} \end{cases}$$

This tell us that irrespective of the sign of B_1 , if $R_0 > 1$, their is a unique drug persistent equilibrium. If $R_0 < 1$ that is $C_1 < 0$ and

$$B_1 \begin{cases} < 0 & \text{then two distinct negative roots,} \\ > 0 & \text{then two distinct positive roots.} \end{cases}$$

This indicates the existence of multiple equilibria when $R_0 < 1$ and $B_1 > 0$, hence possibility of backward bifurcation.

4.3.4 Existence of drug persistent equilibrium

If $\tau > 0$, we have the polynomial (4.11). So the presence of innovators, can potentially lead to the persistence of drug use. In this case there is no drug free equilibrium. To determine the roots of this polynomial, we also consider the signs of the coefficients A , B , C and D . The coefficient A is negative and D is positive. We need to check for B and C . The expression for B is simplified to

$$B = B_{11} - B_{12},$$

where

$$\begin{aligned} B_{11} &= \pi r \mu \psi \theta N_P (\beta + \tau) + \pi r \theta \mu b_1 N_P (\beta \eta + \tau) + \pi r \mu b_2 N_P (1 - \theta) (\beta + \tau) \\ &\quad + \pi r \mu \sigma N_P (1 - \theta) (\beta \eta + \tau) + \pi r \mu \sigma \psi N_P + \pi r \gamma \mu b_1 N_P + \pi r \tau \theta \psi \rho_2 N_P \\ &\quad + \pi r \tau b_2 \rho_2 N_P (1 - \theta), \\ B_{12} &= \pi \mu N_P (1 - \theta) [r \beta \gamma + \gamma \sigma + r \gamma \tau + \sigma b_3] + \pi N_P (1 - \theta) [\mu b_2 b_3 + \gamma \sigma \rho_1 + b_2 b_3 \rho_2] \\ &\quad + \pi r \gamma \tau \rho_2 N_P (1 - \theta) + \pi \theta \mu N_P [\gamma b_1 + \psi b_3 + b_1 b_3] + \pi N_P [r \mu b_1 b_2 + \gamma \theta b_1 \rho_1 + \theta \psi b_3 \rho_2]. \end{aligned}$$

And C becomes

$$\begin{aligned} C &= \pi \mu b_3 N_P (\beta + \tau) [\theta \psi + b_2 (1 - \theta)] + \pi \mu b_3 N_P (\beta \eta + \tau) [\sigma (1 - \theta) + \theta b_1] \\ &\quad + \pi \gamma \mu \tau N_P [\sigma (1 - \theta) + \theta b_1] + \pi \gamma \tau \rho_1 N_P [\sigma (1 - \theta) + \theta b_1] \\ &\quad + \pi \tau b_3 \rho_2 N_P [\theta \psi + b_2 (1 - \theta)] + \pi r \mu \tau N_P [(\mu + \delta_1)(\mu + \sigma + \rho_2) + \psi(\mu + \rho_2)] \\ &\quad - \pi \mu b_1 b_2 b_3 N_P (1 - q_1), \\ &= \pi \mu b_1 b_2 b_3 N_P (1 - q_1) \left\{ \frac{(\beta + \tau)}{(1 - q_1)} \left[\frac{\theta \psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} \right] + \frac{(\beta \eta + \tau)}{(1 - q_1)} \left[\frac{\sigma (1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right] \right\} \\ &\quad + \pi \mu b_1 b_2 b_3 N_P (1 - q_1) \left\{ \frac{\gamma \tau}{(1 - q_1)} \left[\frac{\sigma (1 - \theta)}{b_1 b_2 b_3} + \frac{\theta}{b_2 b_3} \right] + \frac{\gamma \tau \rho_1}{\mu (1 - q_1)} \left[\frac{\sigma (1 - \theta)}{b_1 b_2 b_3} + \frac{\theta}{b_2 b_3} \right] \right\} \\ &\quad + \pi \mu b_1 b_2 b_3 N_P (1 - q_1) \left\{ \frac{\tau \rho_2}{\mu (1 - q_1)} \left[\frac{\theta \psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} \right] + \frac{r \tau}{(1 - q_1)} \left[\frac{(\mu + \delta_1)(\mu + \sigma + \rho_2)}{b_1 b_2 b_3} \right] \right\} \\ &\quad + \pi \mu b_1 b_2 b_3 N_P (1 - q_1) \left\{ \frac{\psi(\mu + \rho_2)}{b_1 b_2 b_3} - 1 \right\} \\ &= \pi \mu b_1 b_2 b_3 N_P (1 - q_1) [R(\tau) - 1], \end{aligned}$$

where

$$\begin{aligned}
R(\tau) = & \frac{(\beta + \tau)}{(1 - q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} \right] + \frac{(\beta\eta + \tau)}{(1 - q_1)} \left[\frac{\sigma(1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right] \\
& + \frac{\gamma\tau}{(1 - q_1)} \left[\frac{\sigma(1 - \theta)}{b_1 b_2 b_3} + \frac{\theta}{b_2 b_3} \right] + \frac{\gamma\tau\rho_1}{\mu(1 - q_1)} \left[\frac{\sigma(1 - \theta)}{b_1 b_2 b_3} + \frac{\theta}{b_2 b_3} \right] \\
& + \frac{\tau\rho_2}{\mu(1 - q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} \right] + \frac{r\tau}{(1 - q_1)} \left[\frac{(\mu + \delta_1)(\mu + \sigma + \rho_2) + \psi(\mu + \rho_2)}{b_1 b_2 b_3} \right].
\end{aligned}$$

Note that when $\tau = 0$, $R(\tau) = R_0$. $R(\tau)$ can be expressed as

$$R(\tau) = \beta v + \varrho \tau \quad (4.15)$$

where

$$\begin{aligned}
v = & \frac{1}{(1 - q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} \right] + \frac{\eta}{(1 - q_1)} \left[\frac{\sigma(1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right], \\
\varrho = & \frac{1}{(1 - q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} \right] + \frac{1}{(1 - q_1)} \left[\frac{\sigma(1 - \theta)}{b_1 b_2} + \frac{\theta}{b_2} \right] \\
& + \frac{\gamma}{(1 - q_1)} \left[\frac{\sigma(1 - \theta)}{b_1 b_2 b_3} + \frac{\theta}{b_2 b_3} \right] + \frac{\gamma\rho_1}{\mu(1 - q_1)} \left[\frac{\sigma(1 - \theta)}{b_1 b_2 b_3} + \frac{\theta}{b_2 b_3} \right] \\
& + \frac{\rho_2}{\mu(1 - q_1)} \left[\frac{\theta\psi}{b_1 b_2} + \frac{(1 - \theta)}{b_1} \right] + \frac{r}{(1 - q_1)} \left[\frac{(\mu + \delta_1)(\mu + \sigma + \rho_2) + \psi(\mu + \rho_2)}{b_1 b_2 b_3} \right].
\end{aligned}$$

From the equation (4.15), $R(\tau)$ is the sum of two terms which represents the contribution of drug users who start using drug due to interaction with drug users and the contribution of innovators respectively.

From the expression of C in terms of $R(\tau)$ and B in terms of B_{11} and B_{12} we know that $C < 0$ if $R(\tau) < 1$ and $C > 0$ if $R(\tau) > 1$. $B < 0$ if $B_{11} < B_{12}$ and $B > 0$ if $B_{11} > B_{12}$ while $A < 0$ and $D > 0$. Using Descartes' rule of signs, it follows that:

- If $C < 0$ and $B < 0$, there is one change of sign and hence there is one positive root.
- If $C < 0$ and $B > 0$, there are three change of sign, so there are three or one positive roots.
- If $C > 0$ and $B < 0$, there is one change of sign and therefore there is one positive

root.

- If $C > 0$ and $B > 0$, then one positive root exists as there is one change of sign.

Theorem 4.3.1 : *When $q = 0$, the model (4.2) will always have drug persistent equilibrium for values of R_7 . However, it has a unique drug persistent equilibrium point if $R_7 > 1$.*

Remark 2 :

In the presence of innovators, drug persistence is always guaranteed. We were unable to explicitly determine the equilibria, but the analysis has been helpful in showing that drug use will always persist.

4.4 Sensitivity analysis

In this section we perform sensitivity analysis for the methamphetamine model with non linear incidence. We perform this to determine important parameters in the dynamics of methamphetamine abuse. To perform sensitivity analysis we use the same method described in Chapter 3.

4.4.1 Sensitivity indices of R_0

We use the same definition used in Chapter 3 to compute the normalized forward sensitivity index of R_0 . The sensitivity index of R_0 with respect to each parameter are given in TABLE. 4.1. The parameter values from TABLE. 4.3 were used to compute these sensitivity indices. The expression for the sensitivity index for R_0 with respect to β is

$$\Upsilon_{\beta}^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1,$$

which means R_0 is an increasing function of β as in Chapter 3. From the sensitivity indices in TABLE. 4.1, R_0 is most sensitive to changes in β .

Changing β will result in a change in R_0 by the same amount. For example if β changes by 10 %, R_0 will also change by 10 %. This is as expected because as the transmission is

TABLE. 4.1. Sensitivity indices of R_0

Parameter	Sensitivity index
β	+1.0000
ρ_2	-0.221652
μ	-0.590786
θ	-0.00047493
γ	-0.126156
ψ	+0.118761
η	+0.0148894
σ	-0.180165
δ_1	-3.03373×10^{-6}

increased then it means more individuals will become methamphetamine users and hence an increase in the spreading of methamphetamine abuse. Other parameters which increase with R_0 are η and ψ . These also agree with our intuition because increasing η increases initiation to methamphetamine abuse and increasing ψ means increasing the number of light drug users who have a higher probability of initiating their acquaintances. For more illustration we include FIG. 4.1, which shows the relationship between R_0 and transition rate σ , reversion rate ψ , the rate in which light drug users quite drug use ρ_2 , and proportion of individuals who progress fast into hard drug use θ .

FIG. 4.1 (a) shows that increasing transition rate decreases R_0 . This is because more light drug users will progress into hard drug use which is less effective in initiation process. In FIG. 4.1 (b), we observe that as reversion rate increases R_0 also increases. This means that more hard drug users will revert into light drug use and hence more light drug users. Furthermore FIG. 4.1 (c) and (d) shows that R_0 is a decreasing function of recovery rate of light drug users and proportion of individuals who progress fast into hard drug use respectively. Hence increasing these results decrease R_0 . This is due to the fact that increasing recovery rate decreases the number of light drug users. Also an increase in the proportion of individuals who progress fast to hard drug use decrease the number of light drug users through decrease in the proportion of susceptibles who become light drug users. This in turn reduces R_0 due to the fact that hard drug users are not as effective as light drug users in recruiting new initiates.

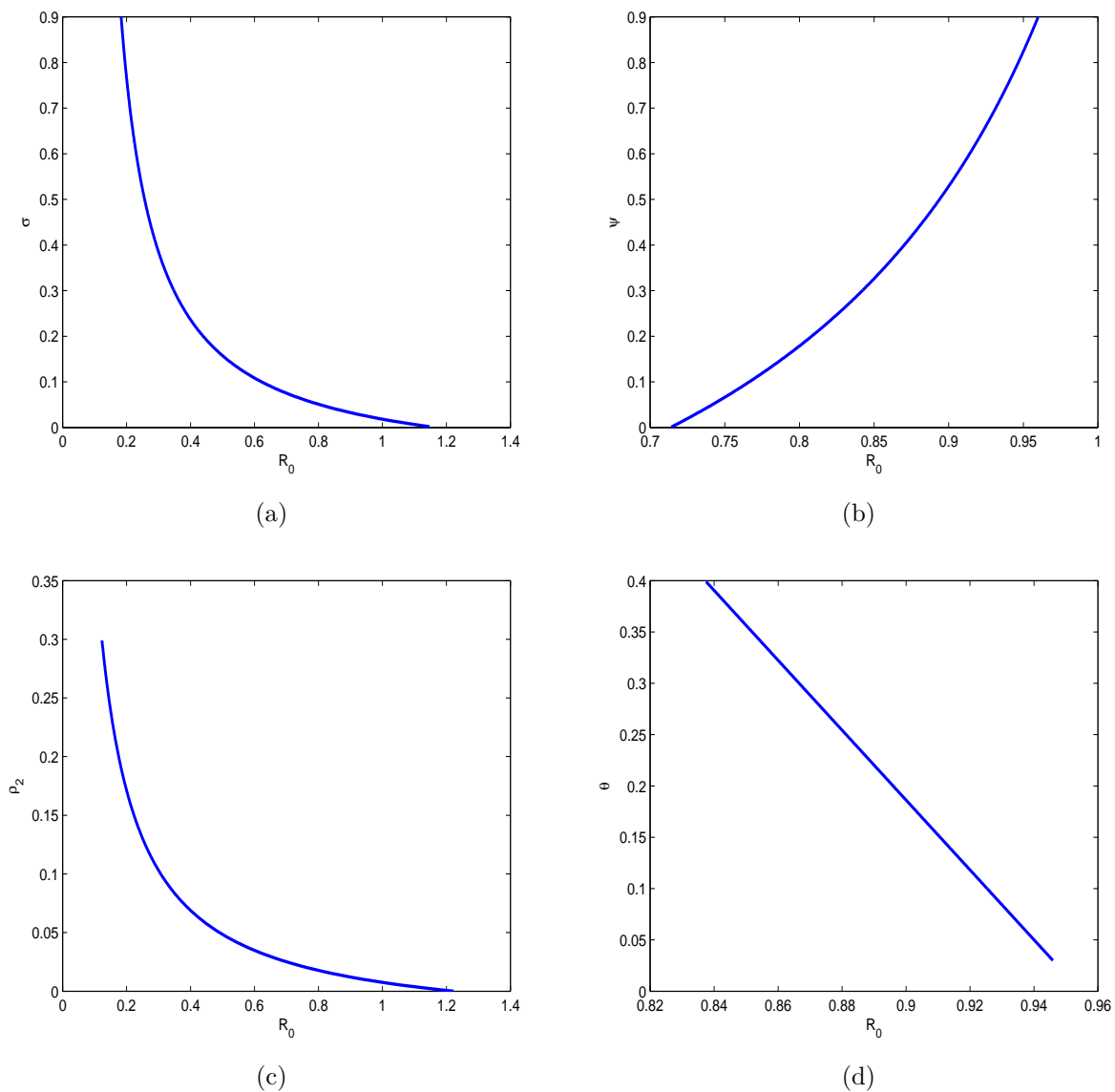


FIG. 4.1. Shows how R_0 relate with transition, reversion and recovery rates as well as proportion of individuals who progress fast into hard drug use. Parameter values are given in TABLE. 4.3

4.5 Numerical fitting

4.5.1 Parameter estimation

The equations of the system (4.2) are integrated by the Runge Kutta numerical scheme in Matlab. We also fit the methamphetamine epidemic model using the least square fitting

method in matlab. It is fitted as from 1996 to 2009 due to the availability of the data. The data was collected by the South Africa Community Epidemiology Network on Drug use (SACENDU) [37] for individuals who attend specialist treatment center in the Western Cape. Data on treatment demand trends is used to model the growth in the U_T class in our model. The data for growth of methamphetamine users in Western Cape are given in TABLE. 4.2. The data were collected in six month intervals that is twice a year. The

TABLE. 4.2. Primary or secondary methamphetamine abuse from year 1996b to 2009a

Year	1996b	1997a	1997b	1998a	1998b	1999a	1999b	2000a	2000b
MA users	0	0	2	0	1	2	6	10	12
Year	2001a	2001b	2002a	2002b	2003a	2003b	2004a	2004b	2005a
MA users	14	17	21	32	81	121	429	668	884
Year	2005b	2006a	2006b	2007a	2007b	2008a	2008b	2009a	
MA users	952	1232	1451	1413	1356	1209	1241	1837	

letter ‘a’ in years represents first six months of the year, that is January to June and ‘b’ represents the second six months from July to December. Due to unavailability of data on transmission and progression rates we estimate most of the parameters. This makes the setting of initial conditions difficult. Nevertheless for the purpose of the simulations and illustrating the usefulness of the model we assume an initial population of one million for the population of individuals who are prone to become methamphetamine abuser. We set the natural death rate of 0.025 taken from [32], where natural per capita death rate was between (0.025, 1). The parameter values obtained from the fitting are shown in TABLE. 4.3

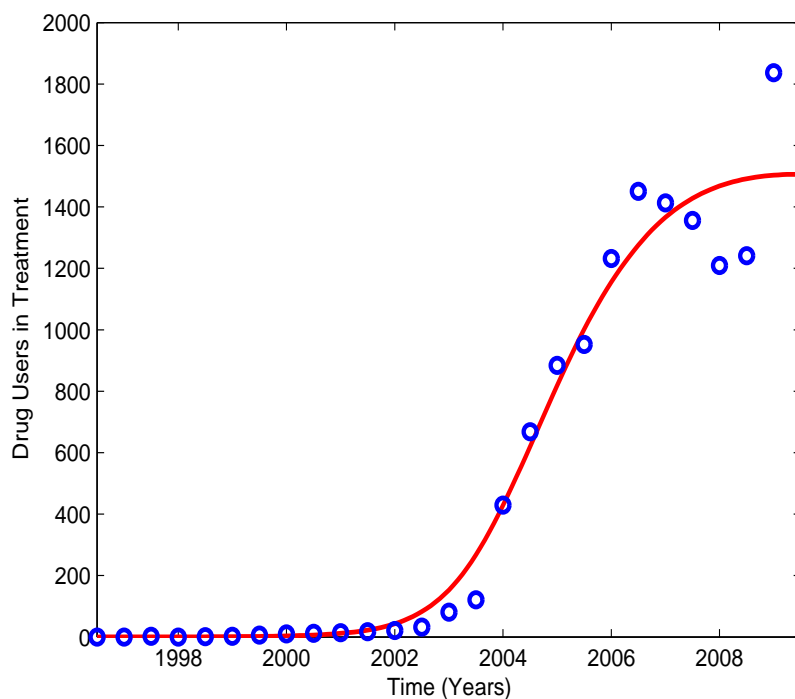
4.5.2 Numerical results

In this subsection numerical results are presented in figures. FIG. 4.2 is a graphical representation of the model fitted to data for individuals seeking treatment of methamphetamine abuse related problem. In FIG. 4.2, the model fits well with the data where by the continuous line shows the fit from the model and circles represent the actual data.

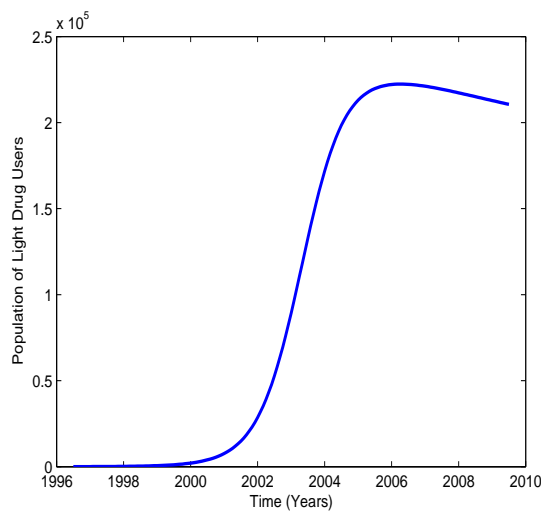
FIG. 4.2 shows that there were no drug users in treatment for some time, for instance in 1996b and 1997a. This does not mean that there were no drug users in the community. In fact if we look at FIG. 4.3 which shows the number of light and hard drug users we observe

TABLE. 4.3. Parameter values obtained from the best fit

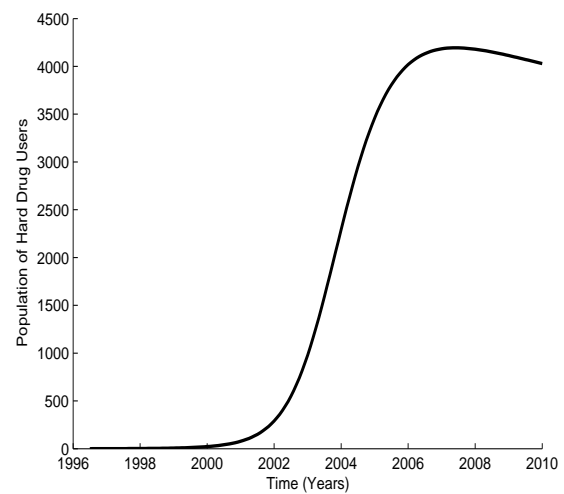
Parameter	Range	Estimated Parameter Values	Source
τ	$(7 \times 10^{-7}, 0.009)$	$7.0346 \times 10^{-7}/\text{year}$	Fitted
q	$(0, 0.9)$	0.0303	Fitted
π	$(0, 0.04)$	0.04/year	Fitted
σ	$(0, 0.9)$	0.0244/year	Fitted
r	$(0.00002, 0.9)$	0.0011/year	Fitted
ψ	$(0, 0.9)$	0.8560/year	Fitted
η	$(0, 0.9)$	0.8044	Fitted
γ	$(0, 0.99)$	0.4210/year	Fitted
θ	$(0.0015, 0.5)$	0.03	Fitted
β	$(0, 0.9399)$	0.9031/year	Fitted
δ_1	$(0.00001, 0.9)$	$1.0124 \times 10^{-5}/\text{year}$	Fitted
δ_2	$(0.001, 0.9)$	0.0998/year	Fitted
μ	0.025/year		[[32]]
ρ_1	$(0, 0.91)$	0.8312 /year	Fitted
ρ_2	$(0, 0.3)$	0.0095 /year	Fitted

FIG. 4.2. Shows the change in the population of individuals under treatment U_T . Parameter values produced this fit are in TABLE. 4.3

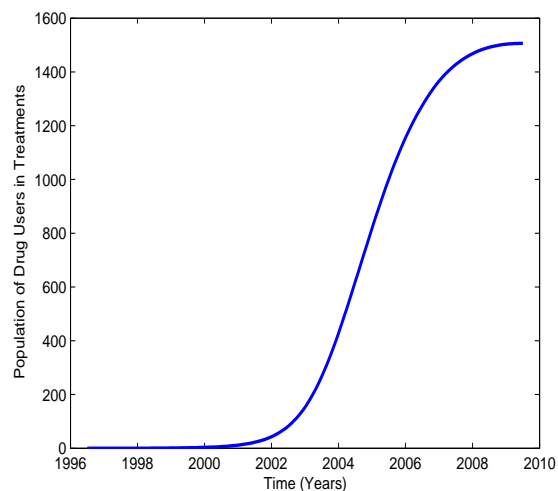
that there were drug users even at the time where there were no drug users in treatments. FIG. 4.3 (a) shows the number of light drug users while FIG. 4.3 (b) shows the number of hard drug users. FIG. 4.3 (c) shows the number of drug users in treatment estimated by the model. FIG. 4.3 also shows that there are more light drug users followed by the number of hard drug users and then drug users in treatment. FIG. 4.3 indicates that there were about 220,000 light drug users and around 4000 hard methamphetamine users.



(a)



(b)



(c)

FIG. 4.3. Shows the change in numbers of light, hard and drug users in treatment estimated by the model over time respectively. Parameter values are given in TABLE. 4.3

We also include the figures for prevalence, incidence and the force of infection in FIG. 4.4 (a), (b) and (c) respectively using the same parameter values which provided the best fit. From FIG. 4.4 (a), we observe that there about 227,600 individuals who are methamphetamine users in Western Cape. This compares well to the estimated number of methamphetamine users in Cape Town which is more than 200,000 [29]. FIG. 4.4 (b) shows the incidence of methamphetamine users which is around 2.8% and FIG. 4.4 (c) indicates the percentage in force of infection which is about 2.9%. Projection of prevalence

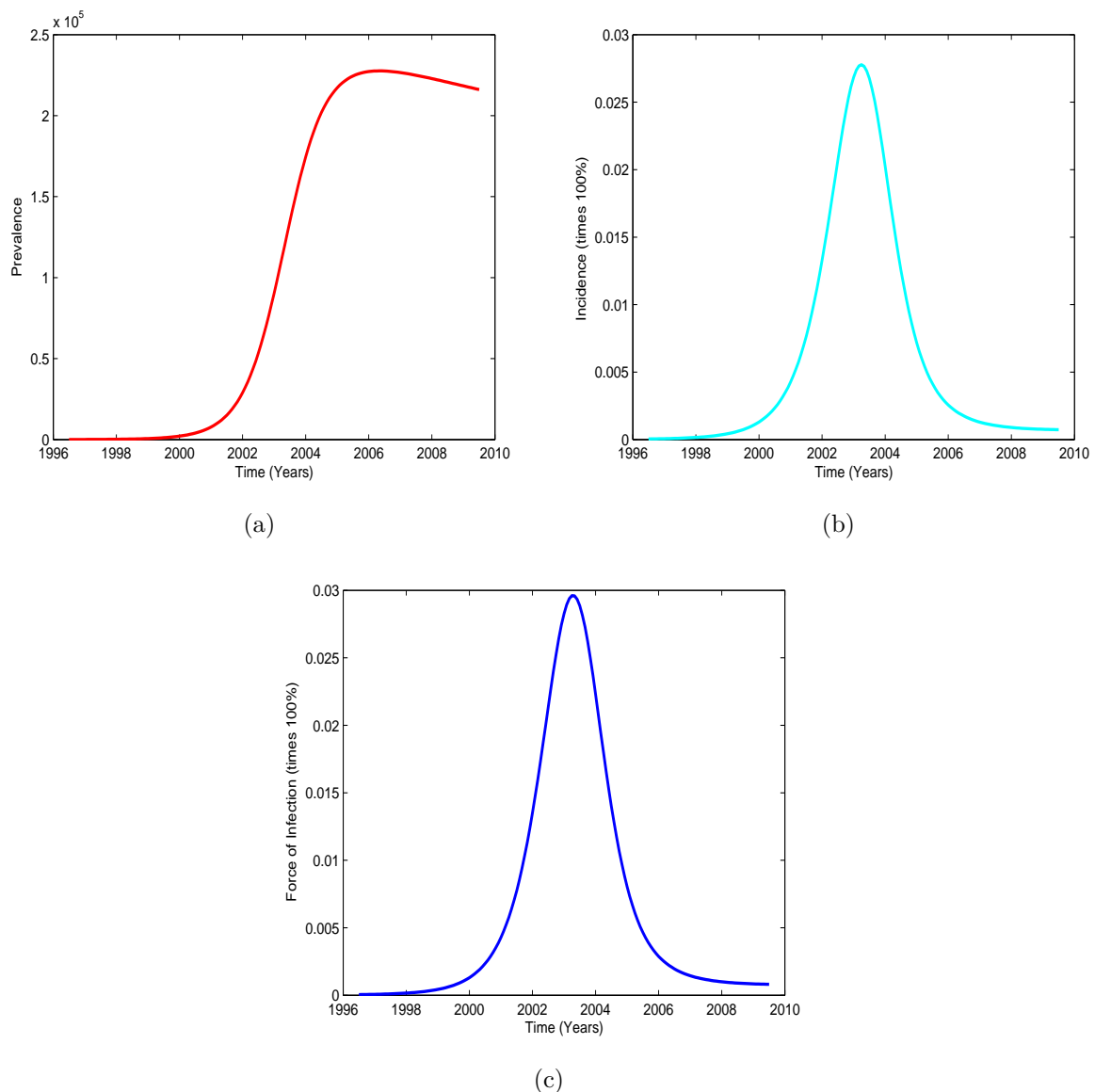


FIG. 4.4. Shows the change on prevalence, incidence and force of infection over time. Parameter values are given in TABLE. 4.3

by the model for five years is shown in FIG.4.5. The model projects that there will be a decrease on prevalence. The same parameter values are used to investigate how prevalence

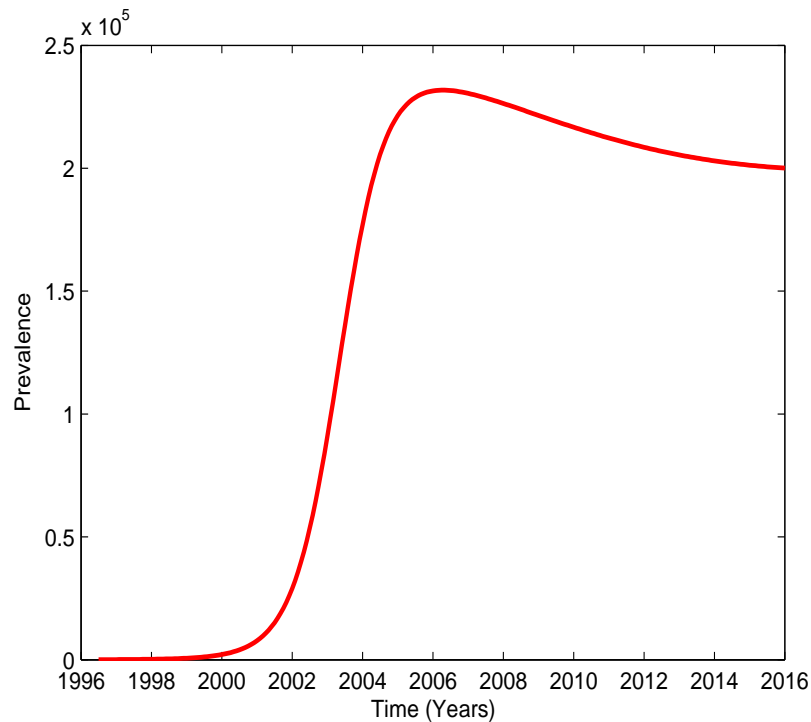


FIG. 4.5. Shows projection of prevalence to 2015. Parameter values are given in TABLE. 4.3

and incidence change with an increase in the values of q . The results are shown in FIG. 4.6, where by as q increases, the prevalence and incidence lowers. This tells us that as individuals change their behaviour, the prevalence as well as incidence decrease.

We also investigate how the populations respond to the changes in the values of q . The results are shown in FIG. 4.7. We observe that drug users' populations decrease with increasing values of q . This gives us some insights in that, as individuals change their behaviour, they will not be involved in drug abuse and hence reduce the number of individuals who are recruited into drug use.

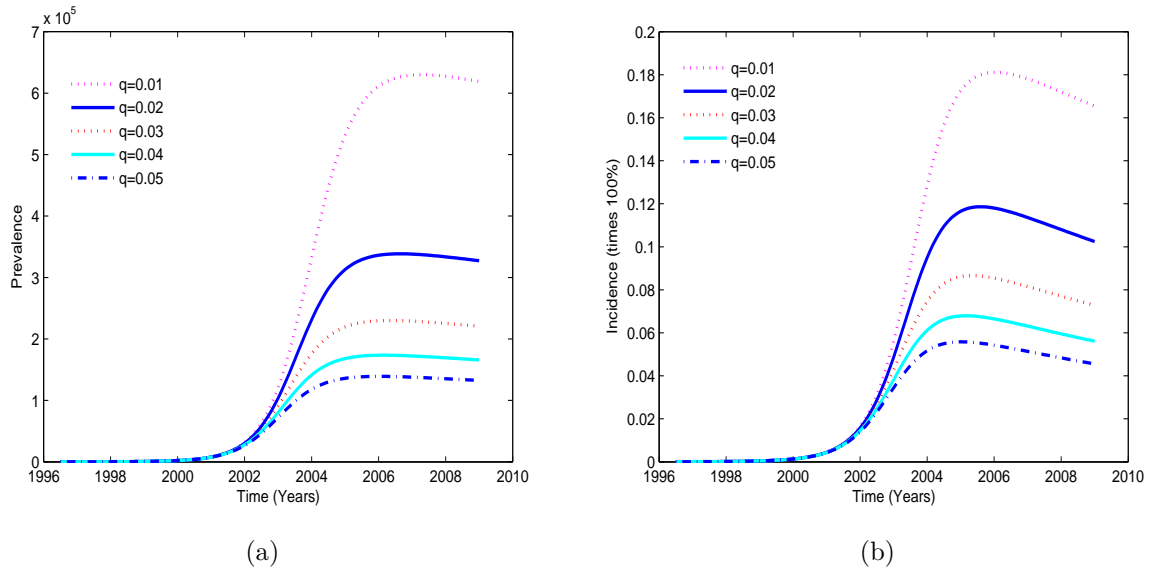


FIG. 4.6. Shows the impact of behaviour change on prevalence and incidence. As q increases, there is a noted decrease on prevalence as well as incidence.

4.5.3 Contribution of ‘reinfection’ r and uptake rate into treatment γ on prevalence

We investigate the impact of ‘reinfection’ and uptake rate into treatment on prevalence. ‘Reinfection’ in this case depicts the reversion to drug use for those in treatment. It is interesting to see how ‘reinfection’ and uptake rate into treatment impact the prevalence. For ‘reinfection’ we consider two cases, when there is ‘reinfection’ and when there is no ‘reinfection’. This is shown in FIG. 4.8 (a), where the area with dark red represents the contribution of ‘reinfection’ $r = 1$ on prevalence and the area with gray colour shows the prevalence on the absence of ‘reinfection’ $r = 0$. It is important to note that when $r = 1$ then the ability to recruit initiates by light drug users and hard drug users is the same. The area in between the curves gives the number of drug users that arise as a result of ‘reinfection’. FIG. 4.8 (b) shows the impact of uptake rate on prevalence. We observe that the prevalence decreases when the uptake rate into treatment increases. We change the uptake rate as from the years 2010 to determine the likely course of the epidemic as γ varies. The reason being that increase in γ would mean increase in treatment centers or making treatment centers accessible to many drug users. This can be done in the future as an intervention and prevention strategy.

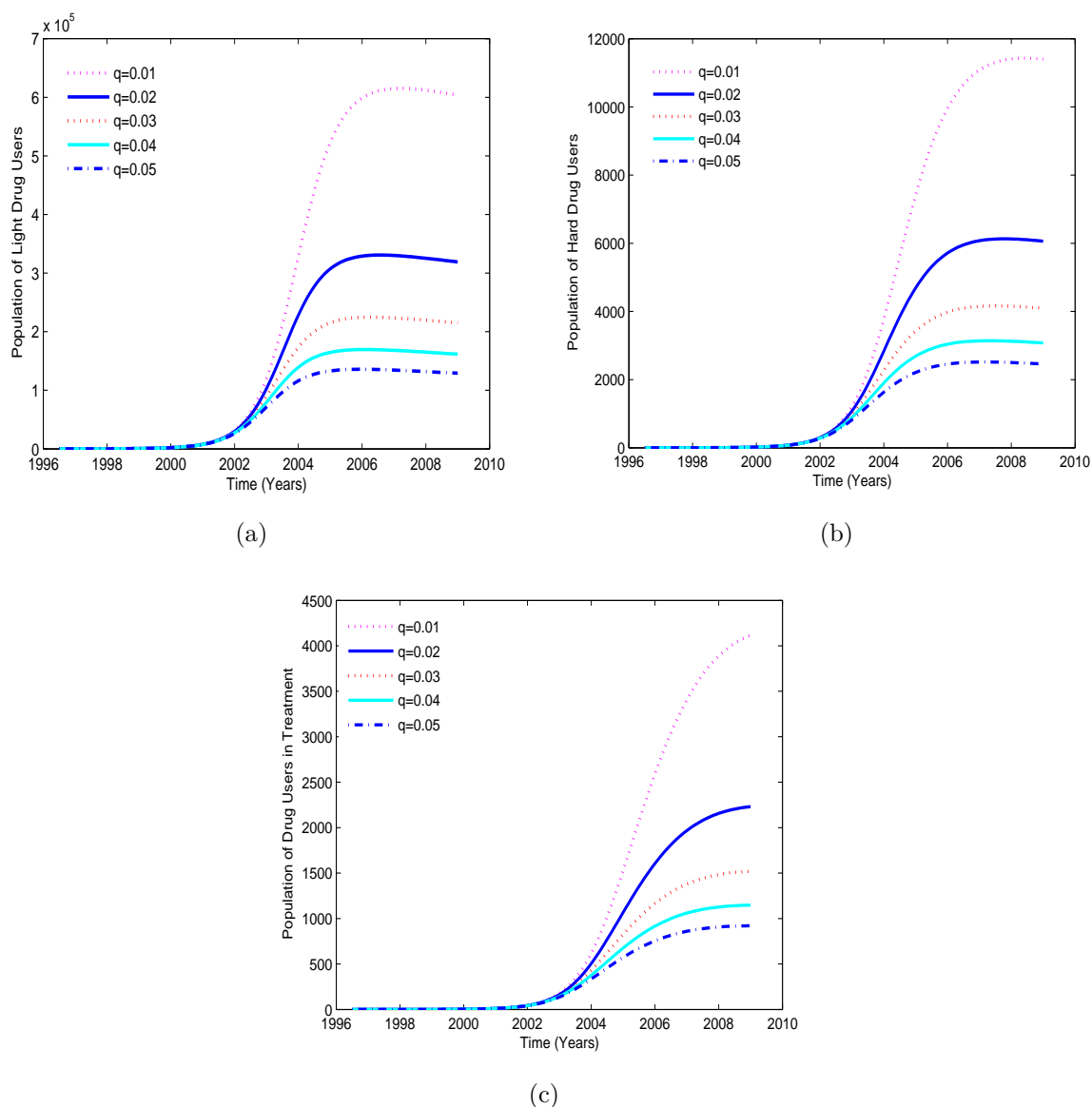


FIG. 4.7. Illustrates the impact of behaviour change in the drug user's populations. (a), (b), and (c) shows the decrease in the number of, light drug users, hard drug users and drug users in treatment individuals respectively, as q increases. Parameter values are given in TABLE. 4.3.

4.6 Summary

In this chapter, we formulated a mathematical model which incorporates innovators and behavioral change. We analysed the model by considering two cases. Firstly we analyse the model in the absence of behaviour change analytically and secondly in the presence

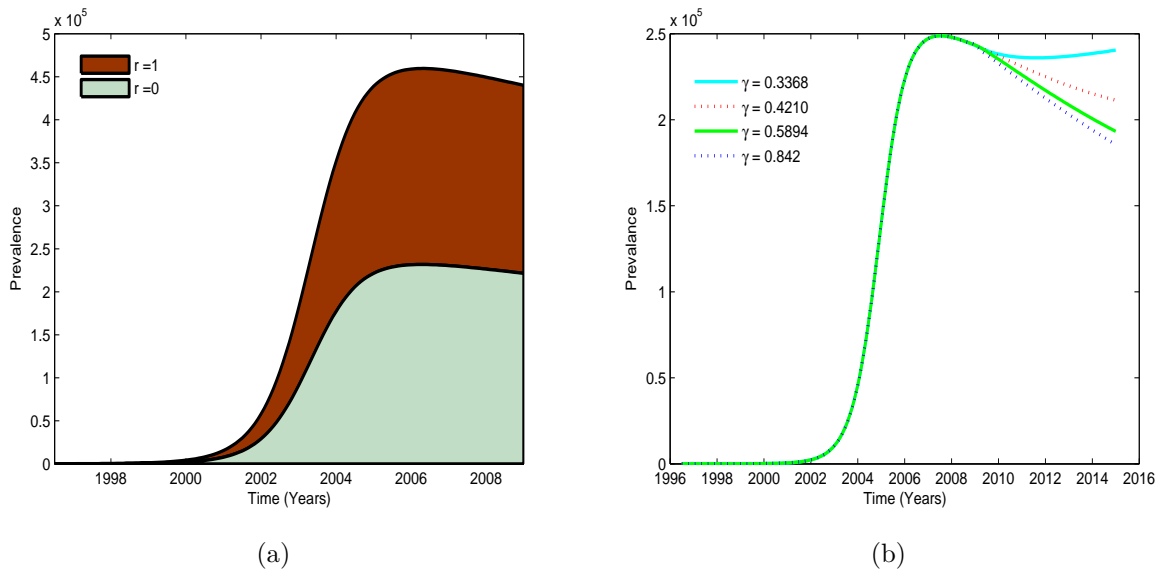


FIG. 4.8. Demonstrates the contribution of ‘reinfection’ r and uptake rate into treatment γ on prevalence respectively. (a) shows the changes in the prevalence as a result of ‘reinfection’, and (b) shows the changes in the prevalence with an increasing uptake rate. Parameter values are given in TABLE. 4.3

of behaviour change numerically. The first case considers the case when there are no innovators (i.e. $\tau = 0$). By considering $\tau = 0$, the non linear incidence function reduces to standard incidence function. In fact the model reduces to the model in Chapter 3 but with a standard incidence function. The model in this case has drug free equilibrium and multiple drug persistent equilibria when $R_0 < 1$. This indicates that the model with standard incidence also exhibits backward bifurcation. We also performed sensitivity analysis of the model using R_0 . The analysis shows that R_0 is most sensitive to transmission rate. R_0 is also an increasing function of relative infectivity and reversion rate. This means that if relative infectivity and reversion rate increase, R_0 also increases and vice versa. It is a decreasing function of permanent recovery rates, removal rate, uptake rate into treatment and transition rate to hard drug use. The dynamics of methamphetamine abuse in the first case is thus similar to that of mass action in Chapter 3.

In the second case we include innovators, and we observe that the model does not have a drug free equilibrium. This is due to constant recruitment of innovators. Similar cases has been observed in the study of infectious disease which considers constant flow of infectives through immigration [6, 25]. Numerically, we explore the model with both innovators and

behavioral change. We fit the model into the data and estimate the parameter values. We also investigate the impact of behaviour change on prevalence, incidence, force of infection and all the three drug users subpopulation. We observe that if people change their behaviour, then the number of drug users, incidence as well as prevalence will be reduced. Finally, we investigate the contributions of ‘reinfection’ and uptake rate into treatment on prevalence. Generally the model enables us to investigate the dynamics of methamphetamine abuse using standard incidence and in a situation where some individuals can start using drugs on their own. It also helps us to understand how interventions focused on behavioral change may have impact on the dynamics of drug abuse.

Chapter 5

Discussion and Conclusion

In this thesis, two mathematical models for the dynamics of methamphetamine abuse are presented. Ordinary differential equations are used to understand the dynamics of methamphetamine abuse in both models. The first model describes the dynamics of methamphetamine abuse assuming that all individuals have the same chance of being a methamphetamine abusers. It also assumed that initiation to methamphetamine abuse is only through contact between drug users and susceptibles. This is presented in Chapter 3. In Chapter 4, the second model which incorporates innovators and behavioral change is discussed. Qualitative and numerical analysis for both models are performed.

The qualitative analysis for the first model and the second model without innovators shows that there exist drug free equilibrium and multiple drug persistent equilibria for $R_0 < 1$ and a unique drug persistent equilibrium when $R_0 > 1$. In the second model with innovators, the analysis shows that there is always a drug persistent equilibrium. This is due to constant inflow of innovators. The existence of a drug persistent equilibrium when $R_0 < 1$ shows possibility of backward bifurcation. In Chapter 3 the stability of drug persistent equilibrium is determined using center manifold theory. The result shows that the model exhibits backward bifurcation under some specific given conditions. This indicates that the classical epidemiological requirement for effective eradication of methamphetamine abuse to be $R_0 < 1$ is not sufficient, even though it is necessary. Rather for eradication of methamphetamine abuse, reproduction number must be smaller than some critical reproduction number R_c .

The relative importance of parameters of the model to the spread of methamphetamine abuse is done through sensitivity analysis. Forward normalization of basic reproduction number with respect to each parameter are performed. Results show that for both models, the reproduction number is most sensitive to transmission rate. It is also an increasing function of relative infectivity, recruitment rate and reversion rate. These agree with our intuition because increase in these parameters results to an increase in initiation to methamphetamine abuse and therefore increase on the spread of methamphetamine abuse. This suggests that the number of drug users can be reduced by reducing reproduction number through a reduction in relative infectivity, transmission, recruitment and reversion rates. It can also be reduced through increased interventions at light drug user phase that lead to recovery. Also the number of methamphetamine abuse can be reduced by increasing the uptake rate into treatment, which can be done by having many treatment centers which are accessible to drug users. Furthermore the number of methamphetamine abusers as well as prevalence can be reduced by preventing reinfection.

We analysed the stability of the first model numerically where by for $R_0 < 1$, the populations stabilized at the drug free equilibrium. When $R_0 > 1$, the populations tend to drug persistent equilibrium. This indicates that drug free equilibrium is asymptotically stable when $R_0 < 1$ and unstable if $R_0 > 1$. Furthermore numerical analysis for the model with innovators and behavioral change was done. We first fitted the model to data. Then we explored the dynamics of drug abuse by the three classes of drug users and prevalence for different values of measure of behavioral change. The result showed that as the measure of behavioral change increased, the populations of methamphetamine abusers as well as prevalence decreased. The implications of this is that if prevention or intervention programs focus on the change of individual's behaviour, there will be a reduction in methamphetamine users and leading to a decrease in prevalence. We also note a decrease in prevalence from the projection.

The study helped to understand the dynamics of methamphetamine abuse in Western Cape. It also enabled us to investigate what can be done in controlling the epidemic. The results presented in this thesis rely on the parameter values estimated from the fitted model. In so doing we had difficulties in estimating parameters especially those related to the level of addiction, that is, the rate at which an individual will move from light to hard drug users or the level of methamphetamine usage which can lead to a person being

categorised as a hard drug user. Therefore these result should be taken with caution, for decision making rather other studies can be done to compliment the one presented in this thesis. We state also that the data used in this study, for the year 1996b to 2006a was collected in the Cape Town metro only. This is because there were no specialist treatment centers/programs in the other parts of the Western Cape other than Cape Town. But as from 2006b to 2009a the total number of methamphetamine users in treatment is a result from all treatment centers in the Western Cape. We suggest the following

- The data collected should include the level of addiction. This is frequency of methamphetamine usage and the amount of methamphetamine usage in a given time interval, for example per week.
- Increase in the number of specialist centers, so as to allow more people to be able to access the services.
- Making these services free or affordable to everyone or majority of methamphetamine users and other illicit drug users.
- Data related to methamphetamine death may be useful.
- Data on arrest related to methamphetamine should be recorded.
- Data on those who relapse to drug use when in treatment and after quitting permanently should be also be recorded.

All these will help on estimating parameters related to addictiveness and also help in comparing results from different sources of data.

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