Modelling in- and out-patient rehabilitation for substance abuse in dynamic environments

by

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Thesis presented in partial fulfilment of the requirements for the degree of Master of Science in the Faculty of Science at Stellenbosch University

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Declaration

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Date: November 10, 2015 .....

Abstract

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Thesis: MSci (Math)

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Substance abuse is a major problem globally with immeasurable consequences to the health of users. Rehabilitation is one of the strategies that can help to fight against substance abuse. It is divided into two forms: in-patient and out-patient rehabilitation. In this study, we consider a compartmental model of substance users in rehabilitation, where a periodic function is included to illustrate seasonal oscillations of drug users entering rehabilitation. In this thesis, we derive two basic reproduction numbers R_0 and $[R_0]$, where R_0 is the model with periodicity and $[R_0]$ the model without periodicity. We show that the model has a drug-free equilibrium when the basic reproduction number R_0 is less than one and drug persistent equilibrium when R_0 is greater than one. We fit the model to data and obtained sneak preview of the future of these forms of rehabilitation. Our results indicate that when R_0 is less than one, the in- and out-patient populations decrease quickly and when R_0 is greater than one drugs persists and after a long period of time, in-

dividuals in rehabilitation approaches $\omega-$periodic solution. Sensitivity analysis is performed and the results show that control measures should focus on the effective contact rate between susceptibles and drug users so as to control the epidemic. These results have significant implications on the management and planning of rehabilitation programs in South Africa.

Uittreksel

Modellering van binne- en buitepasiënt-rehabilitasie vir substansie-misbruik in dinamiese omgewings

("Modelling in- and out-patient rehabilitation for substance abuse in dynamic environments ")

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Dwelm misbruik is wêreldwyd 'n ernstige problem met onmeetbare gevolge vir die gesondheid van gebruikers. Rehabilitasie is een van die strategieë wat dwelm misbruik kan help beveg. Dit word in twee vorms verdeel: binnepasiënt- en buitepasiënt-rehabilitasie. In hierdie studie ondersoek ons 'n kompartementele model van dwelmgebruikers in rehabilitasie, waar 'n periodieke funksie ingesluit word om seisoenale skommelings aan te toon met betrekking tot dwelmgebruikers wat rehabilitasie aanpak. In hierdie tesis lei ons twee basiese reproduksienommers af, R_0 en $[R_0]$, waar R_0 die model met periodisiteit en $[R_0]$ die model sonder periodisiteit is. Ons toon aan dat die model 'n dwelmvrye ekwilibrium het wanneer die basiese reproduksienommer R_0 minder as een is en 'n dwelm-voortsettingsekwilibrium het wanneer R_0 meer as een is. Ons pas die model op die data toe en verkry 'n voor-

uitskouende blik op die toekoms van hierdie vorms van rehabilitasie. Ons resultate dui aan dat wanneer R_0 minder as een is, die binne- en buitepasiënt-bevolkings vinnig verminder en wanneer R_0 meer as een is, die gebruik van dwelms voortduur en dat nà 'n lang tydperk individue in rehabilitasie nader aan $\omega-$periodieke oplossing beweeg. Sensitiwiteitsontleding word uitgevoer en die resultate toon aan dat daar 'n bewustheid moet bestaan dat die graad van effektiewe kontak tussen vatbare individue en dwelmgebruikers beperk moet word ten einde die epidemie onder beheer te bring. Hierdie resultate het betekenisvolle implikasies vir die bestuur en beplanning van rehabilitasieprogramme in Suid-Afrika.

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Dedications

This thesis is dedicated to my God for giving me wisdom and I say Ebenezer, you were with me upto this far. To my mother Noluvuyo Gatyeni for her love and support. To my siblings Ndaxola and Sibabalwe Gatyeni. My love to you all. May God bless you.

Publications

The following publication is taken from this thesis. It is added at the end of the thesis.

1. Modelling in- and out-patient rehabilitation for substance abuse in a dynamic environment. To be submitted.

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Chapter 1

Introduction

1.1 Substance abuse

Substance abuse, also known as drug abuse, is an influenced use of a drug where a user consumes a substance in amounts or with methods which are detrimental to themselves or to others [37]. It remains a problem globally with endless health consequences, high rates of suicide, crime and increased government spending [51, 62].

Every 6 months in South Africa, drug abuse data is collected by South African Community Epidemiology Network on Drug Use (SACENDU) as a regular treatment monitoring system [47]. This is a network of researchers, practitioners and policy makers from eight sites in South Africa who meet twice a year and provide community-level public health surveillance information about substance abuse. The SACENDU reports have shown a significant increase in demand for drug abuse rehabilitation [64].

The problem of drug abuse in South Africa is a major public health responsibility, since the increase of drug abuse causes an increase in the spread of HIV [50]. In sub-Saharan Africa there were several studies that suggest a strong link between substance abuse and risky sex behaviour; such as having two or more sex partners, unprotected sex and engaging in commercial sex [16]. Drug abuse has also been linked to crime [41].

The World Health Organisation (WHO) reported that 40% of the treatment of drug use is served by the government and 60% from the private sector [67]. The report also shows that 10% of the addicts have access to treatment as in-patient clients and 10-50% as out-patient.

Compared to the other provinces in South Africa, the Western Cape province has higher rates of the substance abuse [19]. This province is particularly causing trouble with the higher proportion of alcohol and drug positive arrestees [41].

Methamphetamine drug is also associated with sexual risk behaviour, increasing the likelihood of exposure to sexually transmitted infections (STIs) and HIV [44]. Figure 1.2 shows the treatment trends on methamphetamine in the Western Cape [47]. 'Tik' is the main drug of choice for 42% of Cape Town users.

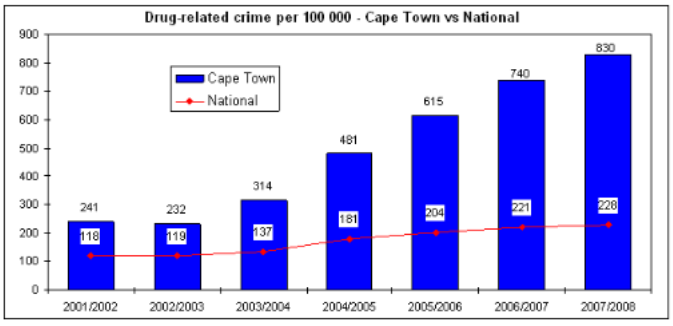


Figure 1.1: Results of the Christian Drug Support, comparing Cape Town statistics on drugs with the national statistics on drugs. Source [8].

Figure 1.1 shows that from 2001 to 2008 drug related crime in Cape Town increased more rapidly compared to other provinces [8]. The United Nations Office on Drugs and Crime (UNODC), in 2011 on the world drug report showed that Cape Town has topped in the drug called Methamphetamine commonly known as 'tik', in people who are seeking treatment in for rehabilitation [61].

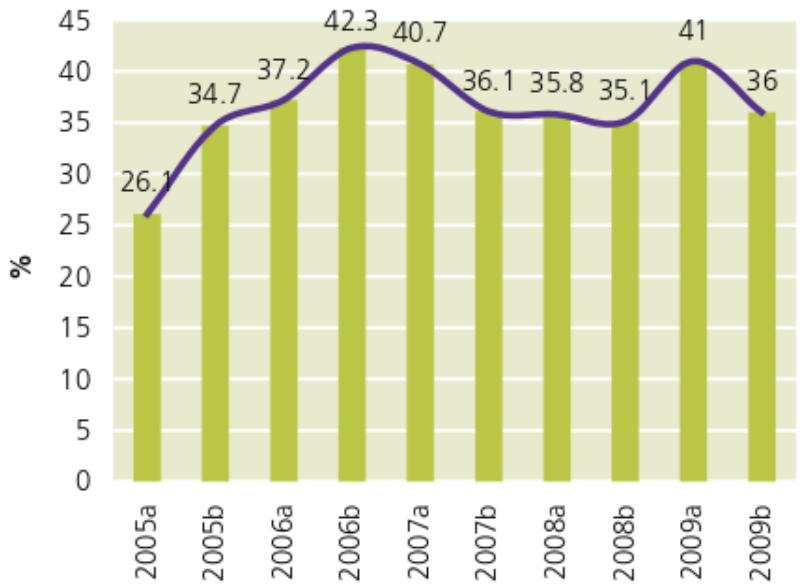


Figure 1.2: Treatment demand for methamphetamine as the primary substance abuse in the Western Cape. Where 'a' represent the first half of the year (January - June) and 'b' represent the second half of the year (July - December). Source [47].

1.2 Substance abuse types

1.2.1 Heroin

Heroin drug is the most dangerous and addictive narcotic drug that is produced from the resin of the opium poppy [13]. It is mixed with other substances like chalk powder, zinc oxide and even strychnine [11]. This drug leads to suppression of pain, heaviness of limbs and shallow breathing. It also damages the liver and affects the heart lining and valves. Pregnant women who are addicted to heroin can bear addicted babies. It destroys the chemical balance in the brain to an extend that when the user who uses heroin, starts to experience pain in the absence of any injuries.

1.2.2 Marijuana

Marijuana refers to the dried leaves, flowers, stems and seeds from the hemp plant, *Cannabis sativa* [22]. Cannabis sativa is a plant which grows annually in all parts of the world, such as the Canadian-American border primarily by Asian gangs [22] and in South Africa [42]. This plant contains mind-altering chemical delta-9-tetrahydrocannabino (THC) and other compounds related. In 1980, the number of natural compounds identified in Cannabis sativa was 423 and by 1995 it has increased to 483 [21]. It is the most used drug worldwide and 20% is the youth [54].

Marijuana is commonly self-administered by the smoking route, by rolling marijuana leaves in tobacco paper and smoking as a cigarette and may produce a variety of pharmacological effects such as sedation, euphoria, hallucinations and temporal distortion [22].

1.2.3 Alcohol

Alcohol abuse is a pattern of drinking that results in harm to health or ability to work. It is also a psychiatric condition in which there is recurring harmful use of ethanol despite its negative consequences [7, 10].

Alcohol abuse to pregnant women cause their fetus to develop conditions that can affect an unborn child, such as abnormal appearance, short height, low body weight, small head, poor coordination, low intelligence, behaviour problems and problems with hearing or seeing [26]. Fetal alcohol syndrome is the pattern of physical abnormalities and the impairment of mental development which is seen with increasing frequency among children with alcoholic parents [26].

1.2.4 Methamphetamine

The National Institute on Drug Abuse (NIDA) defines Methamphetamine (MA) as an extremely addictive drug that is chemically similar to amphetamine (which stimulates the central nervous system) [35]. In the Western Cape province of South Africa, this drug is known as ‘tik’ and is the common drug that is used. It is a much more potent version of its parent drug amphetamine, which was the first drug introduced into medical practice as a nasal decongestant but due to its abuse

potential it is limited to certain rare conditions [9].

(a) Heroin. (b) Marijuana.

(c) Alcohol. (d) Methamphetamine.

Figure 1.3: Types of substance abuse used in South Africa.

According to [40, 45], the rates of methamphetamine are increasing in Cape Town, and is particularly used by young people, more especially in coloured communities [46] it also commonly used by individuals under the age of 20 [46]. Methamphetamine is an illegal drug similar to cocaine and other powerful drugs and it is a dangerous drug that damages the brain. It also increases the amount of neurotransmitter dopamine in the brain.

Methamphetamine abusers get affected in the brain by experiencing nervousness, confusion, insomnia and mood disturbances. Also long-term methemphetamine users face consequences on physical health and skin sores caused by scratching. There is also high risk of contracting infectious diseases like HIV, by sharing contaminated drug injection equipment and having two or more partners and practice

of unsafe sex and it may also worsen the progression of HIV/AIDS and its consequences [29].

1.3 Common substances of abuse in Cape Town

In Cape Town, SACENDU [47] reported that between January and June 2013, 76% of drug users were male, 71% coloured people, 59% were not working, 67% were single and 59% were between the ages of 15 and 29. In 2006, individuals who received treatment as in and out-patients were 1428 (summing up all drug types victims) [43]. The latest report from SACENDU shows that the number of people who received treatment between January and June 2013 was 3137 and were between the ages of 15 and 19.

SACENDU also reported that most the drug users who have been admitted for treatment in rehabilitation centres; 33% primarily used Methamphetamine commonly known as 'tik', 22% used alcohol, and 22% used cannabis known as 'marijuana'. Tik remain as the most common drug in Cape Town. One of the reasons that makes 'tik' to be common in the province is that, it is cheap, widely available, easy to make and the recipe is on the internet.

The proportion of patients admitted for heroin dependence remained the same in the past years as 13% in Cape Town.

1.4 In-patient and out-patient rehabilitation

The rehabilitation of drug users (often known as drug rehab) is a process of medical treatment, where a patient is assisted to stop the use of drugs and becomes a normal person. In rehabilitation, various types of programs are offered to help drug users to stop using drugs. This can be done at a rehabilitation centre with the patient staying in the centre for the duration of the treatment process. It can also be done when an individual visits the treatment centre on a daily basis.

In-patient treatment also known as residential treatment, can be part of a hospital program or found in special clinics, where a patient stays at the facility and gets therapy in the day or evening. Out-patient treatment happens in mental health

clinics, counsellors offices, hospital clinics, or local health department offices, where a patient is not required to stay overnight.

In-patient rehabilitation programs help patients by removing them from their community and placing them into medically supervised treatment facilities. It eliminates stress by removing individuals from the temptation to use drugs again and the ability to relapse. This form of treatment does not allow individuals to contact family and friends during the first portion of the rehabilitation process, so that individuals can focus on their recovery without disturbances from outside the world.

Out-patient rehabilitation programs on the other hand also helps patients recover from drug abuse but the addict is allowed to return home each night. If a patient has responsibilities, such as caring for children or work obligations, out-patient rehabilitation allows them to maintain those responsibilities. This rehabilitation is best for those with short lived addiction and is not recommended for those with long lived addictions. According to the National Institute on Drug Abuse, being addicted to drugs is a serious illness that is uncontrollable, along with compulsive drug seeking and use that remain even in the face of destructive consequences; but also a treatable disease [36]. Drug addiction results from the effects of persistent drug exposures on brain functions , since addiction is a brain disease that affects brain circuits.

Rehabilitation can help drug users to stop using drugs, avoid relapse and become recovered successfully. Medications from rehabilitation centres can be used to help re-establish normal brain function and to prevent relapse. Drug rehabilitation is a term for the processes of medical treatment, for dependency on psychoactive substances such as alcohol, prescription drugs and street drugs such as cocaine, heroin or amphetamines [36].

1.5 Data on rehabilitation

Data on rehabilitation in South Africa shows a fluctuating behaviour. Below we present the data from SACENDU on in- and out-patient rehabilitants in the Western Cape [47]. The data is connected using spline fitting interpolation.

We argue here that variability of the data trends is certainly driven by community

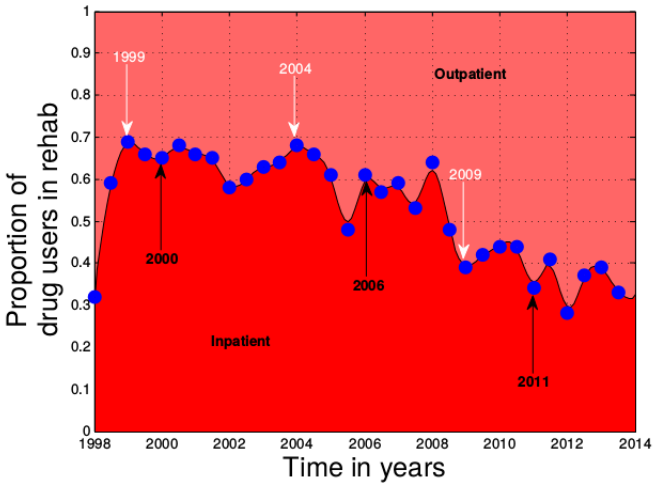


Figure 1.4: Source [47]. Spline fitting interpolation for in- and out-patient treatment users. Dark red area shows the proportion of in-patient in rehabilitation and light red area shows the proportion of out-patient in the rehabilitation. The white arrows indicate the years of parliamentary elections of South Africa which are held every five years and black arrows indicate the municipal elections of South Africans to elect new councils for all municipalities in the country, as potential causes of data variability.

and social dynamics. The drivers of the fluctuations could be financial, social or political. We postulate the following:

(i) Medical aid driven rehabilitation:
Rehabilitation supported by medical aid schemes often covers alcohol, substance and drug rehabilitation for a maximum of three weeks per year [18]. On the other hand, complete recovery often requires at least four weeks [3]. This means that individuals that seek rehabilitation at the beginning of the year may have to wait for the following year to enter into rehab again using medical aid as a result of incomplete treatment protocols.

(ii) Political dynamics:
The demand for basic services including rehabilitation of addicts often increase prior to elections in South Africa. This is accompanied by service delivery protests, which decrease after the elections [25]. We indicated on the figure above the times when national and provincial elections were held [14, 58] and a correlation is clearly observed, where white arrows indicate the years of

parliamentary elections of South Africa which were held every five years and black arrows indicate the municipal elections of South Africans to elect new councillors for all municipalities in the country. In every election year there is a peak in either in-patient or out-patient rehabilitation as potential election candidates try to impress the electorate.

1.6 Project motivation and objectives of the study

1.6.1 Motivation

In South Africa, substance abuse is a major challenge, especially in the Western Cape province. There are many ways to fight substance abuse. Rehabilitation is one of the strategies. Rehabilitation is divided into two forms: in-patient rehabilitation and out-patient rehabilitation. In this research, we focus on these two forms with a particular emphasis on determining the current trends and link the available data with the South African political elections, since the available data seem to suggest that government support comes during election period.

1.6.2 Objectives

The main objective of this research is to model the dynamics of substance abuse in a dynamic environment. In particular we construct a periodic function that includes variations in communities.

The specific objectives include

- Formulating a model for in- and out-patient rehabilitation processes.
- Carrying out the mathematical analysis of the in- and out-patient model, to gain the understanding of how model behaves based on the equilibrium points, reproduction number, stability analysis and the extinction of drugs.
- Fitting the model to the available data on individuals under treatment for substance abuse in the Western Cape province.
- Carrying out the sensitivity analysis to establish parameters that are vital in the model.

- Model substance abuse rehabilitation in the presence of noise, to capture the fluctuations in the data.

1.7 Mathematical preliminaries

There are mathematical concepts and tools that are used for analysing and developing mathematical models.

1.7.1 Equilibrium points and their stability

According to [56], an equilibrium point or steady state of a dynamical system from an autonomous system of ordinary differential equations (ODEs) is defined as a solution that does not change with time. In differential equations, equilibrium points are constant solutions of differential equation [5].

Definition 1. *The point $x^* \in \mathbb{R}^n$ is an equilibrium point for the differential equation [5]:*

$$\frac{dx}{dt} = f(t, x) \tag{1.7.1}$$

if

$$f(t, x^*) = 0 \quad \textit{for all} \quad t$$

and is uniquely determined by its initial conditions $x(0) = x_0$ and the solution is denoted by $x(t, x_0)$.

The Jacobian matrix of a system of ordinary differential equations is the matrix of first order partial derivatives of a vector-valued function [1]. In general Jacobian matrix gives the gradient of a scalar function of multiple variables, which itself generalizes the derivative of a scalar function of a single variable.

Definition 2. *Let $\boldsymbol{F} : \mathbb{R}^n \to \mathbb{R}^m$ be a function that takes the vector $x \in \mathbb{R}^n$ and produce the vector output of $\boldsymbol{F(x)} \in \mathbb{R}^m$ [1], then the Jacobian matrix J of function $\boldsymbol{F}$ is $m \times n$ matrix, such as*

$$J = \frac{d\boldsymbol{F}}{dx} = \begin{bmatrix} \frac{\partial \boldsymbol{F}}{\partial x_1} \cdots \frac{\partial \boldsymbol{F}}{\partial x_n} \end{bmatrix} = \begin{bmatrix} \frac{\partial \boldsymbol{F}_1}{\partial x_1} & \frac{\partial \boldsymbol{F}_1}{\partial x_2} & \cdots & \frac{\partial \boldsymbol{F}_1}{\partial x_n} \\ \frac{\partial \boldsymbol{F}_2}{\partial x_1} & \frac{\partial \boldsymbol{F}_2}{\partial x_2} & \cdots & \frac{\partial \boldsymbol{F}_2}{\partial x_n} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial \boldsymbol{F}_m}{\partial x_1} & \frac{\partial \boldsymbol{F}_m}{\partial x_2} & \cdots & \frac{\partial \boldsymbol{F}_m}{\partial x_n} \end{bmatrix},$$

where the the entries of Jacobian matrix are evaluated at $x = (x_1, \ldots, x_n)$.

x^* is an equilibrium point if $f(x^*, t) = 0$. So the stability of x^* depends on the eigenvalues of $Df(x^*)$. The solution x^* is locally stable if all solutions which start near x^* remain near x^*. If the solutions that start near x^* tend towards x^* as $t \to \infty$, then x^* is locally asymptotically stable.

Definition 3. *The equilibrium point* $x^* \equiv 0$ *of equation* (1.7.1) *is stable at* $t = t_0$ *if for any* $\epsilon > 0 \; \exists \; \delta(t_0, \epsilon) > 0$ *such that*

$$\| \, x(t_0) \, \| < \delta \quad \Longrightarrow \quad \| \, x(t_0) \, \| < \epsilon, \quad \forall \quad \epsilon > t_0.$$

Definition 4. *An equilibrium point* $x^* \equiv 0$ *of equation* (1.7.1) *is asymptotically stable at* $t = t_0$, *if*

1. $x^* \equiv 0$ *is stable and*
2. $x^* \equiv 0$ *is locally attractive (sink),* $\exists \quad \delta(t_0)$ *such that* $\| \, x(t_0) \, \| < \delta \quad \Longrightarrow \lim_{t \to \infty} x(t) = 0$.

1.7.2 The basic reproduction number

Fraser et al. [15] defines the basic reproduction number as the number of cases that one case generates on average over the course of infectious period, in an uninfected population. Sometimes basic reproduction number is called basic reproductive ratio or threshold parameter and denoted by R_0.

The basic reproduction number can be calculated by using the next generation matrix method, for a compartmental model of the spread of diseases. This method has been developed by [12, 70]; where the population has to be divided into n compartments and $m < n$ infected compartments. We let $x_i, i = 1, 2, 3 \ldots, m$ to be the number of infected individuals in the i^{th} infected compartment at time t. Then the epidemic model is given by

$$\frac{dx_i}{dt} = F_i(x) - V_i(x),$$

where $F_i(x)$ is the fertility matrix that represents the rate of appearance of new infections in the compartment i and $V_i(x)$ is the transition matrix that represents the

rate of transfer of individuals and is divided into two sub-compartments, $V_i^-(x)$ and $V_i^+(x)$ which represents the rate of transfer of individuals into and out of compartment i. The matrices $m \times m$ of F and V are defined as

$$F = \frac{\partial F_i}{\partial x_j}(x_0) \quad \text{and} \quad V = \frac{\partial V_i}{\partial x_j}(x_0),$$

then FV^{-1} is the next generation matrix and the largest eigenvalue or the spectral radius of the matrix FV^{-1} is the basic reproduction number of the model.

1.7.3 Spline fitting

Spline functions are formed by joining polynomials together at fixed points called knots and defined as piecewise polynomials of degree n [49]. Spline functions [68] are approximating functions in mathematics and numerical analysis. In numerical analysis, spline interpolation is used as a form of interpolation where the interpolant is a special type of piecewise polynomial called spline.

Definition 5. *Interpolation is a method of constructing new data points with the range of a discrete set of known data points.*

Spline was a term referring to elastic ruler that were able to bent to pass through a number knots, in order to make technical drawings for construction by using hand. This approach to mathematical modelling $\{(x_i, y_i) : i = 0, 1, \ldots, n\}$ is to interpolate between all the pairs of knots $\{x_{i-1}, y_{i-1}\}$ and (x_i, y_i) with polynomials $y = q_i(x), i = 1, 2, \ldots, n$. The arc of a curve $y = f(x)$ is given by

$$k = \frac{y''}{(1 + y'^2)^{\frac{3}{2}}}.$$

As the spline will take a shape that minimizes bending both y' and y'' will be continuous everywhere and at the knots.

1.7.4 Inclusion of noise in differential equations

A stochastic dynamical system is a system that is subjected to the effects of noise [55]. In stochastic dynamics of deterministic systems, the dynamics at each point in time are subject to some random variability and this variability is propagated

forward in time by the underlying equations [23]. Let us consider the stochastic differential equation (SDE) model:

$$\frac{dx}{dt} = Noise. \tag{1.7.2}$$

The Euler's method of integration is the most simple means of solving such equations, breaking time into small components δt,

$$\begin{aligned} x_{t+\delta t} &= x_t + \delta t \frac{dx}{dt} \\ &= x_t + \delta t \quad Noise \\ &= x_0 + \delta t \sum_{1}^{\frac{t}{\delta t}} Noise. \end{aligned}$$

Thus, the equations progress as the summation of many small noise terms with mean zero. If noise terms are independent, as the step size is smaller then the variance of x at any time go down to zero. When the updating method is exact, the limit $\delta t \to 0$ then all the noise terms effectively cancel [23].

Therefore, this shows that there is no simple mathematical method that can be used to express the noise term. The simplest way to this problem is to scale the noise term with respect to the integration step, such that we assume $Noise = RANDN$, independent Gaussian with mean 0 and variance 1, so that

$$\xi = \frac{Noise}{\sqrt{\delta t.}} \tag{1.7.3}$$

Definition 6. *$RANDN$ is the function that generates arrays of random numbers whose elements are normally distributed with mean 0, variance $\sigma^2 = 1$ and standard deviation $\sigma = 1$.*

As the time step of integration decreases, the amplitude of the noise in each step step ξ, increases. Thus, this new definition of ξ has the properties that we require, such that if

$$\frac{dx}{dt} = f\xi,$$

then

$$Noise = f\xi$$

and averaged over multiple simulations, the mean of x is zero while the standard deviation grows like $f = \sqrt{(t)}$ and thus the dynamics correspond to a random walk.

1.8 Outline of the thesis

The thesis is organized into five chapters. In Chapter 1, an introduction of substance abuse in South Africa is provided, types of substance abuse used in Cape Town area and the rehabilitation process. In Chapter 2, we provide literature review based on substance abuse models, periodic models in general and stochastic dynamics of deterministic systems. In Chapter 3, the model is formulated and analysed. In this chapter, equilibrium points are established and their stability analysis presented. Furthermore, we obtained two basic reproduction numbers, with and without periodic function. Finally in this chapter, numerical results are presented and discussed. In Chapter 4, we model substance abuse rehabilitation with noise, sensitivity analysis and simulations are presented. In Chapter 5, we conclude with relevant discussions and recommendations.

Chapter 2

Literature review

2.1 Mathematical models

Modelling describes a typical way of understanding reality, using mathematical concepts and language [53]. Building models for real-world is important, especially for human development. The main interest of modelling a process is to fit realistic mathematical models to data, and use models and data to estimate parameters of that particular model. The initiation and spreading of infectious diseases is a complex phenomenon with interacting factors, such as the environment with which the pathogen and host are situated. We can use compartmental models to analyse the dynamics of epidemics in the population, model how disease spread and what approaches of control are mostly likely to succeed in reduction of the burden of epidemics.

Kermack and McKendrick developed a SIR model. They considered a fixed population with three compartments, such as S for susceptible population who are at risk of becoming infected to the disease, I infected population and R recovered class for those who have been infected and then recover from the disease [24].

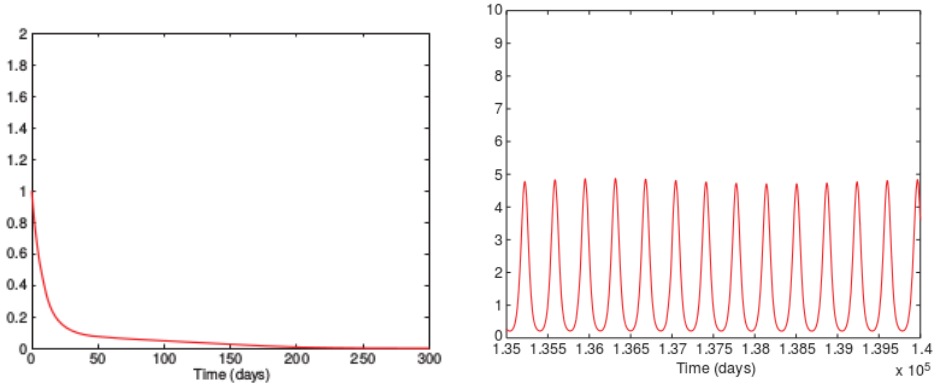
2.2 Model with periodicity

Periodicity and other oscillatory behaviours have been observed in the incidence of many infectious diseases such as chickenpox, cholera, mumps, influenza and

poliomyelitis [20]. The incidence of some diseases like chickenpox, mumps and poliomyelitis increases and decreases every year. Thus, this one year period appears to be due to a seasonal variation in some factors such as contact rate. The contact rate may fluctuate periodically due to weather changes, periodic aggregation of children in schools and due to socio-political issues.

Many researchers discovered that periodic coefficients in deterministic epidemiological models, lead to periodic solutions [20, 27, 48]. Billings and Schwartz identified a mechanism for chaos in the presence of noise using SEIR model which predicts epidemic model outbreaks in childhood diseases [4]. They assumed that the contact rate vary seasonally for childhood diseases due to opening and closing of schools.

In 2014, Posny and Wang proposed a deterministic compartmental model for cholera dynamics in periodic environments [48]. The basic reproduction numbers with and without periodicity, R_0 and $[R_0]$ respectively were derived. Several examples were presented to demonstrate this general model and numerical simulation results were used to analyse prediction.



(a) (b)

Figure 2.1: Source [48]. A typical infection curve, in (a) when $R_0 < 1$ and (b) when $R_0 > 1$. When $R_0 < 1$, the solution quickly converges to zero and when $R_0 > 1$, a periodic solution with $\omega = 365$ days forms after a long transient.

Figure 2.1 shows a typical infection curve for cholera dynamics in a periodic envi-

ronments, when $R_0 < 1$ and when $R_0 > 1$. This shows that when $R_0 < 1$, then the solution quickly converges to zero and stays there forever. Similar patterns were observed for various initial conditions and this shows that the disease-free equilibrium is globally asymptotically stable. When $R_0 > 1$, the disease persists and after a long period of time, the infection approaches a positive $\omega-$periodic solution [48].

2.3 Substance abuse models

Whitey and Comiskey [66], in 2007, modelled the heroin epidemics, treatment using ordinary differential equations in a similar way to modelling diseases. Their aim was to identify parameters of interest for further study, with a view to informing and assisting policy makers in targeting prevention and treatment resources for maximum effectiveness. They found the condition under which a backward bi-

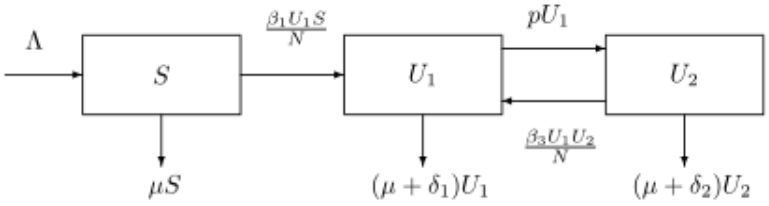


Figure 2.2: Source [66]. Flow diagram used in modelling heroin drug. S stands for susceptible individuals in the population, U_1 is the number of drug users not in treatment and U_2 is the number of drug users in treatment.

furcation may exist, as there were conditions that permit the existence of multiple endemic equilibria. Their results showed that the prevention of drug initiation is better than treatment [66]. Figure 2.2 shows the dynamics of heroin drug where each compartment represents a stage in the drug-using career.

Mulone and Straughan, [34] studied at the modelling of drug epidemics as a note to the work in [66]. They assumed that initiation into drug use is based only on the contact between the susceptible population and the drug user. They showed that equilibrium solution of heroin epidemic model is stable in both linear and nonlinear stability under the realistic condition that the relapse rate of those in treat-

ment returning to untreated drug use is greater than the prevalence rate of susceptibles who become drug users. If their endemic equilibrium were to be unstable that could signal an epidemic in heroin use.

Burattini et al. [6] modelled the dynamics of smoking of crack-cocaine (same mode of transmission is related to that of drug use). The structure of their model adapted from SIR model structure and they assumed that the population is divided into four classes namely, susceptibles, injecting drug users, crack-cocaine users and users of both crack-cocaine and injecting drugs. Their results suggested that the impact of the introduction of crack-cocaine use on the prevalence of HIV/AIDS depends on several factors and could result on the complex demographic interactions of dynamic system in the population of drug users and its relationship with the HIV/AIDS epidemic.

In 2010, Nyabadza and Hove-Musekwa [38], modelled substance abuse in Western Cape province and their model was an extension of the work of White and Comiskey [66]. They modified the model, to model the dynamics of Methamphethamine. Their modification included the addition of two compartments to cater for the recovered and light drug users (see Figure 2.3), the class of drug users who are not on treatment is divided into two compartments: light drug users and heavy drug users. They fitted the model to data which showed projections on the future of heroin.

Nyabadza et al. [39] modelled the dynamics of crystal meth ('tik') abuse in the presence of drug-supply chains in South Africa (see Figure 2.4). They considered a model for 'tik' use that accounts for rehabilitation, tracks drug-supply chains and amelioration for the addicted. They considered both slow and fast dynamics in their model that were driven by drugs in the population and community respectively. Sensitivity analysis revealed that parameters with the most control over the epidemic are the quitting rate of light-drug users and the person-to-person contact rate between susceptible individuals and 'tik' users.

In 1998, van den Bree et al. [69] studied about genetic and environmental influences on drug use and abuse in male and female twins. They analysed males and females separately and their models included thresholds based on population prevalence of abuse and treatment. Environmental influences played a greater role in use than

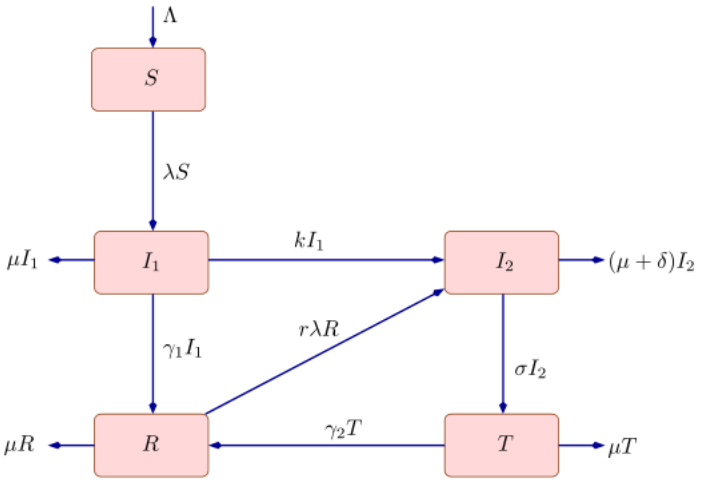


Figure 2.3: Source [38]. Epidemic on methamphetamine drug use.

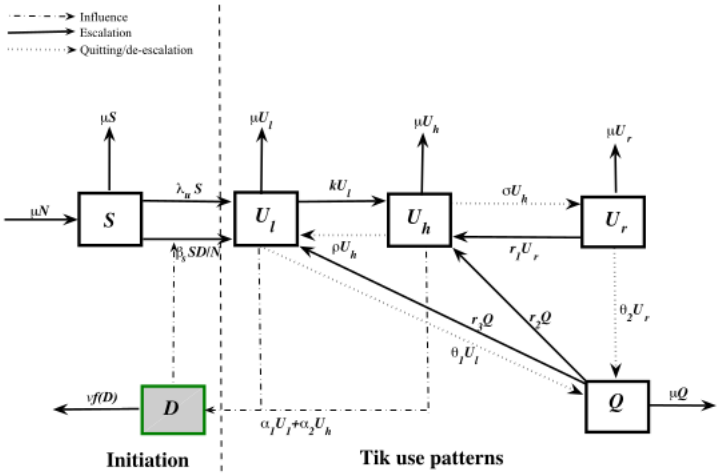


Figure 2.4: Source [39]. A compartmental representation of the epidemic of 'tik' use.

abuse. Their findings indicated that genetic and environmental influences contributes both to illicit drug use and to the clinical diagnosis of illicit drug abuse/ dependence.

Recently Sharma and Samanta [57], developed a mathematical model of alcohol abuse that has four compartments: moderate and occasions drinkers, heavy drinkers, drinkers in treatment and temporarily recovered class. Their aim was to develop

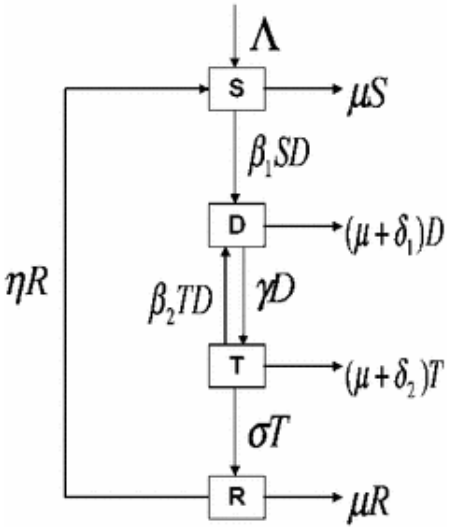


Figure 2.5: Source [57]. Alcohol abuse model.

an alcohol abuse model by introducing a treatment programme in the population considering all possible relapses and the dynamical behaviour of the model was investigated. The numerical findings were illustrated through computer simulations which indicate that the optimal control is efficient to reduce the spread of alcoholism. Figure 2.5 shows the dynamics of the alcohol model.

All models discussed in this chapter help us to understand on modelling the dynamics of substance abuse in general and understand the concept of periodicity in mathematical modelling. Thus in this thesis, we present a mathematical model for substance abuse in dynamic environments in which in- and out-patient rehabilitants are considered with the aim of constructing the periodic function that include variations both forms of rehabilitation. We propose a drug epidemic model in which initiation, addiction, treatment, quitters and relapse are considered. We fit the the model data of individuals seeking treatment services on an in- and outpatient basis in the rehabilitation resulting from drug abuse in different rehabilitation centres within the Western Cape Province as presented by SACENDU reports. Basic properties and model analysis will be established. We now present the details of the model in the next chapter.

Chapter 3

Substance abuse model

3.1 Introduction

Mathematical modelling describes systems using mathematical concepts and language. Mathematical models have been used in many fields such as sciences, engineering, statistics as well as in epidemiology. In this chapter, we formulate and analyse a mathematical model for substance abuse in dynamic environments. The model proposed in [39, 48], will help us in designing a model for substance abuse in dynamic environments driven by community dynamics. The following differentiates our model from the models presented in [39] and [48].

(i) We introduce a compartment that represents the density of drugs in a given community at any time t. We assume that susceptible individuals become drug users jointly as a result of contact with active drug users and through the availability of drugs in the community.

(ii) We allow drug users not in treatment and out-patient individuals to increase the availability of drugs in the community.

(iii) We allow drug users to enter into rehabilitation in a fluctuating manner and this is approximated by the use of a periodic function.

(iv) We also include the removal rate of drugs in the community due to law enforcement, community policy and justice system.

(v) We allow in-patient rehabilitants either quit or become out-patient rehabilitants.

3.2 Model description

We consider a dynamic model of substance abuse with rehabilitation in a fluctuating environment. The population size N at any time t is divided into five compartments: those individuals that are susceptible *i.e* those at risk of using drugs, $S(t)$; drug users $U(t)$; in-patient rehabilitants $R_{in}(t)$; out-patient rehabilitants $R_{out}(t)$ and temporary quitters $Q(t)$. Thus

$$N(t) = S(t) + U(t) + R_{in}(t) + R_{out}(t) + Q(t).$$

The population is assumed to die naturally at a per capita rate μ. We introduce a compartment that represent the amount (density) of drugs in a given community at any time t, denoted by $D(t)$.

Susceptible individuals are recruited at a rate π by means of immigration or birth, and the recruits are assumed susceptible. We assume that susceptible individuals become drug users as a result of their interaction with active drug users at a rate β_1 and through the available drugs in the community at a rate β_2. Thus the force of initiation, λ can be written as a sum of two sub-forces of initiation, so that

$$\lambda = \lambda_U + \lambda_D,$$

where

$$\lambda_U = \frac{\beta_1 (U + \varsigma R_{out})}{N} \quad \text{and } \lambda_D = \frac{\beta_2 D}{K}.$$

λ_U represents the force of initiation associated with person-to-person contact and λ_D represents the force of initiation associated with drugs in the environment-to-person contact. The parameter ς is a relative initiation parameter that measures the ability of individuals in class R_{out} to initiate individuals in class S when compared to individuals in U. It is reasonable to assume that $0 < \varsigma < 1$ due to the assumption that rehabilitation reduces an individual's ability to initiate new users. Assume that the density of drugs in any community has a limiting value and in this case, K is the carrying capacity, i.e. the largest density of drugs a community can tolerate or accommodate.

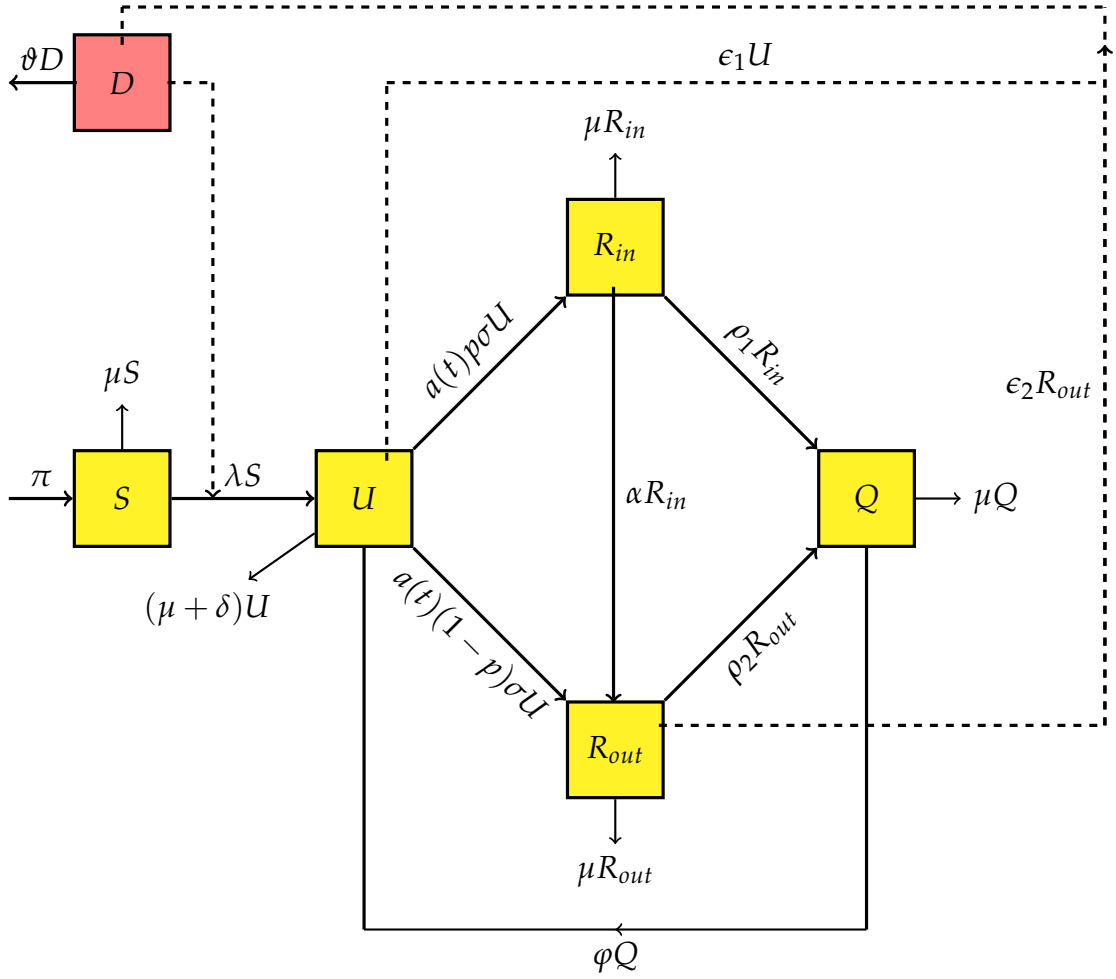


Figure 3.1: A compartmental representation of substance abuse in the presence of rehabilitation.

The population of drug users not in treatment is increased by initiation and relapse. The per capita relapse rate is φ. We assume that quitters in compartment Q, relapse and become drug users again. Drug users not in treatment also die as a result of their use of drugs at a rate δ. The up take of drug users into rehabilitation occurs at a rate σ. The rehabilitation is divided into two: 1) in-patient rehabilitation and 2) out-patient rehabilitation. A proportion p of rehabilitants become in-patient while the remainder $(1-p)$, become out-patient. Individuals in rehabilitation are assumed to quit temporarily. The quitting rates for in-patient and out-patient rehabilitants are

respectively ρ_1 and ρ_2. We assume that the number of out-patient rehabilitants who become in-patient rehabilitants is negligible. Thus only in-patient rehabilitants can become out-patient rehabilitants.

An increase in the density of drugs in a community is fuelled by drug users, since they provide a perpetual market. The availability of drugs in the community, has a profound influence on the initiation of the susceptible population into drug use. The class D decreases as a result of removing drugs in the environment at a rate ϑ often driven by law enforcement, community policing and justice system.

The flow of individuals from one class to another as their status with respect to drug abuse changes is shown in Figure 3.1. Based on the flow diagram, assumptions and the parameter descriptions, the ordinary differential equations that represent the compartmental model are given as

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - (\mu + \lambda)S, \\
\frac{dU}{dt} &= \lambda S + \varphi Q - a(t)\sigma U - a_1 U, \\
\frac{dR_{in}}{dt} &= a(t)p\sigma U - a_2 R_{in}, \\
\frac{dR_{out}}{dt} &= a(t)(1-p)\sigma U + \alpha R_{in} - a_3 R_{out}, \\
\frac{dQ}{dt} &= \rho_1 R_{in} + \rho_2 R_{out} - a_4 Q, \\
\frac{dD}{dt} &= \epsilon_1 U + \epsilon_2 R_{out} - \vartheta D,
\end{aligned}\right\} \tag{3.2.1}$$

where

$a(t) = \overline{a}\left[1 + \widehat{a}\sin\left(\frac{2\pi t}{\omega}\right)\right], a_1 = \mu + \delta, a_2 = \mu + \alpha + \rho_1, a_3 = \mu + \rho_2$ and $a_4 = \mu + \varphi$, with initial conditions $x(0) = \{S_0, U_0, R_{in0}, R_{out0}, Q_0, D_0\}$ such that $S_0 = S(0), U_0 = U(0), R_{in0} = R_{in}(0), R_{out0} = R_{out}(0), Q_0 = Q(0)$ and $D_0 = D(0)$.

Following [34], we assume that the population is constant within modelling time period, so that

$$\pi = \mu N + \delta U. \tag{3.2.2}$$

From system (3.2.1) we obtain

$$\left.\begin{aligned}
\frac{dS}{dt} &= a_1U + \mu(R_{in} + R_{out} + Q) - \lambda S,\\
\frac{dU}{dt} &= \lambda S + \varphi Q - a(t)\sigma U - a_1U,\\
\frac{dR_{in}}{dt} &= a(t)p\sigma U - a_2R_{in},\\
\frac{dR_{out}}{dt} &= a(t)(1-p)\sigma U + \alpha R_{in} - a_3R_{out},\\
\frac{dQ}{dt} &= \rho_1R_{in} + \rho_2R_{out} - a_4Q,\\
\frac{dD}{dt} &= \epsilon_1U + \epsilon_2R_{out} - \vartheta D.
\end{aligned}\right\} \tag{3.2.3}$$

Since the total population, $N = S + U + R_{in} + R_{out} + Q$ is constant, we non-dimensionalize the system by setting

$s = \frac{S}{N}, v = \frac{U}{N}, r_{in} = \frac{R_{in}}{N}, r_{out} = \frac{R_{out}}{N}, q = \frac{Q}{N}, w = \frac{D}{K}$, with $s + v + r_{in} + r_{out} + q = 1$.

Thus, non-dimensionalized system is given by

$$\left.\begin{aligned}
\frac{ds}{dt} &= a_1v + \mu r_{in} + \mu r_{out} + \mu q - \widehat{\lambda}s,\\
\frac{dv}{dt} &= \widehat{\lambda}s + \varphi q - a(t)\sigma v - a_1v,\\
\frac{dr_{in}}{dt} &= a(t)p\sigma v - a_2r_{in},\\
\frac{dr_{out}}{dt} &= a(t)(1-p)\sigma v + \alpha r_{in} - a_3r_{out},\\
\frac{dq}{dt} &= \rho_1r_{in} + \rho_2r_{out} - a_4q,\\
\frac{dw}{dt} &= \widehat{\epsilon_1}v + \widehat{\epsilon_2}r_{out} - \vartheta w,
\end{aligned}\right\} \tag{3.2.4}$$

where $\widehat{\epsilon_1} = \frac{\epsilon_1}{K}, \widehat{\epsilon_2} = \frac{\epsilon_2}{K}$ and $\widehat{\lambda} = \beta_1(v + \varsigma r_{out}) + \beta_2 w$.

In our model, we consider the epidemiological parameters to be constant. The parameters and their description is given in Table 3.1.

Parameter	Description
π	Rate at which new comers are at risk of being initiated into drug abuse.
μ	Natural death rate.
δ	Death rate due to drugs.
σ	Rate at which drug users become in-patients or out-patients in the rehabilitation.
ρ_1, ρ_2	Rates at which those under rehabilitation quit from drugs.
ϕ	Rate at which quitters relapse and become drug users again.
β_1	Effective contact rate from person to person.
β_2	Effective contact rate due to drugs in the environment.
ς	Relative initiation parameter.
p	Proportion of drug users being an in-patient.
α	Rate at which in-patient individuals become out-patients.
$\overline{a}$	Average time for rate of drug users in rehabilitation, $a(t)$.
$\widehat{a}$	Amplitude of the seasonal oscillation in $a(t)$.
ϑ	Removal rate of drugs in the environment due to law enforcement, community policing and justice system.
ϵ_1	Escalation rate of drugs as a result of drug users not in treatment.
ϵ_2	Escalation rate of drugs as a result of out-patient rehabilitants.
ω	Frequency of the oscillations.

Table 3.1: Description of parameters used in the model.

Since $q = 1 - s - v - r_{in} - r_{out}$, we consider a reduced system of s, v, r_{in} and r_{out}, such that

$$\left.\begin{aligned}
\frac{ds}{dt} &= a_1 v + \mu(1 - s - v) - \widehat{\lambda} s, \\
\frac{dv}{dt} &= \widehat{\lambda} s + \varphi(1 - s - v - r_{in} - r_{out}) - a(t)\sigma v - a_1 v, \\
\frac{dr_{in}}{dt} &= a(t) p \sigma v - a_2 r_{in}, \\
\frac{dr_{out}}{dt} &= a(t)(1 - p)\sigma v + \alpha r_{in} - a_3 r_{out}, \\
\frac{dw}{dt} &= \widehat{\epsilon_1} v + \widehat{\epsilon_2} r_{out} - \vartheta w.
\end{aligned}\right\} \tag{3.2.5}$$

Since the available data of in- and out-patient individuals from rehabilitation show a periodic behaviour and medical aid can drive rehabilitation by means of individuals that seek rehabilitation at the beginning of the year have to wait for the following year to enter rehabilitation again using medical aid, thus we introduce a periodic function that describe how drug users enter rehabilitation facilities through medical aid, such that seasonal oscillations of the rate of drug users to rehabilitation, $a(t)$ is a periodic function of time with a common period, ω =365 days such that,

$$a(t) = \overline{a}\left[1 + \widehat{a}\sin\left(\frac{2\pi t}{\omega}\right)\right]. \tag{3.2.6}$$

$\overline{a}$ is the time average of the rate of drug users in the rehabilitation $a(t)$ who uses medical aid. $\widehat{a}$ is the amplitude of the seasonal oscillations in $a(t)$. To ensure that $a(t)$ is positive, we require that $0 < \widehat{a} < 1$.

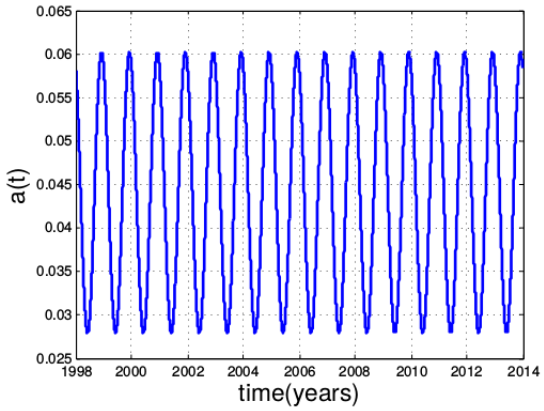


Figure 3.2: Rate of drug users in the rehabilitation treatment centres over 16 years.

Figure 3.2 represents the rate at which seasonal oscillations are exposed to drug users individuals in the rehabilitation.

3.3 Basic properties of the model

3.3.1 Feasible region

The system (3.2.4) is analysed in the region Ω of biological interest. Since the model monitors changes in the human population, then the variables and the parameters must be positive for all $t \geq 0$.

Theorem 3.3.1. *The feasible region Ω defined by*

$$\Omega = \{x \geq 0 : s + v + r_{in} + r_{out} + q = 1\} \tag{3.3.1}$$

is bounded, positively invariant and attracting with respect to system (3.2.4) for all $t > 0$.

$x = (s, v, r_{in}, r_{out}, q, w)$ is a vector space which represents the state space of the system (3.2.4). The solutions of the system (3.2.4) starting from any point in Ω remains Ω.

3.3.2 Positivity of solutions of the model

Since initial conditions are positive, we show that solutions of $x = (s, v, r_{in}, r_{out}, q, w)$ remain positive for all $t > 0$ in Ω.

Theorem 3.3.2. *Let the initial conditions be $(s(0), v(0), r_{in}(0), r_{out}(0), q(0), w(0)) > 0$, then the solutions $x(t)$ are positive for all $t > 0$.*

Proof :

Lets consider the first equation in system (3.2.5),

$$\frac{ds}{dt} = a_1 v + \mu(1 - s - v) - \widehat{\lambda} s \geq -(\mu + \widehat{\lambda})s$$

we obtain the solution

$$s(t) \geq s_0 e^{-\left(\mu t + \int_0^t \widehat{\lambda}(\tau) d\tau\right)} > 0.$$

Since the exponential function is positive always and $s(0) > 0$, then we are guaranteed that the solution of $s(t)$ remains positive for all $t > 0$.

Then, from the second equation of the system (3.2.5),

$$\frac{dv}{dt} = \widehat{\lambda}s + \varphi(1 - s - r_{in} - r_{out}) - (\varphi + a(t)\sigma + a_1)v \geq -(\varphi + a(t)\sigma + a_1)v,$$

$$v(t) \geq v_0 e^{-(\varphi t + a_1 t + \int_0^t \sigma a(\tau) d\tau)} > 0.$$

From the third equation of the system (3.2.5),

$$\frac{dr_{in}}{dt} = a(t)p\sigma v - a_2 r_{in} \geq -a_2 r_{in},$$

$$r_{in}(t) \geq r_i e^{-a_2 t} > 0.$$

Thus, this can be easily shown that r_{out}, q and $w > 0$ for all $t > 0$.

3.4 Model analysis

In this section, we analyse the model by deriving steady states of the model and investigate their stability.

3.4.1 Steady states

At equilibrium, we equate our systems of equations in system (3.2.5) to zero,

$$0 = a_1 v + \mu(1 - s - v) - \widehat{\lambda}s, \tag{3.4.1}$$

$$0 = \widehat{\lambda}s + \varphi(1 - s - v - r_{in} - r_{out}) - a(t)\sigma v - a_1 v, \tag{3.4.2}$$

$$0 = a(t)p\sigma v - a_2 r_{in}, \tag{3.4.3}$$

$$0 = a(t)(1 - p)\sigma v + \alpha r_{in} - a_3 r_{out}, \tag{3.4.4}$$

$$0 = \widehat{\epsilon_1} v + \widehat{\epsilon_2} r_{out} - \vartheta w. \tag{3.4.5}$$

Express r_{in}^* in terms of v^* from (3.4.3),

$$r_{in}^* = \Psi_1 v^*, \quad \text{where} \quad \Psi_1 = \frac{a(t)p\sigma}{a_2}. \tag{3.4.6}$$

Substitute (3.4.6) into (3.4.4) and express r_{out}^* in terms of v^*,

$$r_{out}^* = \Psi_2 v^*, \quad \text{where} \quad \Psi_2 = \frac{a(t)(1 - p)\sigma + \alpha\Psi_1}{a_3}. \tag{3.4.7}$$

Substitute (3.4.7) into (3.4.5) and get,

$$w^* = \Psi_3 v^*, \quad \text{where} \quad \Psi_3 = \frac{\widehat{\epsilon_1} + \widehat{\epsilon_2}\Psi_2}{\vartheta}. \tag{3.4.8}$$

The force of infection at equilibrium, $\widehat{\lambda}^*$ is given by

$$\widehat{\lambda}^* = \xi_0 v^*, \quad \text{where} \quad \xi_0 = \beta_1(1 + \varsigma\Psi_2) + \beta_2\Psi_3. \tag{3.4.9}$$

Solving equations (3.4.1) and (3.4.2) simultaneous, we obtain

$$(s^*, v^*) = (1, 0) \tag{3.4.10}$$

and

$$(s^*, v^*) = \left(\frac{1}{R_0}, K(R_0 - 1)\right), \tag{3.4.11}$$

and v^* exists when $R_0 > 1$, so that $v^* > 0$,

where

$$R_0(t) = \frac{a_4(\beta_1(1 + \varsigma\Psi_2) + \beta_2\Psi_3)}{a(t)\mu\sigma + a_1a_4 + \mu\varphi(\Psi_1 + \Psi_2)}$$

and

$$K(t) = \frac{a(t)\mu\sigma + a_1a_4 + \mu\varphi(\Psi_1 + \Psi_2)}{\mu + a(t)\sigma + \varphi + \varphi(\Psi_1 + \Psi_2)(\beta_1(1 + \varsigma\Psi_2) + \beta_2\Psi_3)}.$$

From (3.4.10), if $v^* = 0$, then

$$r^*_{in} = r^*_{out} = w = 0.$$

Thus, we have a drug free equilibrium

$$DF = (s^*, v^*, r^*_{in}, r^*_{out}, w^*) = (1, 0, 0, 0, 0)$$

which represent a situation where no drugs in the population exist over time (the whole population is susceptible to drugs).

From (3.4.11), since we know v^*, then it is easily to show that

$$DPE = (s^*, v^*, r^*_{in}, r^*_{out}, w^*)$$

is the drug persistent steady state, where

$$\begin{aligned} s^* &= \frac{1}{R_0}, \\ r_{in}^* &= \Psi_1 K(R_0 - 1), \\ r_{out}^* &= \Psi_2 K(R_0 - 1) \quad \text{and} \\ w^* &= \Psi_3 K(R_0 - 1). \end{aligned}$$

If $R_0 = 1$, then DPE collapses to DFE. We thus have the following theorem on the existence of the endemic equilibrium.

Theorem 3.4.1. *The model* (3.2.5) *has a unique drug persistent equilibrium,DPE if* $R_0 > 1$.

3.5 Basic reproduction numbers, $[R_0]$ and R_0

In epidemiological models, the basic reproduction number $[R_0]$ is the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual [12]. In this case we evaluate $[R_0]$ to measure the average number of new substance abusers that are generated by a single case of a drug using individual in a susceptible population. If $[R_0] < 1$, then on average the drug using individual produces less than one user over the course of his/her ability to initiate, and the drug will vanish. Otherwise, if $[R_0] > 1$, a drug user produces more than one drug user. We use the next generation matrix method [12, 70] to derive the basic reproduction number $[R_0]$ of the model.

In periodic models [48], $[R_0]$ is defined as a spectral radius of the time-averaged reproduction number using the next generation matrix method $[F][V]^{-1}$ given by

$$[R_0] = \rho([F][V]^{-1}). \tag{3.5.1}$$

In the absence of periodicity we have

$$[F] = \begin{pmatrix} \beta_1 & 0 & \beta_1\varsigma & \beta_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$[V] = \begin{pmatrix} \varphi + \bar{a}\sigma + a_1 & \varphi & \varphi & 0 \\ -\bar{a}p\sigma & a_2 & 0 & 0 \\ -\bar{a}(1-p)\sigma & -\alpha & a_3 & 0 \\ -\widehat{\epsilon_1} & 0 & -\widehat{\epsilon_2} & \vartheta \end{pmatrix}.$$

$[F]$ is the fertility matrix that represents the rate of appearance of new infections and $[V]$ is the transition matrix that represents the rate of transfer of individuals. We have 4×4 in both matrices, since there are four drug state vectors $X^d = (v, r_{in}, r_{out}, w)$ in the model. Thus

$$[R_0] = \rho([F][V]^{-1}) = R_U + R_D. \tag{3.5.2}$$

$$R_U = \frac{\beta_1(1 + \varsigma((1-p)\sigma a_2 + \alpha p\sigma))}{a_1 a_2 a_3(1 + \Phi_0)}$$

represents the average number of new drug users who may be generated by a single drug user from a susceptible population and

$$R_D = \frac{\beta_2 \bar{a}(a_2 a_3 + ((1-p)\sigma a_2 + \alpha p\sigma))}{a_1 a_2 a_3(1 + \Phi_0)}$$

measure the average number of new users who may be initiated into drug use by the influence of drugs in the environment, where

$$\Phi_0 = \frac{\mu}{a_4}\left[\frac{\bar{a}\sigma}{a_1} + \frac{\varphi}{a_1 a_2 a_3}\left(p\sigma a_2 + ((1-p)\sigma a_2 + \alpha p\sigma)\right)\right].$$

Following [70], we have the following results on the local stability of DF.

Theorem 3.5.1. *The drug-free equilibrium DF is locally asymptotically stable if $[R_0] < 1$ and unstable if $[R_0] > 1$.*

In the presence of periodicity, the basic reproduction number R_0 is defined as the spectral radius of an integral operator, see for instance [2]. We thus ave

$$F(t) = \begin{pmatrix} \beta_1 & 0 & \beta_1\varsigma & \beta_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V(t) = \begin{pmatrix} \varphi + a(t)\sigma + a_1 & \varphi & \varphi & 0 \\ -a(t)p\sigma & a_2 & 0 & 0 \\ -a(t)(1-p)\sigma & -\alpha & a_3 & 0 \\ -\widehat{\epsilon_1} & 0 & -\widehat{\epsilon_2} & \vartheta \end{pmatrix}.$$

Following [27], let $\Phi_V(t)$ and $\rho(\Phi_V(\omega))$ be the inverse of a fundamental (monodromy) matrix of the linear ω-periodic system $dz/dt = V(t)z$ and the spectral radius of $\Phi_V(\omega)$. Assume that $Y(t,s)$ is the evolution operator of the linear ω-periodic system

$$\frac{dy}{dt} = -V(t)y, t \geq s. \tag{3.5.3}$$

That is for each $s \in \mathbb{R}$, the 4×4 matrix $Y(t,s)$ satisfies

$$\frac{dY(t,s)}{dt} = -V(t)Y(t,s), \quad \text{for all } t \geq s, Y(s,s) = I,$$

where I is the 4×4 identity matrix and the monodromy matrix $\Phi_{-V}(t)$ of (3.5.3) is equal to $Y(t,0), t \geq 0$. We assume that $F(s)\phi(s)$ is the rate of new drug users produced by drug users individuals who were introduced at time s. Since $t \geq s$, $Y(t,s)F(s)\phi(s)$ gives the distribution of new drug users who were infected at time s and remain in drug users compartment at time t. Thus

$$\psi(t) := \int_{-\infty}^{t} Y(t,s)F(s)\phi(s)ds = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da$$

is the distribution of accumulative new drug users at time t produced by all drug users $\phi(s)$ that were introduced at time previous to t.

Based on [48, 71], R_0 is defined as the the spectral radius of an integral operator. They introduced the next infection operator given by L

$$(L\phi)(t) = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da, \quad \text{where} \tag{3.5.4}$$

$\phi(s)$ is the initial distribution of infectious individuals and is ω-periodic and positive. Thus the basic reproduction number is defined as the spectral radius of L,

$$R_0 = \rho(L). \tag{3.5.5}$$

We obtain $a(t) \equiv \bar{a}$, $F(t) \equiv F$ and $V(t) \equiv V$, for all $t \geq 0$. Thus we have

$$R_0 = \frac{\beta_1(1+\varsigma((1-p)\sigma a_2 + \alpha p\sigma)) + \beta_2 a(t)(a_2a_3 + ((1-p)\sigma a_2 + \alpha p\sigma))}{a_1a_2a_3(1+\Phi_0)}, \quad (3.5.6)$$

where

$$\Phi_0 = \frac{\mu}{a_4}\left[\frac{\bar{a}\sigma}{a_1} + \frac{\varphi}{a_1a_2a_3}(p\sigma a_2 + ((1-p)\sigma a_2 + \alpha p\sigma))\right].$$

The basic reproduction number defined in equation (3.5.5) can be numerically solved by using the method presented in [63] and then we obtain the following result regarding the local stability of DF :

Theorem 3.5.2. *Let R_0 be defined as (3.5.5). Then the drug-free equilibrium of the system (3.2.5) is locally asymptotically stable if $R_0 < 1$, and unstable if $R_0 > 1$.*

We have do numerical simulations on the computed basic reproduction number and the average basic reproduction number R_0 and $[R_0]$ for various values of $a(t)$. In Figure 3.3a and 3.3b , we vary $\bar{a}$ and $\widehat{a}$, respectively, keeping other parameter values fixed: $\pi = 0.1891, \beta_1 = 0.0497, \mu = 0.02, \rho_1 = 0.1976, \rho_2 = 1.0, \delta = 1 \times 10^{-8}, \sigma = 0.0203, \varsigma = 0.5768, p = 0.2360, \varphi = 0.5005, \alpha = 1.2, \beta_2 = 0.03, \widehat{\epsilon_1} = 0.0083, \widehat{\epsilon_2} = 3.028 \times 10^{-10}$ and $\vartheta = 0.0268$. In Figure 3.3a, $R_0 = 1$ when $\bar{a} \approx 1.5648$ and $[R_0] = 1$ when $\bar{a} \approx 1.8887$, $\widehat{a}$ is set to be 0.662. We can see that the basic reproduction number R_0 is always greater than the average basic reproduction number $[R_0]$ when $\bar{a}$ varies from 0.4 to 2.0. This shows that if R_0 is used then risk of being involved in drug abuse will be overestimated.

On the other hand, Figure 3.3b shows that $R_0 = 1$ when $\widehat{a} \approx 0.0928$ and $[R_0] \approx 0.9938$ for all $\widehat{a}$, thus this illustrate inaccuracy on using $[R_0]$ for drug abuse prediction. The value of $\bar{a}$ is set to be 4.5 in this case.

(a) (b)

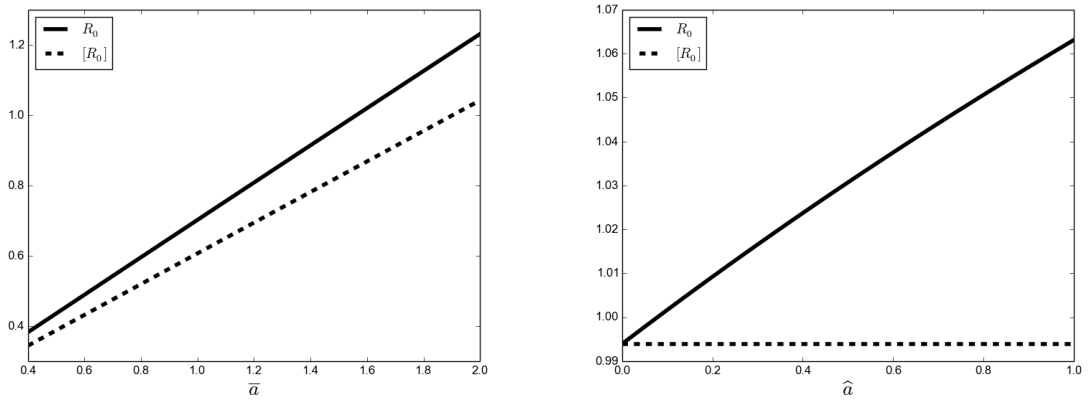


Figure 3.3: Plots of the periodic threshold of R_0 for various $\overline{a}$ and $\widehat{a}$. In (a) this shows $R_0 = 1$ when $\overline{a} \approx 1.5648$, and $[R_0] = 1$ when $\overline{a} \approx 1.8887$; in (b) $R_0 = 1$ when $\widehat{a} \approx 0.0928$ and $[R_0] \approx 0.9938$ for all $\widehat{a}$. We vary $\overline{a}$ and $\widehat{a}$, respectively, keeping other parameter values fixed: $\pi = 0.1891, \beta_1 = 0.0497, \mu = 0.02, \rho_1 = 0.1976, \rho_2 = 1.0, \delta = 1 \times 10^{-8}, \sigma = 0.0203, \varsigma = 0.5768, p = 0.2360, \varphi = 0.5005, \alpha = 1.2, \beta_2 = 0.03, \widehat{\epsilon_1} = 0.0083, \widehat{\epsilon_2} = 3.028 \times 10^{-10}$ and $\vartheta = 0.0268$.

3.6 Drug abuse extinction

We investigate the global stability of DFE for our model. We consider the following matrix function $F(t) - V(t)$:

$$F(t) - V(t) = \begin{pmatrix} \beta_1 - (\varphi + a(t)\sigma + a_1) & -\varphi & \beta_1\varsigma - \varphi & \beta_2 \\ a(t)p\sigma & -a_2 & 0 & 0 \\ a(t)(1-p)\sigma & \alpha & -a_3 & 0 \\ \widehat{\epsilon_1} & 0 & \widehat{\epsilon_2} & -\vartheta \end{pmatrix}, \tag{3.6.1}$$

where the matrix function is ω-periodic.

We let $\Phi_{(F-V)(\cdot)}(t)$ be the solution of fundamental matrix of the system of ordinary differential equation:

$$x' = \Big(F(t) - V(t)\Big)\, x, \tag{3.6.2}$$

and $\rho(\Phi_{(F-V)(\cdot)}(\omega))$ is the spectral radius of the fundamental matrix, $\Phi_{(F-V)(\cdot)}(t)$. Then we have the following results [48]:

Theorem 3.6.1. *Let* $\nu = (1/\omega)\ln\rho(\Phi_{(F-V)(\cdot)}(\omega))$. *Then there exists a positive* ω*-periodic function* $y(t)$ *such that* $e^{\nu t}y(t)$ *is a solution to equation* (3.6.2).

Definition 7. *Spectral radius: Let* A *be an* $n\times n$ *matrix with complex or real elements with eigenvalues* $\lambda_1,\ldots,\lambda_n$ *[65]. Then the spectral radius* $\rho(\Phi_{(F-V)(\cdot)}(\omega))$ *of* A *is*

$$\rho(\Phi_{(F-V)(\cdot)}(\omega)) = \max_{1\leq i\leq n}|\lambda_i|.$$

Let us consider the equation 2, 3, 4, and 5 in the system (3.2.5) such that

$$\frac{d}{dt}\begin{bmatrix} v \\ r_{in} \\ r_{out} \\ w \end{bmatrix} \leq [F(t)-V(t)]\begin{bmatrix} v \\ r_{in} \\ r_{out} \\ w \end{bmatrix}.$$

Based on Theorem 3.6.1, there exist $y(t)$ such that

$$x(t) = (\hat{v}(t), \hat{r_{in}}(t), \hat{r_{out}}(t), \hat{w}(t)) = e^{\nu t}y(t)$$

is a solution of equation (3.6.2). Thus, $(v(t), r_{in}(t), r_{out}(t), w(t)) \leq (\hat{v}(t), \hat{r_{in}}(t), \hat{r_{out}}(t), \hat{w}(t))$ when t is large.

From [48], Theorem 2.2 state that $R_0 < 1$, if $\rho(\Phi_{(F-V)(\cdot)}(\omega)) < 1$. Thus, $\nu < 0$ such that

$$\lim_{t\to\infty} v(t) = 0, \quad \lim_{t\to\infty} r_{in}(t) = 0, \quad \lim_{t\to\infty} r_{out}(t) = 0 \quad \text{and} \quad \lim_{t\to\infty} w(t) = 0.$$

Since we have a constant population, then the total population $s + v + r_{in} + r_{out} + w = 1$, thus we have

$$\lim_{t\to\infty} s(t) = 1.$$

Finally, we have the following result:

Theorem 3.6.2. *If* $R_0 < 1$, *then the drug-free equilibrium for system* (3.2.5) *is globally asymptotically stable, and and* $\lim_{t\to\infty} x(t) = DFE = (1,0,0,0,0)$ *for any solution* $x(t)$ *of system* (3.2.5).

Thus, above result shows that as long $R_0 < 1$, then drug use will vanish completely in the population. Keeping $R_0 < 1$ would be sufficient to remove drug use in the community, even in a fluctuating environment.

3.7 Simulation results

In this section, we use the rehabilitation data to fit the model into it, carry out estimation of parameters and obtain numerical simulation of model system (3.2.1). The fitting of the model to data is carried out in Matlab programming language using the least squares fitting routine *(lsqcurvefit)* with optimisation and get estimated parameters in Table 3.3. The simulations are carried out using Python programming language using the set of estimated parameters in Table 3.3.

3.7.1 Rehabilitation data

According to 2011 census, Cape Town has 3.74 million inhabitants [28]. The population has grown due to migration from other provinces as well as from outside South Africa. The largest percentage are migrants from Eastern Cape and followed by migrants from other countries [33]. This growth has increased the high rate of unemployment and poverty, especially in the Cape Flats area (low-lying, flat area situated to the south east of the central business district of Cape Town) where there are high rates of crime and drugs in the province and since the process of rehabilitation start with medication then patients cannot afford rehabilitation especially residential rehabilitation known as in-patient.

The rehabilitation cost varies great in South Africa [60] and since it depends on the duration of the program and the facility of choice on which type of drug a patient is addicted. 28 days in the rehabilitation can cost $R10,000 - R150,000$ depending on the type of facility. In 2009, Western Cape government provides treatment service at 24 centres at an increase of 7%. Eight were in-patient centres, while sixteen were out-patient centres. Many of the problems in rehabilitation centres arises due to lack of financial resources, such that this may cause difficulty in regularly continuation of getting medication and afterwards relapse on drug users.

We fit the model (3.2.1) to data in Table 3.2 using the least squares fitting routine

(lsqcurvefit) in Matlab with optimisation. The modelling time is from 1998 to 2013 because the data for both in- and out-patient treatment is available for the given time. The data was collected by the South African Community Epidemiology Network on Drug Use (SACENDU) for drug using individuals who attended the rehabilitation centre in Cape Town. This data is used to predict future projections on the number of individuals who will need rehabilitation. According to the data (both in- and out-patient), the majority of patients are treated on an out-patient basis. The reason could be, in-patient rehabilitation programmes are expensive compared to out-patient and Cape Town residents are faced with high rates of unemployment. The data is given in the table below.

Year	98a	98b	99a	99b	00a	00b	01a	01b	02a	02b	03a
% In-patient	32	59	69	68	66	68	66	65	58	60	63
% Out-patient	64	40	27	32	34	32	34	35	42	40	37
% Both	4*	< 1*	3*	2*	< 1*	< 1*	-	-	< 1*	-	-
Year	03b	04a	04b	05a	05b	06a	06b	07a	07b	08a	08b
% In-patient	64	68	66	61	48	61	57	59	53	64	48
% Out-patient	36	32	34	39	52	39	43	41	47	36	52
Year	09a	09b	10a	10b	11a	11b	12a	12b	13a	13b	
% In-patient	39	42	44	44	34	41	28	37	39	33	
% Out-patient	61	58	56	56	66	59	72	63	61	67	

Table 3.2: Type of treatment received in rehabilitation for the period 1998a to 2013b (%); $a-$represent January$-$June, $b-$represent July$-$December; * indicates those who received treatment on both in- and out-patient basis. Source: [47].

3.7.2 Parameter estimation

The table below shows the estimated parameter values that are used in the fitting of model using the least squares fitting routine in Matlab for both in- and out-patient rehabilitation. Most of the parameter values are obtained from the fitting of the model to in- and out-patient data collected by SACENDU in the Western Cape Province of South Africa [47]. The average life expectancy in South Africa is approximately 62 years [59], thus the natural mortality rate is $\mu \approx 0.02$ per year.

We set the recruitment rate π to be greater than the natural mortality rate so that $(\pi \approx 0.1891 \quad \text{per year})$ hypothetically.

The effective contact rate for person to person contact, β_1, is assumed to be higher than that of drugs to person, β_2. We thus have $\beta_1 = 0.0497$ and $\beta_2 = 0.0003325$. The proportion p of drug users who become in-patient rehabilitants is 23.6%.

Symbol	Range	Value	Source
π	0.028 - 1.000	0.1891	Estimated
δ	0.000 - 0.020	1.43×10^{-8}	Estimated
σ	0.000 - 1.000	0.0203	Estimated
μ	0.019 - 0.021	0.0200	[59]
ρ_1	0.000 - 0.500	0.1976	Estimated
ρ_2	0.000 - 1.000	1.000	Estimated
φ	0.000 - 1.000	1.000×10^{-5}	Estimated
β_1	0.000 - 1.000	0.0497	Estimated
β_2	0.000 - 0.020	3.325×10^{-4}	Estimated
ς	0.000 - 1.000	0.5768	Estimated
p	0.000 - 1.000	0.2360	Estimated
α	0.000 - 1.000	2.498×10^{-6}	Estimated
$\overline{a}$	0.000 - 1.000	0.0441	Estimated
$\widehat{a}$	0.000 - 1.000	0.3662	Estimated
ϑ	0.000 - 1.000	0.0268	Estimated
ϵ_1	0.000 - 1.000	0.0083	Estimated
ϵ_2	0.000 - 1.000	3.028×10^{-10}	Estimated

Table 3.3: Estimated parameters used in the model.

3.7.3 Numerical results

In Figure 3.4, we observe that when $R_0 < 1$, both in- and out-patient rehabilitants decreases quickly to zero and stays there forever and the solution converges to the drug-free equilibrium DF with $r^*_{in} = r^*_{out} = 0$, thus DF is globally asymptotically stable; since similar patterns were observed for various initial conditions. Figure

3.5 illustrates in- and out-patient individuals when $R_0 > 1$. In this case, drugs persists and after long period of time, individuals in rehabilitation approaches a $\omega-$periodic solution.

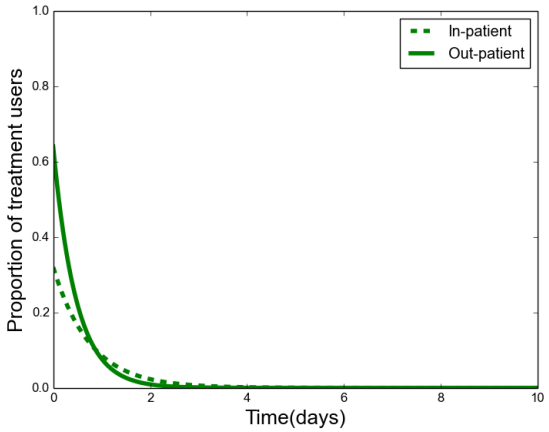


Figure 3.4: A typical curve of in- and out-patient rehabilitation dynamics for model (3.2.3) when $R_0 < 1$, with initial conditions $r_{in}(0) = 0.32$ and $r_{out}(0) = 0.64$. Parameter values: $R_0 = 0.26136, \mu = 0.02, \pi = 0.1891, \delta = 1.43 \times 10^{-8}, \sigma = 0.0203, \rho_1 = 0.1976, \rho_2 = 1.000, \varphi = 1.0 \times 10^{-5}, \beta_1 = 0.0497, \beta_2 = 3.325 \times 10^{-4}, \varsigma = 0.5768, p = 0.2360, \alpha = 2.498 \times 10^{-6}, \overline{a} = 0.0441, \widehat{a} = 0.3662, \vartheta = 0.0268, \epsilon_1 = 0.0083$ and $\epsilon_2 = 3.028 \times 10^{-10}$.

(a) (b)

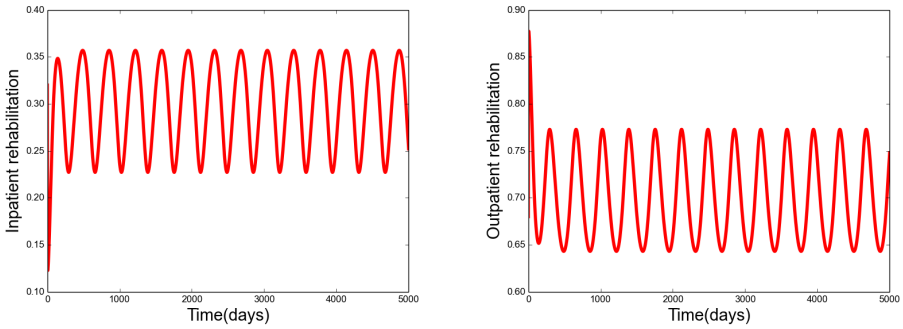


Figure 3.5: A typical curve of in- and out-patient rehabilitation dynamics for model (3.2.3) when $R_0 > 1$, with initial conditions $r_{in}(0) = 0.32$ and $r_{out}(0) = 0.64$. A periodic solution with $\omega = 365$ days forms after a long period. Parameter values: $R_0 = 1.7714, \mu = 0.02, \pi = 0.1410, \delta = 0.1876, \sigma = 0.90, \rho_1 = 0.0639, \rho_2 = 0.993, \varphi = 0.50, \beta_1 = 0.205, \beta_2 = 0.02, \varsigma = 0.999, p = 0.2014, \alpha = 0.50, \overline{a} = 5, \widehat{a} = 0.5, \vartheta = 0.2056, \epsilon_1 = 0.0083$ and $\epsilon_2 = 0.04$.

3.7.4 Model fit to in- and out-patient data

We fit the model (3.2.1) to data in Table 3.2 using the least squares fitting routine *(lsqcurvefit)* in matlab with optimisation. The fitting starts from 1998 to 2013 due to the availability of data for both in- and out-patient treatment users. This data was collected by the South African Community Epidemiology Network on Drug Use (SACENDU) for drug users individuals who attended the rehabilitation centre in Cape Town. This data will be used to predict future projections on rehabilitation.

The data was collected from different specialist treatment centres on a monthly basis from individuals who attended in the monitoring program during that particular time. According to the data (both in- and out-patient), the majority of patients are treated on an out-patient basis. The reason could be, in-patient rehabilitation programmes are expensive compared to out-patient and Cape Town residents face high rate in unemployment.

Curve fitting is the process of constructing a curve or mathematical function that has the best fit to a series of data points [17]. Curve fitting can either be involve interpolation or smoothing. This process can fits equations of approximating curves to the raw field data. Thus, the best fitting curve can be obtained by the method

of least squares. The least squares method is a standard approach in regression analysis the approximate solution of overdetermined systems.

The most important application of least squares fitting is in data fitting, where a best fit minimizes the sum of squared residuals, a residual which is a difference between an observed value and the fitted value provided by a model.

In this research, we are interested in the construction of a smooth curve that gives the best fit from our data points. We are using the least squares method to construct a suitable curve that produce the best model fit to in- and out-patient data.

Figure 3.6a and Figure 3.7a represent the model system (3.2.1) on fitting to data for individuals receiving treatment on an in- and out-patient basis. The data is obtained from [47]. The blue circles represent the actual data and a red solid line represents the fitting model to data. The model fits well in both data points (in- and out-patient) for the given estimated parameter values. It is important to state future projections using the model beyond 2013 as Figure 3.6b and Figure 3.7b demonstrated. Figure 3.6b shows a continued declined and stable in a long run, while Figure 3.7b shows continued increase and stable in a long run.

(a) (b)

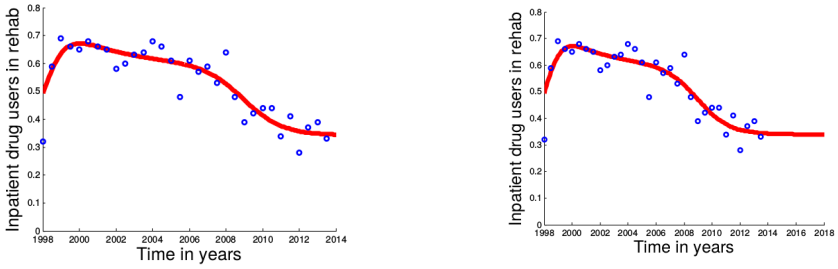
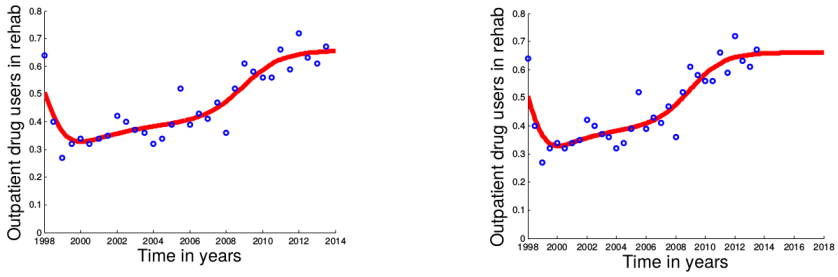


Figure 3.6: Model system (3.2.3) fitted to data for individuals seeking treatment as in-patients in rehabilitation and projected population for 4 years (%).



(a) (b)

Figure 3.7: Model system (3.2.3) fitted to data for individuals seeking treatment as outpatients in rehabilitation and projected population for 4 years (%).

Chapter 4

A model for substance abuse rehabilitation with scaled noise

4.1 Introduction

A stochastic dynamical system is a system that is subjected to the effects of noise and where such fluctuations are classified as noisy or stochastic, when their suspected origin implicates the action of a very large number of variables. Stochastic processes are concerned with approximating this random element [23]. In general, stochastic process is used whenever the infectious individuals is relatively small, which can be when the population size is small, when an infectious disease is invaded, when control measures are applied successfully or during the trough phase of an epidemic cycle.

The form of noise that we are going to introduce directly into deterministic differential equations in Chapter 3 is a scaled noise. As such, the dynamics at each point in time are subject to some random variability and this variability is propagated forward in time by the underlying equations [23]. We want to include the noise term in each term, such that each event is associated with a noise term.

Our model is extended in a more realistic formulation by some changes to the following formulations:

1. In each event type, the noise is included.

2. Following [23], the magnitude of this noise term is a function of the rate of each process. The events are assumed to be Poisson distributed such that the standard deviation of the noise scales with the square-root of the mean.

4.2 The model with scaled noise

In this chapter, we extend the model given in Chapter 3, by incorporating the noise into each event term using stochastic dynamics and the periodic function in this chapter is not included.

The ordinary differential equations in equation (3.2.1) with added scaled noise are given as follows

$$\left.\begin{aligned}
\frac{dS}{dt} &= \left[\pi + \sqrt{\pi}\xi_1\right] - \left[\mu S + \sqrt{\mu S}\xi_2\right] - \left[\lambda S + \sqrt{\lambda S}\xi_3\right], \\
\frac{dU}{dt} &= \left[\lambda S + \sqrt{\lambda S}\xi_3\right] + \left[\varphi Q + \sqrt{\varphi Q}\xi_4\right] - \left[A_1 U + \sqrt{A_1 U}\xi_5\right], \\
\frac{dR_{in}}{dt} &= \left[\bar{a}p\sigma U + \sqrt{\bar{a}p\sigma U}\xi_6\right] - \left[a_2 R_{in} + \sqrt{a_2 R_{in}}\xi_7\right], \\
\frac{dR_{out}}{dt} &= \left[\bar{a}(1-p)\sigma U + \sqrt{\bar{a}(1-p)\sigma U}\xi_8\right] + \left[\alpha R_{in} + \sqrt{\alpha R_{in}}\xi_9\right] - \left[a_3 R_{out} + \sqrt{a_3 R_{out}}\xi_{10}\right], \\
\frac{dQ}{dt} &= \left[\rho_1 R_{in} + \sqrt{\rho_1 R_{in}}\xi_{11}\right] + \left[\rho_2 R_{out} + \sqrt{\rho_2 R_{out}}\xi_{12}\right] - \left[a_4 Q + \sqrt{a_4 Q}\xi_{13}\right], \\
\frac{dD}{dt} &= \left[\epsilon_1 U + \sqrt{\epsilon_1 U}\xi_{14}\right] + \left[\epsilon_2 R_{out} + \sqrt{\epsilon_2 R_{out}}\xi_{15}\right] - \left[\vartheta D + \sqrt{\vartheta D}\xi_{16}\right],
\end{aligned}\right\} \tag{4.2.1}$$

with

$A_1 = a_1 + \bar{a}\sigma, a_1 = \mu + \delta + \sigma, a_2 = \mu + \alpha + \rho_1, a_3 = \mu + \rho_2$ and $a_4 = \mu + \varphi$.
The parameter descriptions are detailed in Table 4.1.

Parameter	Description
ξ_i	A set of sixteen noise terms which are generated as functions of the time step.
π	Rate at which new comers are at risk of being initiated into drug abuse.
μ	Natural death rate.
δ	Death rate due to drugs.
σ	Rate at which drug users become in-patients or out-patients in the rehabilitation.
ρ_1, ρ_2	Rates at which those under rehabilitation quit from drugs.
ϕ	Rate at which quitters relapse and become drug users again.
β_1	Effective contact rate from person to person.
β_2	Effective contact rate due to drugs in the environment.
ς	Relative initiation parameter.
p	Proportion of drug users being an in-patient.
α	Rate at which in-patient individuals become out-patients.
$\overline{a}$	Average time for rate of drug users in rehabilitation, $a(t)$.
ϑ	Removal rate of drugs in the environment due to law enforcement, community policing and justice system.
ϵ_1	The fraction of drug users whose presence contributes to increase the availability of drugs in the environment.
ϵ_2	The fraction of those who receive treatment as out-patients whose presence contributes to increase the availability of drugs in the environment
K	Carrying capacity

Table 4.1: Description of parameters used in the model with scaled noise.

This provides a direct means of determining the magnitude of the noise term, such that $f = \sqrt{\text{rate}}$. In equation (4.2.1), we have sixteen noise terms $(\xi_1, \xi_2, \cdots, \xi_{16})$, one for each event type; but the same noise is used for each event when it appear in more than one equation.

4.3 Sensitivity analysis

According to Saltelli et al. [52], sensitivity analysis is defined as the study of how uncertainty in the output of a system that can be distributed to different sources

of uncertainty in the model output. This analysis is used to determine the effects of such changes in the parameters of a model. The objective of sensitivity analysis is to identify parameters of a model and quantify how input uncertainty impacts outcomes of the model [32].

In this section, we use Latin Hypercube Sampling (LHS) to determine the Partial Rank Correlation Coefficients (PRCCs) with 1000 simulations per run to indicate parameters that have a significant influence in the basic reproduction number $[R_0]$, see equation (3.5.2). We carry out the sensitivity analysis by assessing the PRCC for each parameter value that is discovered by LHS method.

Definition 8. *Latin Hypercube Sampling (LHS) is defined as a statistical method for generating a sample of possible collections of parameter values from a multidimensional distribution [32].*

LHS belongs to the Monte Carlo class of sampling methods, which are popular algorithms in solving different types of computational problems. These methods also include any technique of statistical sampling employed to approximate solutions to quantitative problems and were first introduced by McKay et al. [32]. PRCCs provides a measure of the strength of a linear association between an input and output [30].

4.3.1 Results of our analysis

Figure 4.1 shows the effects of parameter variations on $[R_0]$. This figure shows that the effective contact rate from person to person β_1, in the model have the highest positive influences on $[R_0]$, this means that an increase in the size of β_1 will result an increase in $[R_0]$ ($[R_0] > 1$), thus drug abuse will spread in the community. On the other hand, the rate at which drug users are rehabilitated σ and the rate at which in-patient treatment users quits from drugs ρ_1 have shown the highest negative influences on $[R_0]$. This shows that σ and ρ_1 are important parameters in the fight against substance abuse. This shows that increasing rehabilitation and successful rehabilitation of in-patient rehabilitants will be effective ways to control the epidemic.

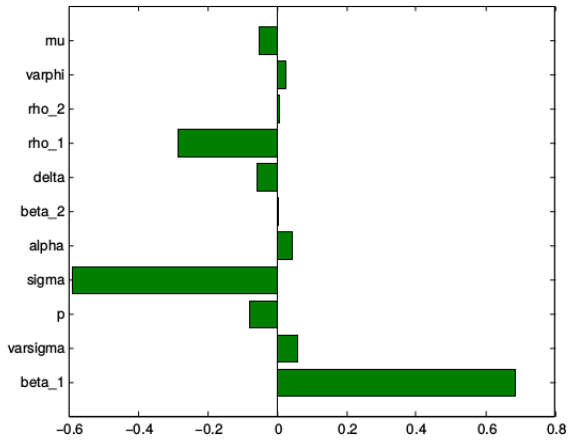
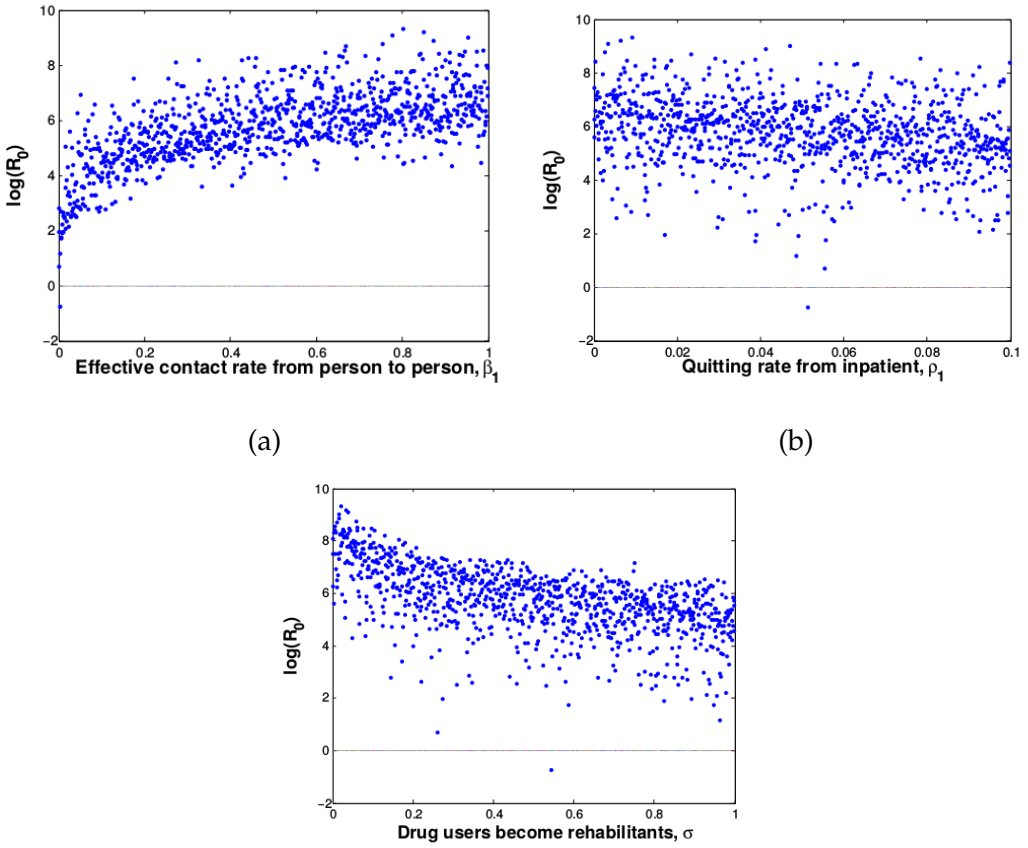


Figure 4.1: PRCCs plot showing the effects of parameters on $[R_0]$.

Increasing β_1 increases $[R_0]$. So a reduction in the in the person to person contact is vital in control of substance abuse. The person to person contact in this case is viewed as contacts that will result in peer influence.

In this case, we conclude that from the sensitivity analysis we have, more awareness should be targeted at reducing the effective contact between susceptible individuals and drug users such that the epidemic can be controlled and by means of improving in-patient rehabilitation programmes, drugs in the community can be controlled.

We further produced scatter plots of Monte Carlo simulations for parameters with the greatest influence towards the reproduction number $[R_0]$ in Figure 4.2. The PRCC scatter plots also show that $[R_0]$ is influenced by the effective contact rate from person to person β_1, whereas the rate at which drug users receive treatment σ and the rate at which in-patient treatment users quits from drugs ρ_1 have shown in reducing the $[R_0]$. Thus control measures should similarly focus on the effective contact rate and improve in-patient rehabilitation facilities.



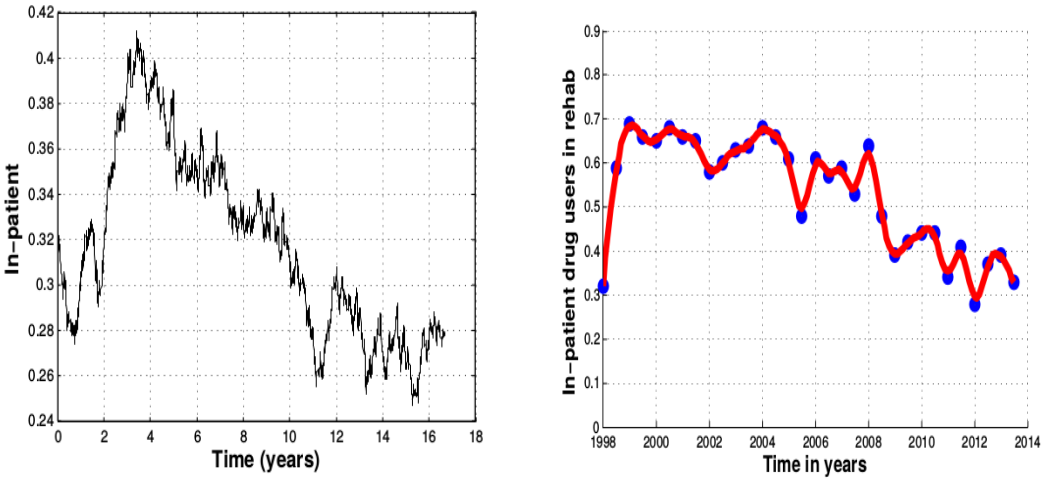
(a) (b)

(c)

Figure 4.2: Monte Carlo simulations for three parameters with the greatest PRCC magnitude in the model system (3.2.1). In Figure 4.2a, β_1 shows that when there is an increase in contact between susceptible individuals and a drug user, $[R_0]$ also increases ($[R_0] > 1$), whereas in Figure 4.2b and Figure 4.2c, shows the highest negative influence towards the $[R_0]$, thus $R_0 < 1$. Parameter values used in Table 3.3 and per run $1,000$ simulations were used.

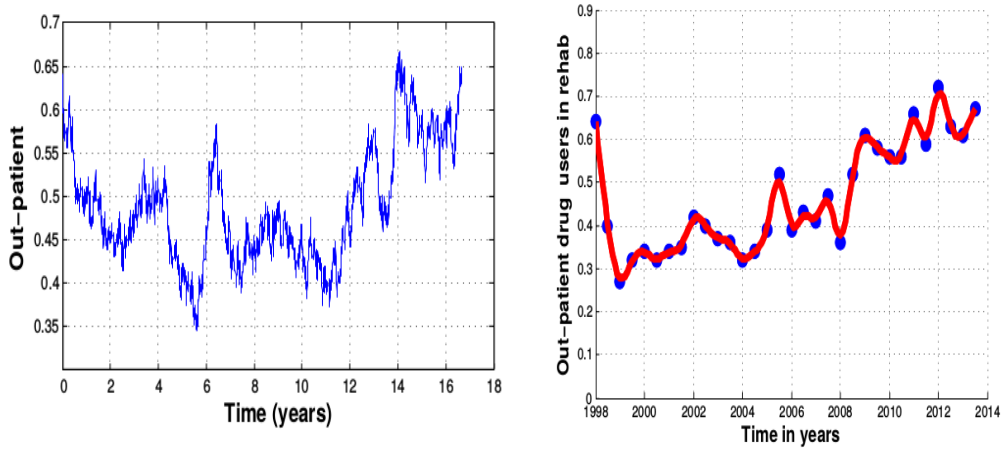
4.4 Numerical simulation

Figure 4.3 and Figure 4.4 compare the time series of in- and out-patient data with stochastic simulation results in rehabilitation classes using the complete stochastic system of the time series. In these figures, we used parameter values that fit the model to data in Table 3.3. Thus, results are comparable.



(a) (b)

Figure 4.3: Comparison of in-patient data with stochastic simulation time series over a period of years. Figure 4.3a is the time series plot using stochastic dynamics of deterministic systems and Figure 4.3b shows the in-patient treatment data that is connectected using spline fit interpolation.



(a) (b)

Figure 4.4: Comparison of out-patient data with stochastic simulation time series over a period of years. Figure 4.4a is the time series plot using stochastic dynamics of deterministic systems and Figure 4.4b shows the out-patient treatment data that is connectected using spline fit interpolation.

Figure 4.5 shows the time series of substance abuse rehabilitants with scaled noise over a period of time using the stochastic dynamic of deterministic systems in equation (4.2.1). Using the estimated parameters that fit the model to data in Table 3.3, we link in- and out-patient data with the stochastic simulation results and this shows that our results are comparable.

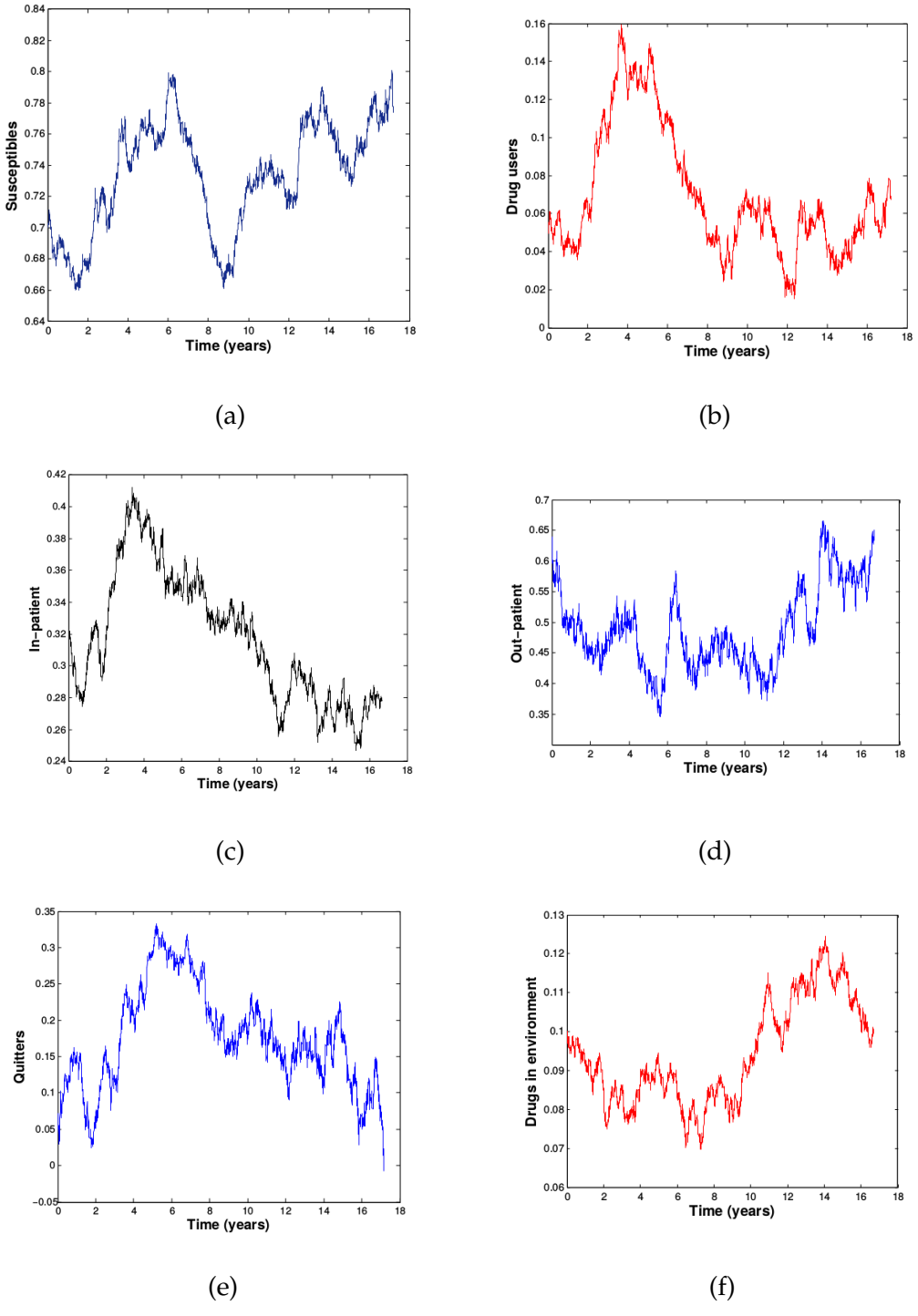


Figure 4.5: The dynamics of substance abuse rehabilitants with a scaled noise (%). Parameter values used in Table 3.3: $\mu = 0.02, \pi = 0.1891, \delta = 1.43 \times 10^{-8}, \sigma = 0.0203, \rho_1 = 0.1976, \rho_2 = 1.000, \varphi = 1 \times 10^{-5}, \beta_1 = 0.0497, \beta_2 = 3.325 \times 10^{-4}, \varsigma = 0.5768, p = 0.2360, \alpha = 2.498 \times 10^{-6}, \bar{a} = 0.0441, \vartheta = 0.0268, \epsilon_1 = 0.0083$ and $\epsilon_2 = 3.028 \times 10^{-10}$.

Chapter 5

Conclusions

In this thesis, we presented a dynamical model of substance abuse with in- and out-patient rehabilitants in a fluctuating environment. We assumed 'seasonal' recruitment into rehabilitation centres due to some defined social dynamics reminiscent of the communities in South Africa. The model was analysed qualitatively by determining the invariant region, positivity of solutions and stability of the steady states. The drug-free equilibrium has shown to be globally asymptotically stable if $[R_0] < 1$ and unstable otherwise, whereas the endemic equilibrium has shown to be asymptotically stable if $[R_0] > 1$.

The average basic reproduction number $[R_0]$ was evaluated. Using the next infection operator introduced in [63], we have derived and computed the basic reproduction number R_0 with periodicity and results shown numerically. Our results established R_0 as a sharp threshold for dynamics of substance abuse in a dynamic environment such that if $R_0 < 1$ drug abuse dies out completely and if $R_0 > 1$ it persists in the population.

Numerical simulations were performed to fit the model to data. Projections on the future of the two forms of rehabilitation were also made. The effects of the periodicity are observed in the fluctuations observed in Figure 3.5. These results have significant implications on the management and planning of rehabilitation programs in South Africa.

In Chapter 4, we modelled substance abuse rehabilitation in the presence of scaled

noise, where dynamics of the model are classified as noisy or stochastic. We extend the model by incorporation the noise term into each event term of the system equations. Simulations were performed to show the dynamics of the model with noise. A comparison is made between the actual data and these simulations. It is important to state that the comparison can not be replicated as each run of the model simulations produces a different result. Lastly, we have shown the sensitivity analysis to identify parameters that influence the basic reproduction number $[R_0]$. We concluded that control measures should focus on the effective contact rate from person to person and improve in-patient rehabilitation programmes.

The model presented here is not without short comings. We model the fluctuations using a sine function. This does not capture the non-uniform fluctuation observed in the data.The model ignores variability and randomness in human behaviour. The model also assumes interactions derived from the modelling of infectious diseases. To correctly model the interactions, the model should have initiation driven by imitation. Despite these shortcomings, the model provides some very useful approach to predicting rehabilitation trends.

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Modelling in- and out-patient rehabilitation for substance abuse in a dynamic environment

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Abstract

Substance abuse is a major problem globally with immeasurable consequences to the health of users. Rehabilitation is the most effective strategy of reversing the effects of substance abuse. The rehabilitations can either be in-patient or out-patient. In this paper, we consider a compartmental model of substance users in the two forms of rehabilitation. A periodic function is used to illustrate fluctuations of drug users entering rehabilitation. The model has two basic reproduction numbers, R_0 and $[R_0]$ where R_0 is the for model with fluctuations and $[R_0]$ for the model without. The model analysis is performed in terms of the two reproduction numbers. The model is fitted to data on the two forms of rehabilitations and projections made. The main results show that the disease goes to extinction if the threshold value R_0 is less than unity, whilst the disease persists if the threshold value is larger than unity. Also, there exists a positive periodic solution when the threshold is above unity.

Key words Substance abuse · rehabilitation · in-patient · out-patient · basic reproduction number.

1 Introduction

Substance abuse, also known as drug abuse, is a patterned use of a drug where a user consumes a substance in amounts or with methods which are harmful to themselves or others [13]. It remains a problem globally with endless health consequences, high rates of suicide, crime and increased government spending. In South Africa for example, substance abuse accounts for most of the criminal offences in the townships [15]. There has been a significant increase in demand for drug abuse rehabilitation in the Western Cape Province of South Africa [27]. The rehabilitation of drug users (often known as drug rehab) is a process of medical treatment, where a patient is assisted to stop the use of drugs and becomes a normal person. In rehabilitation, various types of programs are offered to help drug users to stop using drugs. This can

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be done at a rehabilitation centre with the patient staying in the centre for the duration of the treatment process (in-patient treatment) and can also be done when an individual visits the treatment centre on a daily basis (out-patient treatment).

In-patient treatment, also known as residential treatment, refers to be part of a hospital program or found in special clinics, where a patient stays at the facility and gets therapy daily. Out-patient treatment happens in mental health clinics, counsellors offices, hospital clinics, or local health department offices, where a patient does not require to stay overnight. The rehabilitation cost varies great in South Africa [22] and since it depends on the duration of the program and the facility of choice on which type of drug a patient is addicted. 28 days in the rehabilitation can cost $R10,000 - R150,000$ depending on the type of facility. In-patient treatment cost more than out-patient treatment in rehabilitation centres.

Many researchers have studied the dynamics of substance abuse using mathematical models, see for instance [2, 6, 12, 14, 20, 23, 29]. In these models, systems of differential equations were formulated and analysed. The formulated models were built on modelling principles applied to infectious diseases. Some of the models, see for instance [14], were fitted to data that is collected every six months in South Africa, by the South African Community Epidemiology Network on Drug Use (SACENDU) [16], as a treatment monitoring system. The data shows some fluctuating behaviour. Below we present the data from SACENDU on in-patient and out-patient rehabilitants in the Western Cape. The data is connected using spline fitting interpolation. We argue here that variability of the data trends is certainly driven by commu-

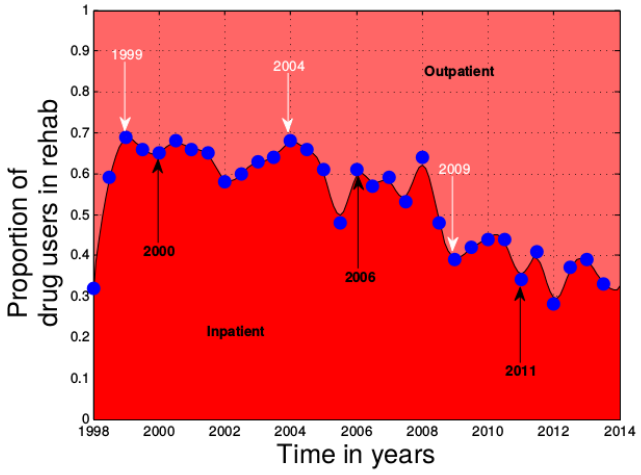

Figure 1: Source [16]. Spline fitting interpolation for in- and out-patient treatment users. Dark red area shows the proportion of in-patient in rehabilitation and light red area shows the proportion of out-patient in the rehabilitation. The white arrows indicate the years of parliamentary elections of South Africa which are held every five years and black arrows indicate the municipal elections of South Africans to elect new councils for all municipalities in the country, as potential causes of data variability.

nity and social dynamics. The drivers of the fluctuations could be financial, social or political. We postulate the following:

(i) Medical aid driven rehabilitation: Rehabilitation supported by medical aid schemes often covers alcohol, substance and drug rehabilitation for a maximum of 21 days per year [7]. On the other hand, complete recovery often requires at least four weeks [30]. This means that individuals that seek rehabilitation at the beginning of the year may have to wait for the following year to enter into rehab again using medical aid as a result of incomplete treatment protocols.

(ii) Political dynamics: The demand for basic services including rehabilitation of addicts often increase prior to elections in South Africa. This is accompanied by service delivery protests, which decrease after the elections [31]. We indicated on the figure above the times when national and provincial elections were held [4, 19] and a correlation is clearly observed, where white arrows indicate the years of parliamentary elections of South Africa which were held every five years and black arrows indicate the municipal elections of South Africans to elect new councillors for all municipalities in the country. In every election year there is a peak in either in-patient or out-patient rehabilitation as potential election candidates try to impress the electorate.

In this paper, we present a compartmental model for substance abuse in a dynamic environment. We assume that drug users not in treatment and users in out-patient treatment play a role in drug initiation. Supply of drugs in communities also fuels initiation into drug use that eventually results in drug abuse. We assume that drug users not in treatment have higher influence on the susceptible population than drug users on out-patient treatment. The objective of this paper is to model the dynamics of substance abuse in a dynamic environment with fluctuations. In particular, we construct a periodic function and link it with the fluctuations in the data. While the data does not show a clear periodic pattern, we can best approximate the oscillations through a periodic function. Using the approach in [26], we determine the basic reproduction number for the model with and without periodicity, i.e $[R_0]$ and R_0 respectively. When $R_0 < 1$, then the drug-free equilibrium is globally asymptotically stable and drug abuse dies out in the population. When $R_0 > 1$, then the system admits a positive periodic solution and drugs in the population persist. We discuss the extinction of drug abuse in the population, using the method described in [17]. The model is the fitted to data.

This paper is arranged as follows; in Section 2, we present the model formulation and description, in Section 3 we analyse the model, followed by drug abuse extinction in Section 4, followed by numerical results in Section 5, followed by discussion and conclusion in Section 6.

2 Model Formulation

We consider a dynamic model of substance abuse with rehabilitation in a fluctuating environment. The population size N at any time t is divided into five compartments: those individuals that are susceptible *i.e* those at risk of using drugs, $S(t)$; drug users $U(t)$; in-patient rehabilitants $R_{in}(t)$; out-patient rehabilitants $R_{out}(t)$ and temporary quitters $Q(t)$. Thus

$$N(t) = S(t) + U(t) + R_{in}(t) + R_{out}(t) + Q(t).$$

The population is assumed to die naturally at a per capita rate μ. We introduce a compartment that represent the amount (density) of drugs in a given community at any time t, denoted by $D(t)$.

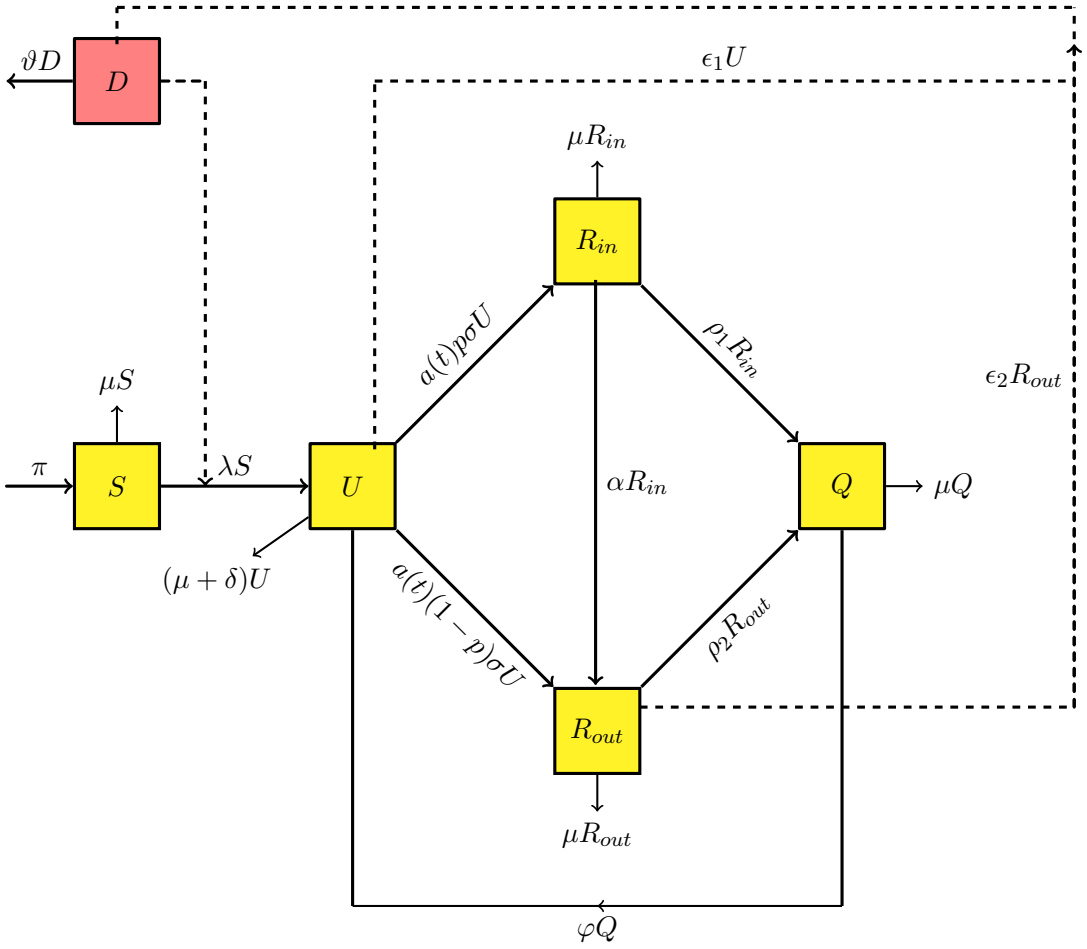

Figure 2: A compartmental representation of substance abuse in the presence of rehabilitation.

Susceptible individuals are recruited at a rate π by means of immigration or birth, and the recruits are assumed susceptible. We assume that susceptible individuals become drug users as a result of their interaction with active drug users at a rate β_1 and through the available drugs in the community at a rate β_2. Thus the force of initiation, λ can be written as a sum of two sub-forces of initiation, so that

$$\lambda = \lambda_U + \lambda_D,$$

where

$$\lambda_U = \frac{\beta_1 \left(U + \varsigma R_{out}\right)}{N} \quad \text{and } \lambda_D = \frac{\beta_2 D}{K}.$$

λ_U represents the force of initiation associated with person-to-person contact and λ_D represents the force of initiation associated with drugs in the environment-to-person contact. The

parameter ς is a relative initiation parameter that measures the ability of individuals in class R_{out} to initiate individuals in class S when compared to individuals in U. It is reasonable to assume that $0 < \varsigma < 1$ due to the assumption that rehabilitation reduces an individual's ability to initiate new users. Assume that the density of drugs in any community has a limiting value and in this case, K is the carrying capacity, i.e the largest density of drugs a community can tolerate or accommodate.

The population of drug users not in treatment is increased by initiation and relapse. The per capita relapse rate is φ. We assume that quitters in compartment Q, relapse and become drug users again. Drug users not in treatment also die as a result of their use of drugs at a rate δ. The up take of drug users into rehabilitation occurs at a rate σ. The rehabilitation is divided into two: 1) in-patient rehabilitation and 2) out-patient rehabilitation. A proportion p of rehabilitants become in-patient while the remainder $(1-p)$, become out-patient. Individuals in rehabilitation are assumed to quit temporarily. The quitting rates for in-patient and out-patient rehabilitants are respectively ρ_1 and ρ_2. We assume that the number of out-patient rehabilitants who become in-patient rehabilitants is negligible. Thus only in-patient rehabilitants can become out-patient rehabilitants.

An increase in the density of drugs in a community is fuelled by drug users, since they provide a perpetual market. The availability of drugs in the community, has a profound influence on the initiation of the susceptible population into drug use. The class D decreases as a result of removing drugs in the environment at a rate ϑ often driven by law enforcement, community policing and justice system.

The flow of individuals from one class to another as their status with respect to drug abuse changes is shown in Figure 2. Based on the flow diagram, assumptions and the parameter descriptions, the ordinary differential equations that represent the compartmental model are given as

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - (\mu + \lambda)S, \\
\frac{dU}{dt} &= \lambda S + \varphi Q - a(t)a_1 U - a_1 U, \\
\frac{dR_{in}}{dt} &= a(t)p\sigma U - a_2 R_{in}, \\
\frac{dR_{out}}{dt} &= a(t)(1-p)\sigma U + \alpha R_{in} - a_3 R_{out}, \\
\frac{dQ}{dt} &= \rho_1 R_{in} + \rho_2 R_{out} - a_4 Q, \\
\frac{dD}{dt} &= \epsilon_1 U + \epsilon_2 R_{out} - \vartheta D,
\end{aligned}\right\} \tag{1}$$

where

$a_1 = \mu + \delta + \sigma$, $a_2 = \mu + \alpha + \rho_1$, $a_3 = \mu + \rho_2$ and $a_4 = \mu + \varphi$, with initial conditions $x(0) = \{S_0, U_0, R_{in0}, R_{out0}, Q_0, D_0\}$ such that $S_0 = S(0), U_0 = U(0), R_{in0} = R_{in}(0), R_{out0} = R_{out}(0), Q_0 = Q(0)$ and $D_0 = D(0)$. A full description of the parameters is given in Table 1.

Parameter	Description
π	Recruitment rate.
μ	Natural death rate.
δ	Death rate due to drug abuse.
σ	Rate at which drug users become in-patients or out-patients rehabilitants.
ρ_1, ρ_2	Quitting rates.
φ	Relapse rate.
β_1	Effective contact rate for person to person contact.
β_2	Effective contact rate for drugs to person contact.
ς	Relative initiation parameter.
p	Proportion of drug users that become in-patient rehabilitants.
α	Rate at which in-patient rehabilitants become out-patient.
ϑ	Removal rate of drugs in the environment due to law enforcement, community policing and justice system.
ϵ_1	Escalation rate of drugs as a result of drug users not in treatment.
ϵ_2	Escalation rate of drugs as a result of out-patient rehabilitants.
ω	Frequency of the oscillations.

Table 1: Description of parameters used in the model

We assume that the population is constant within modelling time period, so that

$$\pi = \mu N + \delta U. \tag{2}$$

From system (1) we obtain

$$\left.\begin{aligned}
\frac{dS}{dt} &= a_1 U + \mu(R_{in} + R_{out} + Q) - \lambda S, \\
\frac{dU}{dt} &= \lambda S + \varphi Q - a(t)\sigma U - a_1 U, \\
\frac{dR_{in}}{dt} &= a(t)p\sigma U - a_2 R_{in}, \\
\frac{dR_{out}}{dt} &= a(t)(1-p)\sigma U + \alpha R_{in} - a_3 R_{out}, \\
\frac{dQ}{dt} &= \rho_1 R_{in} + \rho_2 R_{out} - a_4 Q, \\
\frac{dD}{dt} &= \epsilon_1 U + \epsilon_2 R_{out} - \vartheta D.
\end{aligned}\right\} \tag{3}$$

Since the total population, $N = S+U+R_{in}+R_{out}+Q$ is constant, we can non-dimensionalize the system by setting $s = \frac{S}{N}, v = \frac{U}{N}, r_{in} = \frac{R_{in}}{N}, r_{out} = \frac{R_{out}}{N}, q = \frac{Q}{N}, w = \frac{D}{K}$, with $s + v + r_{in} + r_{out} + q = 1$.

Thus, the non-dimensionalized system is given by

$$\left.\begin{aligned}
\frac{ds}{dt} &= a_1 v + \mu r_{in} + \mu r_{out} + \mu q - \widehat{\lambda} s,\\
\frac{dv}{dt} &= \widehat{\lambda} s + \varphi q - a(t)\sigma v - a_1 v,\\
\frac{dr_{in}}{dt} &= a(t) p\sigma v - a_2 r_{in},\\
\frac{dr_{out}}{dt} &= a(t)(1-p)\sigma v + \alpha r_{in} - a_3 r_{out},\\
\frac{dq}{dt} &= \rho_1 r_{in} + \rho_2 r_{out} - a_4 q,\\
\frac{dw}{dt} &= \widehat{\epsilon_1} v + \widehat{\epsilon_2} r_{out} - \vartheta w,
\end{aligned}\right\} \tag{4}$$

where $\widehat{\epsilon_1} = \frac{\epsilon_1}{K}, \widehat{\epsilon_2} = \frac{\epsilon_2}{K}$ and $\widehat{\lambda} = \beta_1(v + \varsigma r_{out}) + \beta_2 w$.

Since $q = 1 - s - v - r_{in} - r_{out}$, we consider a reduced system of s, v, r_{in} and r_{out}, such that

$$\left.\begin{aligned}
\frac{ds}{dt} &= a_1 v + \mu(1 - s - v) - \widehat{\lambda} s,\\
\frac{dv}{dt} &= \widehat{\lambda} s + \varphi(1 - s - v - r_{in} - r_{out}) - a(t)\sigma v - a_1 v,\\
\frac{dr_{in}}{dt} &= a(t) p\sigma v - a_2 r_{in},\\
\frac{dr_{out}}{dt} &= a(t)(1-p)\sigma v + \alpha r_{in} - a_3 r_{out},\\
\frac{dw}{dt} &= \widehat{\epsilon_1} v + \widehat{\epsilon_2} r_{out} - \vartheta w.
\end{aligned}\right\} \tag{5}$$

Since the available data shows some fluctuating behavior, we introduce a periodic function to describe how drug users enter rehabilitation facilities periodically, say for example, increased rehabilitation demand at the beginning of every year. We define $a(t)$ as a periodic function of time with a common period, ω =365 days such that,

$$a(t) = \overline{a}\left[1 + \widehat{a}\sin\left(\frac{2\pi t}{\omega}\right)\right]. \tag{6}$$

$\overline{a}$ is the baseline value, or the time average, of $a(t)$ and $\widehat{a}$ is the amplitude of the periodic oscillations in $a(t)$. To ensure that $a(t)$ is positive, we require that $0 < \widehat{a} < 1$.

3 Model analysis

3.1 Feasible region

The system (4) is analysed in the region Ω of biological interest. Since the model monitors changes in the human population, then the variables and the parameters must be positive for all $t \geq 0$.

Theorem 1. *The feasible region* Ω*, defined by*

$$\Omega = \{x \geq 0 : s + v + r_{in} + r_{out} + q = 1\} \tag{7}$$

is bounded, positively invariant and attracting with respect to system (4) *for all* $t > 0$.

Here $x = (s, v, r_{in}, r_{out}, q, w)$ is a vector space which represents the state space of the system (4). The solutions of the system (4) starting from any point in Ω remains Ω.

3.2 Positivity of solutions

Since initial conditions are positive, we show that solutions of $x = (s, v, r_{in}, r_{out}, q, w)$ remain positive for all $t > 0$ in Ω.
Theorem 2. *Let the initial conditions be* $(s(0), v(0), r_{in}(0), r_{out}(0), q(0), w(0)) > 0$*, then the solutions* $x(t)$ *are positive for all* $t > 0$.

Proof. From the first equation in system (5), we have

$$\frac{ds}{dt} = a_1 v + \mu(1 - s - v) - \widehat{\lambda} s \geq -(\mu + \widehat{\lambda})s.$$

We thus have

$$s(t) \geq s_0 e^{-\left(\mu t + \int_0^t \widehat{\lambda}(\tau) d\tau\right)} > 0.$$

Since the exponential function is always positive and $s(0) > 0$, then we are guaranteed that the solution of $s(t)$ remains positive for all $t > 0$.

The second equation of the system (5) gives

$$\frac{dv}{dt} = \widehat{\lambda} s + \varphi(1 - s - r_{in} - r_{out}) - (\varphi + a(t)\sigma + a_1)v \geq -(\varphi + a(t)\sigma + a_1)v,$$

$$\Rightarrow v(t) \geq v_0 e^{-(\varphi t + a_1 t + \int_0^t \sigma a(\tau) d\tau)} > 0.$$

From the third equation of the system (5) we have

$$\frac{dr_{in}}{dt} = a(t)p\sigma v - a_2 r_{in} \geq -a_2 r_{in},$$

$$\Rightarrow r_{in}(t) \geq r_i e^{-a_2 t} > 0.$$

Thus, it can be easily shown that r_{out}, q and $w > 0$ for all $t > 0$. □

3.3 Basic Reproduction Numbers, $[R_0]$ and R_0

In epidemiological models, the basic reproduction number $[R_0]$ is the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual [3]. In this case we evaluate $[R_0]$ to measure the average number of new substance abusers that are generated by a single case of a drug using individual in a susceptible population. If $[R_0] < 1$, then on average the drug using individual produces less than one drug

user over the course of his/her ability to initiate, and the drug use will vanish. Otherwise, if $[R_0] > 1$ a drug user produces more than one drug user. We use the next generation matrix method [3, 24] to derive the basic reproduction number $[R_0]$ of the model.

In periodic models, $[R_0]$ is defined as a spectral radius of the time-averaged reproduction number using the next generation matrix method $[F][V]^{-1}$ given by

$$[R_0] = \rho([F][V]^{-1}). \tag{8}$$

In the absence of periodicity we have

$$\begin{pmatrix} \beta_1 & 0 & \beta_1\varsigma & \beta_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad [V] = \begin{pmatrix} \varphi + \overline{a}\sigma + a_1 & \varphi & \varphi & 0 \\ -\overline{a}p\sigma & a_2 & 0 & 0 \\ -\overline{a}(1-p)\sigma & -\alpha & a_3 & 0 \\ -\widehat{\epsilon_1} & 0 & -\widehat{\epsilon_2} & \vartheta \end{pmatrix}.$$

$[F]$ is the fertility matrix that represents the rate of appearance of new infections and $[V]$ is the transition matrix that represents the rate of transfer of individuals.Thus

$$[R_0] = \rho([F][V]^{-1}) = R_U + R_D,$$

where

$$R_U = \frac{\beta_1(1 + \varsigma((1-p)\sigma a_2 + \alpha p\sigma))}{a_1 a_2 a_3(1 + \Phi_0)}$$

represents the average number of new drug users who are generated by a single drug user from compartment U and

$$R_D = \frac{\beta_2\overline{a}(a_2a_3 + ((1-p)\sigma a_2 + \alpha p\sigma))}{a_1 a_2 a_3(1 + \Phi_0)}$$

is the average number of new users who may be initiated into drug use as a result of the availability of drugs in the community, where

$$\Phi_0 = \frac{\mu}{a_4}\left[\frac{\overline{a}\sigma}{a_1} + \frac{\varphi}{a_1a_2a_3}(p\sigma a_2 + ((1-p)\sigma a_2 + \alpha p\sigma))\right].$$

Following [24], we have the following results on the local stability of DF.

Theorem 3. *The drug-free equilibrium DF is locally asymptotically stable if $[R_0] < 1$ and unstable if $[R_0] > 1$.*

In the presence of periodicity, the basic reproduction number R_0 is defined as the spectral radius of an integral operator, see for instance [1]. We thus have

$$F(t) = \begin{pmatrix} \beta_1 & 0 & \beta_1\varsigma & \beta_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad V(t) = \begin{pmatrix} \varphi + a(t)\sigma + a_1 & \varphi & \varphi & 0 \\ -a(t)p\sigma & a_2 & 0 & 0 \\ -a(t)(1-p)\sigma & -\alpha & a_3 & 0 \\ -\widehat{\epsilon_1} & 0 & -\widehat{\epsilon_2} & \vartheta \end{pmatrix}.$$

Following [9], let $\Phi_V(t)$ and $\rho(\Phi_V(\omega))$ be the inverse of a fundamental (loxodromy) matrix of the linear ω-periodic system $dz/dt = V(t)z$ and the spectral radius of $\Phi_V(\omega)$. Assume that $Y(t, s)$ is the evolution operator of the linear ω-periodic system

$$\frac{dy}{dt} = -V(t)y, t \geq s. \tag{9}$$

That is for each $s \in \mathbb{R}$, the 4×4 matrix $Y(t,s)$ satisfies

$$\frac{dY(t,s)}{dt} = -V(t)Y(t,s), \quad \text{for all } t \geq s, Y(s,s) = I,$$

where I is the 4×4 identity matrix and the monodromy matrix $\Phi_{-V}(t)$ of (9) is equal to $Y(t,0), t \geq 0$. We assume that $F(s)\phi(s)$ is the rate of new drug users produced by drug users individuals who were introduced at time s. Since $t \geq s$, $Y(t,s)F(s)\phi(s)$ gives the distribution of new drug users who were infected at time s and remain in drug users compartment at time t. Thus

$$\psi(t) := \int_{-\infty}^{t} Y(t,s)F(s)\phi(s)ds = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da$$

is the distribution of accumulative new drug users at time t produced by all drug users $\phi(s)$ that were introduced at time previous to t.

Following [17,33], R_0 is defined as the spectral radius of an integral operator. They introduced the next infection operator given by L

$$(L\phi)(t) = \int_{0}^{\infty} Y(t,t-a)F(t-a)\phi(t-a)da, \quad \text{where} \tag{10}$$

$\phi(s)$ is the initial distribution of infectious individuals and is ω-periodic and positive. Thus the basic reproduction number is defined as the spectral radius of L,

$$R_0 = \rho(L). \tag{11}$$

We obtain $a(t) \equiv \overline{a}$, $F(t) \equiv F$ and $V(t) \equiv V$, for all $t \geq 0$. Thus we have

$$R_0 = \frac{\beta_1(1 + \varsigma((1-p)\sigma a_2 + \alpha p\sigma)) + \beta_2 a(t)(a_2a_3 + ((1-p)\sigma a_2 + \alpha p\sigma))}{a_1a_2a_3(1+\Phi_0)}. \tag{12}$$

3.4 Steady States

At equilibrium, we equate the equations of system (5) to zero,

$$0 = a_1 v + \mu(1-s-v) - \widehat{\lambda}s, \tag{13}$$
$$0 = \widehat{\lambda}s + \varphi(1-s-v-r_{in}-r_{out}) - a(t)\sigma v - a_1 v, \tag{14}$$
$$0 = a(t)p\sigma v - a_2 r_{in}, \tag{15}$$
$$0 = a(t)(1-p)\sigma v + \alpha r_{in} - a_3 r_{out}, \tag{16}$$
$$0 = \widehat{\epsilon_1} v + \widehat{\epsilon_2} r_{out} - \vartheta w. \tag{17}$$

Expressing r_{in}^* in terms of v^* from (15), we have

$$r_{in}^* = \Psi_1 v^*, \quad \text{where} \quad \Psi_1 = \frac{a(t)p\sigma}{a_2}. \tag{18}$$

Substituting (18) into (16) and expressing r_{out}^* in terms of v^* we obtain

$$r_{out}^* = \Psi_2 U^*, \quad \text{where} \quad \Psi_2 = \frac{a(t)(1-p)\sigma + \alpha\Psi_1}{a_3}. \tag{19}$$

Substituting (19) into (17) we obtain

$$w^* = \Psi_3 v^*, \quad \text{where} \quad \Psi_3 = \frac{\widehat{\epsilon_1} + \widehat{\epsilon_2}\Psi_2}{\vartheta}. \tag{20}$$

The force of infection at equilibrium, $\widehat{\lambda}^*$ is thus given by

$$\widehat{\lambda}^* = \xi_0 v^*, \quad \text{where} \quad \xi_0 = \beta_1(1 + \varsigma\Psi_2) + \beta_2\Psi_3. \tag{21}$$

Solving equations (13) and (14) simultaneously, we obtain

$$(s^*, v^*) = (1, 0) \tag{22}$$

and

$$(s^*, v^*) = \left(\frac{1}{R_0}, K(t)(R_0 - 1)\right), \tag{23}$$

and v^* exists when $R_0 > 1$, so that $v^* > 0$, where

$$R_0(t) = \frac{a_4(\beta_1(1 + \varsigma\Psi_2) + \beta_2\Psi_3)}{a(t)\mu\sigma + a_1a_4 + \mu\varphi(\Psi_1 + \Psi_2)} \text{ and } K(t) = \frac{a(t)\mu\sigma + a_1a_4 + \mu\varphi(\Psi_1 + \Psi_2)}{\mu + a(t)\sigma + \varphi + \varphi(\Psi_1 + \Psi_2)(\beta_1(1 + \varsigma\Psi_2) + \beta_2\Psi_3)}.$$

From (22), if $v^* = 0$, then

$$r^*_{in} = r^*_{out} = w = 0.$$

Thus, we have a drug free equilibrium given by

$$DF = (s^*, v^*, r^*_{in}, r^*_{out}, w^*) = (1, 0, 0, 0, 0)$$

which represent a situation where no drugs in the population exist over time (the whole population is susceptible to drug use).

Given that we know v^*, from (23), we can easily to show that

$$DP = (s^*, v^*, r^*_{in}, r^*_{out}, w^*)$$

is the drug persistent steady state, where

$$s^* = \frac{1}{R_0}, \quad r^*_{in} = \Psi_1 K(R_0 - 1), \quad r^*_{out} = \Psi_2 K(R_0 - 1) \quad \text{and} \quad w^* = \Psi_3 K(R_0 - 1).$$

If $R_0 = 1$, then DP collapses to DF. We thus have the following theorem on the existence of the endemic equilibrium.

Theorem 4. *The model* (5) *has a unique drug persistent equilibrium, DP if $R_0 > 1$.*

Following [26] we have the following result with respect to the local stability of DF :

Theorem 5. *Let R_0 be defined as* (12)*. Then the drug-free equilibrium of the system* (5) *is locally asymptotically stable if $R_0 < 1$, and unstable if $R_0 > 1$.*

We have do numerical simulations on the computed basic reproduction number and the average basic reproduction number R_0 and $[R_0]$ for various values of $a(t)$. In Figure 3a and 3b , we vary $\overline{a}$ and $\widehat{a}$, respectively, keeping other parameter values fixed, see caption. In Figure 3a, $R_0 = 1$ when $\overline{a} \approx 1.5648$ and $[R_0] = 1$ when $\overline{a} \approx 1.8887$, $\widehat{a}$ is set to be 0.662. We can see that the basic reproduction number R_0 is always greater than the average basic reproduction number $[R_0]$ when $\overline{a}$ varies from 0.4 to 2.0. This shows that if R_0 is used then risk of being involved in drug abuse will be overestimated.

On the other hand, Figure 3b shows that $R_0 = 1$ when $\widehat{a} \approx 0.0928$ and $[R_0] \approx 0.9938$ for all $\widehat{a}$, thus this illustrate inaccuracy on using $[R_0]$ for drug abuse prediction. The value of $\overline{a}$ is set to be 4.5 in this case.

(a) (b)

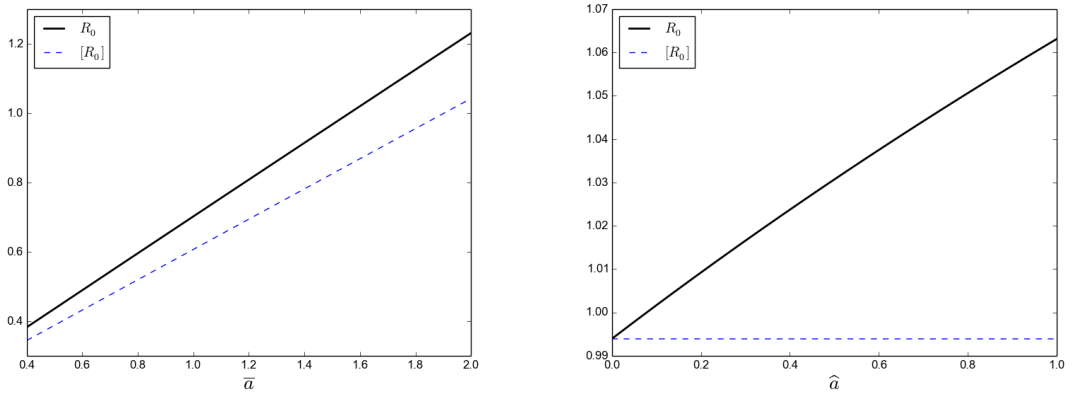

Figure 3: Plots of the periodic threshold of R_0 for various $\overline{a}$ and $\widehat{a}$. In (a) this shows $R_0 = 1$ when $\overline{a} \approx 1.5648$, and $[R_0] = 1$ when $\overline{a} \approx 1.8887$; in (b) $R_0 = 1$ when $\widehat{a} \approx 0.0928$ and $[R_0] \approx 0.9938$ for all $\widehat{a}$. We vary $\overline{a}$ and $\widehat{a}$, respectively, keeping other parameter values fixed: $\pi = 0.1891, \beta_1 = 0.0497, \mu = 0.02, \rho_1 = 0.1976, \rho_2 = 1.0, \delta = 1 \times 10^{-8}, \sigma = 0.0203, \varsigma = 0.5768, p = 0.2360, \varphi = 0.5005, \alpha = 1.2, \beta_2 = 0.03, \widehat{\epsilon_1} = 0.0083, \widehat{\epsilon_2} = 3.028 \times 10^{-10}$ and $\vartheta = 0.0268$.

4 Drug abuse extinction

We investigate the global stability of DF for our model. We consider the following matrix function $F(t) - V(t)$:

$$F(t) - V(t) = \begin{pmatrix} \beta_1 - (\varphi + a(t)\sigma + a_1) & -\varphi & \beta_1\varsigma - \varphi & \beta_2 \\ a(t)p\sigma & -a_2 & 0 & 0 \\ a(t)(1-p)\sigma & \alpha & -a_3 & 0 \\ \widehat{\epsilon_1} & 0 & \widehat{\epsilon_2} & -\vartheta \end{pmatrix}, \tag{24}$$

where the matrix function is ω-periodic.

We let $\Phi_{(F-V)(\cdot)}(t)$ be the solution of fundamental matrix of the system of ordinary differential

equation:

$$x' = \big(F(t) - V(t)\big)\, x, \tag{25}$$

and $\rho(\Phi_{(F-V)(\cdot)}(\omega))$ is the spectral radius of the fundamental matrix, $\Phi_{(F-V)(\cdot)}(t)$. Then we have the following results [17]:

Theorem 6. *Let $\nu = (1/\omega)\ln\rho(\Phi_{(F-V)(\cdot)}(\omega))$. Then there exists a positive ω-periodic function $y(t)$ such that $e^{\nu t}y(t)$ is a solution to equation 25.*

Definition 1. *Spectral radius: Let A be an $n\times n$ matrix with complex or real elements with eigenvalues $\lambda_1, \ldots, \lambda_n$. Then the spectral radius $\rho(\Phi_{(F-V)(\cdot)}(\omega))$ of A is [28]*

$$\rho(\Phi_{(F-V)(\cdot)}(\omega)) = \max_{1\le i\le n} |\lambda_i|.$$

Let us consider the equation 2, 3, 4, and 5 in the system (5) such that

$$\frac{d}{dt}\begin{bmatrix} v \\ r_{in} \\ r_{out} \\ w \end{bmatrix} \le [F(t) - V(t)] \begin{bmatrix} v \\ r_{in} \\ r_{out} \\ w \end{bmatrix}.$$

Based on Theorem 4, there exist $y(t)$ such that

$$x(t) = (\hat{v}(t), \hat{r_{in}}(t), \hat{r_{out}}(t), \hat{w}(t)) = e^{\nu t}y(t)$$

is a solution of equation (25). Thus, $(v(t), r_{in}(t), r_{out}(t), w(t)) \le (\hat{v}(t), \hat{r_{in}}(t), \hat{r_{out}}(t), \hat{w}(t))$ when t is large.

From [17], Theorem 2.2 state that $R_0 < 1$, if $\rho(\Phi_{(F-V)(\cdot)}(\omega)) < 1$. Thus, $\nu < 0$ such that

$$\lim_{t\to\infty} v(t) = 0, \quad \lim_{t\to\infty} r_{in}(t) = 0, \quad \lim_{t\to\infty} r_{out}(t) = 0 \quad \text{and} \quad \lim_{t\to\infty} w(t) = 0.$$

Since we have a constant population, then the total population $s + v + r_{in} + r_{out} + w = 1$, thus we have

$$\lim_{t\to\infty} s(t) = 1.$$

Finally, we have the following result:

Theorem 7. *If $R_0 < 1$, then the drug-free equilibrium for system (5) is globally asymptotically stable, and $\lim_{t\to\infty} x(t) = DFE = (1, 0, 0, 0, 0)$ for any solution $x(t)$ of system (5).*

Thus, above result shows that as long $R_0 < 1$, then drug use will vanish completely in the population. Keeping $R_0 < 1$ would be sufficient to remove drug use in the community, even in a fluctuating environment.

5 Simulation results

5.1 Rehabilitation data

According to the 2011 census, Cape Town has 3.74 million inhabitants [10]. The population has grown due to migration from other provinces as well as from outside South Africa. The

largest percentage are migrants from Eastern Cape and followed by migrants from other countries [11]. This growth has increased unemployment and poverty, especially in the Cape Flats (low-lying, flat area situated to the south east of the central business district of Cape Town) where there are high rates of crime and drug abuse.

We fit the model (1) to data in Table 2 using the least squares fitting routine *(lsqcurvefit)* in Matlab with optimisation. The modelling time is from 1998 to 2013 because the data for both in- and out-patient treatment is available for the given time. The data was collected by the South African Community Epidemiology Network on Drug Use (SACENDU) for drug using individuals who attended the rehabilitation centre in Cape Town. This data is used to predict future projections on the number of individuals who will need rehabilitation. According to the data (both in- and out-patient), the majority of patients are treated on an out-patient basis. The reason could be, in-patient rehabilitation programmes are expensive compared to out-patient and Cape Town residents face high rate in unemployment. The data is given in the table below.

Year	98a	98b	99a	99b	00a	00b	01a	01b	02a	02b	03a
% In-patient	32	59	69	68	66	68	66	65	58	60	63
% Out-patient	64	40	27	32	34	32	34	35	42	40	37
% Both	4^*	$< 1^*$	3^*	2^*	$< 1^*$	$< 1^*$	-	-	$< 1^*$	-	-
Year	03b	04a	04b	05a	05b	06a	06b	07a	07b	08a	08b
% In-patient	64	68	66	61	48	61	57	59	53	64	48
% Out-patient	36	32	34	39	52	39	43	41	47	36	52
Year	09a	09b	10a	10b	11a	11b	12a	12b	13a	13b	
% In-patient	39	42	44	44	34	41	28	37	39	33	
% Out-patient	61	58	56	56	66	59	72	63	61	67	

Table 2: Type of treatment received for the period 1998a to 2013b (%).
Source: [16]; $a-$represent January$-$June, $b-$represent July$-$December; * indicates those who received treatment on both in- and out-patient basis.

5.2 Parameter estimation

The table below shows the estimated parameter values that are used in the fitting of model using Matlab for both in- and out-patient rehabilitation. The average life expectancy in South Africa is approximately 62 years [8], thus the natural mortality rate is $\mu \approx 0.02$ per year. We set the recruitment rate π to be greater than the natural mortality rate so that ($\pi \approx 0.1891$ per year) hypothetically.

Symbol	Range	Value	Source
π	0.028 - 1.000	0.1891	Estimated
δ	0.000 - 0.020	1.43×10^{-8}	Estimated
σ	0.000 - 1.000	0.0203	Estimated
μ	0.019 - 0.021	0.0200	[8]
ρ_1	0.000 - 0.500	0.1976	Estimated
ρ_2	0.000 - 1.000	1.000	Estimated
φ	0.000 - 1.000	1.000×10^{-5}	Estimated
β_1	0.000 - 1.000	0.0497	Estimated
β_2	0.000 - 0.020	3.325×10^{-4}	Estimated
ς	0.000 - 1.000	0.5768	Estimated
p	0.000 - 1.000	0.2360	Estimated
α	0.000 - 1.000	2.498×10^{-6}	Estimated
$\overline{a}$	0.000 - 1.000	0.0441	Estimated
$\widehat{a}$	0.000 - 1.000	0.3662	Estimated
ϑ	0.000 - 1.000	0.0268	Estimated
ϵ_1	0.000 - 1.000	0.0083	Estimated
ϵ_2	0.000 - 1.000	3.028×10^{-10}	Estimated

Table 3: Estimated parameters used in the model

The effective contact rate for person to person contact, β_1, is assumed to be higher than that of drugs to person, β_2. We thus have $\beta_1 = 0.0497$ and $\beta_2 = 0.0003325$. The proportion p of drug users who become in-patient rehabilitants is 23.6%.

5.3 Results

In Figure 4, we observe that when $R_0 < 1$, both in- and out-patient rehabilitants decrease to zero, thus depicting the drug-free equilibrium. Similar patterns are observed for various initial conditions. Figure 5 illustrates in- and out-patient rehabilitants when $R_0 > 1$. In this case, drug use persists and after long period of time, individuals in rehabilitation approaches an $\omega-$periodic solution.

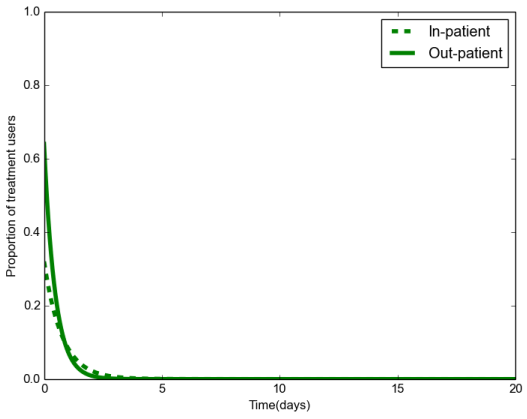

Figure 4: A typical curve of in- and out-patient rehabilitation dynamics for model (3) when $R_0 < 1$, with initial conditions $r_{in}(0) = 0.32$ and $r_{out}(0) = 0.64$. Parameter values: $R_0 = 0.26136, \mu = 0.02, \pi = 0.1891, \delta = 1.43 \times 10^{-8}, \sigma = 0.0203, \rho_1 = 0.1976, \rho_2 = 1.000, \varphi = 1.0 \times 10^{-5}, \beta_1 = 0.0497, \beta_2 = 3.325 \times 10^{-4}, \varsigma = 0.5768, p = 0.2360, \alpha = 2.498 \times 10^{-6}, \overline{a} = 0.0441, \widehat{a} = 0.3662, \vartheta = 0.0268, \epsilon_1 = 0.0083$ and $\epsilon_2 = 3.028 \times 10^{-10}$.

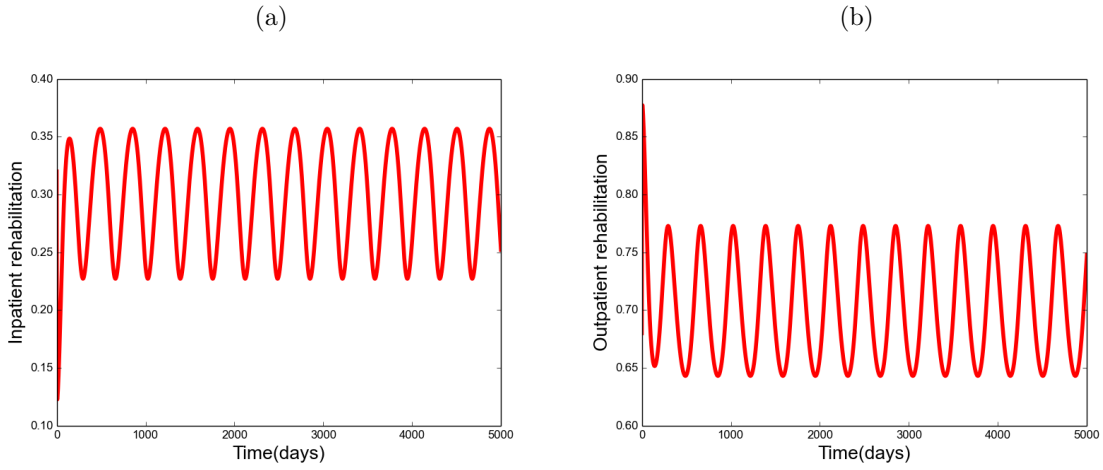

Figure 5: A typical curve of in- and out-patient rehabilitation dynamics for model (3) when $R_0 > 1$, with initial conditions $r_{in}(0) = 0.32$ and $r_{out}(0) = 0.64$. A periodic solution with $\omega = 365$ days forms after a long period. Parameter values: $R_0 = 1.7714, \mu = 0.02, \pi = 0.1410, \delta = 0.1876, \sigma = 0.90, \rho_1 = 0.0639, \rho_2 = 0.993, \varphi = 0.50, \beta_1 = 0.205, \beta_2 = 0.02, \varsigma = 0.999, p = 0.2014, \alpha = 0.50, \overline{a} = 5, \widehat{a} = 0.5, \vartheta = 0.2056, \epsilon_1 = 0.0083$ and $\epsilon_2 = 0.04$.

5.4 Model fit to in- and out-patient data

Figures 6a and 7a represent the model's fits to data on individuals receiving treatment on an in- and out-patient basis. The data is obtained from [16]. The blue circles represent the

actual data and a red solid line represents the model fits. The model fits well in both cases for the given estimated parameter values. The future of the two forms of rehabilitation are shown by the projected graphs is Figures 6b and 7b. Figure 6b shows a continued but steady decline in the number of in-patient rehabilitants, while Figure 7b shows continued but slow increase in the number of out-patient rehabilitants.

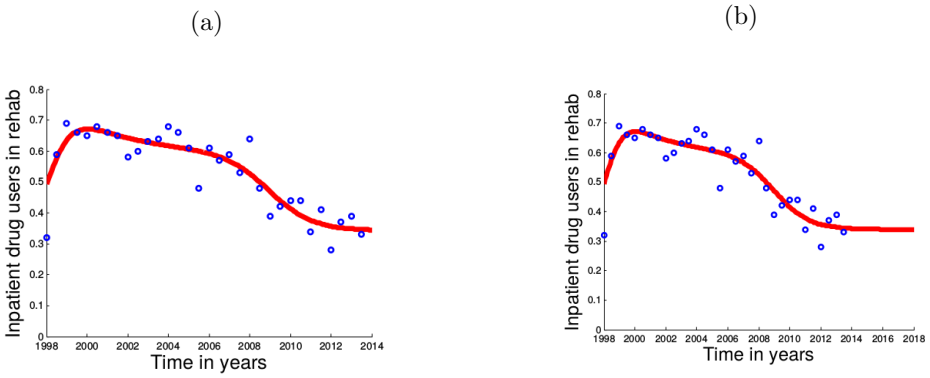

Figure 6: For the parameter values in Table 3, the model system (3) is fitted to data for individuals seeking treatment as in-patient rehabilitants and projected decline over years.

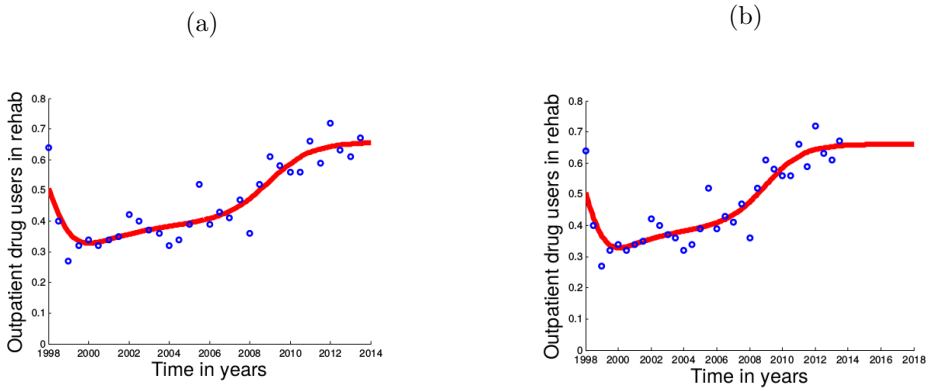

Figure 7: Using the estimated parameter values in Table 3, the model system (3) is fitted to data for individuals seeking treatment as out-patient rehabilitants and the projected increase over years.

6 Conclusion

In this paper, we presented a dynamical model of substance abuse with in- and out-patient rehabilitants in a fluctuating environment. We assumed 'seasonal' recruitment into rehabilitation centers due to some defined social dynamics reminiscent of the communities in South Africa. The model was analysed qualitatively by determining the invariant region, positivity of solutions and stability of the steady states. The drug free equilibrium has shown to be globally asymptotically stable if $[R_0] < 1$ and unstable otherwise, whereas the endemic equilibrium has shown to be asymptotically stable if $[R_0] > 1$.

The average basic reproduction number $[R_0]$ was evaluated. Using the next infection operator introduced in [26], we have derived and computed the basic reproduction number R_0 with periodicity and results shown numerically. Our results established R_0 as a sharp threshold for dynamics of substance abuse in a dynamic environment such that if $R_0 < 1$ drug abuse dies out completely and if $R_0 > 1$ it persists in the population.

Numerical simulations were performed to fit the model to data. Projections on the future of the two forms of rehabilitation were also made. The effects of the periodicity are observed in the fluctuations observed in Figure 5. These results have significant implications on the management and planning of rehabilitation programs in South Africa. The model presented here is not without short comings. We model the fluctuations using a sine function. This does not capture the non-unform fluctuation observed in the data.The model ignores variability and randomness in human behavior. The model also assumes interactions derived from the modelling of infectious diseases. To correctly model the interactions, the model should have initiation driven by imitation. Despite these shortcomings, the model provides some very useful approach to predicting rehabilitation trends.

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