Bull Math Biol
DOI 10.1007/s11538-012-9790-5

ORIGINAL ARTICLE

Modelling the Dynamics of Crystal Meth ('Tik') Abuse in the Presence of Drug-Supply Chains in South Africa

Farai Nyabadza · John B.H. Njagarah · Robert J. Smith?

Received: 20 March 2012 / Accepted: 25 October 2012

Abstract Substance abuse remains a global problem, with immense health and social consequences. Crystal meth, known as 'tik' in South Africa, is a growing problem, and its supply chains have equally grown due to increased numbers of 'tik' users, especially in the Western Cape province of South Africa. We consider a model for 'tik' use that tracks drug-supply chains, and accounts for rehabilitation and amelioration for the addicted. We analyse the model and show that it has a unique drug-free equilibrium. We prove that the drug-free equilibrium is globally stable when the reproduction number is less than one. We also consider both slow and fast dynamics, and show that there is a unique drug-persistent equilibrium when the reproduction number exceeds one. The model is fitted to data on 'tik' users in rehabilitation in the Western Cape province. A sensitivity analysis reveals that the 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. This suggests that programs aimed at light-drug users that encourage them to quit will be significantly more effective than targeting hard-drug users, either in quitting or in rehabilitation. Similarly, the person-to-person contact rate may be reduced by social programs that raise awareness of the dangers of 'tik' use and discourage light users from recruiting others.

Keywords Crystal meth · Reproductive number · Drug-supply chains · 'Tik' · Latin hypercube sampling · Partial rank correlation coefficients

F. Nyabadza (✉) · J.B.H. Njagarah
Department of Mathematics, University of Stellenbosch, P. Bag X1, Matieland 7602, South Africa
e-mail: nyabadzaf@sun.ac.za

R.J. Smith?
Department of Mathematics and Faculty of Medicine, The University of Ottawa, Ottawa, ON, Canada
e-mail: rsmith43@uottawa.ca

1 Introduction

Methamphetamine, commonly known by the street name 'tik' in South Africa or as crystal meth in other countries, is a highly addictive stimulant whose production and abuse has increased dramatically, with similar trends having been observed in the United States during the past decade. Since its advent in 1893, in Japan, the abuse of 'tik' remains a major global health and social problem (Lineberry and Bostwick 2006). Its popularity stems from energy-promoting and performance-enhancing properties. It also gives users appetite suppression; it is this property that drug-supply chains have taken advantage of in luring young women, who would not be typical drug users, into taking 'tik' as a weight-loss remedy. In South Africa, 'tik' is sold in drinking straws, with prices being charged per straw. The bitter white powder can also be placed in the glass enclosure of an incandescent light bulb, heated with a lighter and the fumes inhaled (Kapp 2008).

Generally, research into drug abuse and its impact on the general population presents an insurmountable task. In South Africa, many questions remain unanswered as to how much drug abuse is occurring and the implications of drug use, especially on disease burden, health-care demands, and risky sexual behaviour. We also ask: What policies should be put in place to curtail drug abuse and how can they be evaluated? There is a need to understand the problem, measure drug use trends, design appropriate intervention measures, and evaluate the success of these interventions (Rossi 2004). It is at this stage that mathematical models become useful. Mathematical models can help in designing interventions and evaluating their success, and predicting drug use trends (Mulone and Straughan 2009).

Because 'tik' is made available through drug-supply chains, additional preventive measures can be used. These include scare tactics (as with a policy of zero tolerance, backed up by stern parental, school, and legal penalties for use), educational campaigns (through media campaigns or prevention curricula in the schools), training in refusal skills and promotion of safe non-substance-using activities (Drug Library 1994), coupled with effective policing and a functioning judicial system. In South Africa, in a study on the nature and extent of heroin use in Cape Town, 33 out of 250 heroin users interviewed (13 %) had been arrested at least once and seven of them had been arrested for drug possession. Two were charged and none of them were found guilty of the alleged offence (Plüddemann et al. 2004). The sequence most often reported is that alcohol and cigarette use comes first, followed by marijuana use and then by the use of other illicit substances. Some variations in this sequence have been found for individuals of different sexes, racial and ethnic groups, and cultures (Drug Library 1994).

Many researchers have alluded to drug use spreading like an infectious disease (Burattini et al. 1998; De Alarcon 1969; Hunt and Chambers 1976; Mackintosh and Stewart 1979; Mulone and Straughan 2009; Nyabadza and Hove-Musekwa 2010; White and Comiskey 2007). Their focus has mainly been modelling heroin epidemics. The dynamics of smoking (whose mode of transmission is closely related to that of drug use) have also been modelled recently (Sharomi and Gumel 2008). In these models, the rate of generation of new drug users depends on contacts between non-drug users and drug users. In this paper, in addition to the bilinear interaction that

generates new cases, we also take into consideration the role played by drug-supply chains and person-to-person initiation in fueling the 'tik' epidemic. We extend the compartmental model presented in Nyabadza and Hove-Musekwa (2010) that provides a structure in which individuals in each compartment can be tracked in time as relationships between compartments described in mathematical terms evolve.

Here, our research questions are twofold. First, we ask: can we use data on individuals seeking treatment to estimate the incidence of 'tik' abuse in a community? Second, by quantifying policing levels on drug-supply chains, can we predict subsequent changes in incidence of 'tik' abuse? The former can easily be tackled by using standard epidemiological survey techniques, such as household surveys or by direct enumeration through case findings. The major challenge is that such data are usually incomplete, due to drug abuse being stigmatized, with trafficking and possession of drugs being criminal offences in many countries (Rossi 2004), including South Africa. It is therefore necessary to look at alternative methods that allow the prediction of the number of drug users in communities without necessarily having to go through surveys and case findings, which are usually dangerous due to gang violence. This presents a huge challenge. The difficult part in trying to include the levels of policing is that they cannot easily be measured and are hard to verify. The annual crime statistics do not contain police conquest of drug-supply chains, but rather how drug-related crimes are changing. For example, the South African police statistics showed that drug-related crimes increased from 621 to just over 3,000 between 2001–2002 and 2005–2006 in Mitchell's Plain, a township in Cape Town (Kapp 2008). The work presented in this paper, to the best of our knowledge, is the first attempt to model the levels of policing and their potential impact on drug-use control.

The main objectives of this paper are as follows. First, to develop a mathematical model that takes into account rehabilitation, amelioration, and policing of drug-supply chains. Second, to fit the model to observed data on individuals under rehabilitation and determine the corresponding incidence of 'tik' use using the parameters that produce the best fit to the data. Lastly, we also endeavour to quantify the levels of policing and determine the impact of increased or decreased policing on the dynamics of 'tik' use. The assumption is that drug users fuel the growth of supply chains and new drug initiations arise through two pathways: exposure to drug-supply chains (run by drug lords) and through person-to-person contact.

This paper is organised as follows. In Sect. 2, a dynamic model is formulated and a brief discussion of the model properties is given. The model is analysed in Sect. 3. In Sect. 4, we re-scale parameters to consider two time-scales for a comprehensive analysis of the model. The simulation results, estimation of parameters and determination of their sensitivity are presented in Sect. 5. Section 6 contains a discussion and concluding remarks.

2 The Model

We consider a dynamic model of 'tik' abuse that ignores detailed social and economic characteristics (for example, living conditions, literacy levels, and household income) and simultaneous abuse of substances. We conceptualize the drug epidemic

based on the characterization of individuals' risk, by dividing the population into distinct classes with respect to their drug-use patterns. We thus introduce here a compartmental model that is innovative in three regards. First, it incorporates the density of drugs in the supply chains represented by a compartment D. Second, it includes a recovery process that is ameliorative. Third, it includes aspects of policing that are important in controlling the supply of drugs on the market. Prevention of substance abuse and addiction is best done by cutting out any initial use. This can be done by making sure that abusable substances are out of the communities.

The population density N at time t is divided into five exclusive classes: those at risk of using 'tik', the susceptibles, $S(t)$; light-drug users, $U_l(t)$; hard-drug users, $U_h(t)$; users under rehabilitation, $U_r(t)$; and quitters, $Q(t)$. Thus,

$$N(t) = S(t) + U_l(t) + U_h(t) + U_r(t) + Q(t).$$

We assume a constant size population with a recruitment and non-drug-related death rate t given by μ. The recruitment of susceptibles is proportional to the population and is given by $\mu N(t)$. Initiation occurs through two processes: contact with drug users (i.e. person-to-person contact) and through the influence of drug-supply chains (i.e. supply-chain-to-person contact). We let β_u and β_s be the effective contact rates for person-to-person and supply-chain-to-person contact, respectively. The forces of infection associated with the person-to-person and supply-chain-to-person contact, denoted respectively by λ_u and λ_s, are given by

$$\lambda_u = \beta_u \left(\frac{U_l + \eta U_h}{N} \right) \quad \text{and} \quad \lambda_s = \frac{\beta_s D}{N}. \tag{1}$$

The modification parameter η $(0 < \eta < 1)$ accounts for the decreased initiation potential of hard-drug users. The assumption here is that hard-drug users have a lower potential of generating new drug users than light-drug users do. This is because hard-drug users manifest ill effects of substance abuse as they may have been using drugs for a long time and may be older and socially distant from potential recruits. Drug users thus generate secondary drug users in two ways: first, through direct contact with those susceptible, and secondly by propping up drug-supply chains, which make drugs available to susceptible individuals, resulting in initiation. The remaining rate parameters are k, the escalation rate from light drug use to hard drug use; σ, the uptake rate into rehabilitation programs; and θ_1 and θ_2, respectively, the rates at which light-drug users and those under rehabilitation quit 'tik' use. We assume that individuals who quit, should they relapse, will either go straight into U_h, due to their previous exposure to drugs, or into U_l at rates r_2 and r_3, respectively. Once one quits, one cannot go back to rehabilitation (U_r) unless one has started using drugs again. We also assume that individuals in the compartment U_h have a quitting rate that is negligible and the only way they quit is via rehabilitation. The other parameters are r_1, the relapse rates of rehabilitants; ρ, the amelioration rate as hard-drug users return to light drug use; and α_1 and α_2, the person-drug-supply contact rates for the light- and hard-drug users, respectively.

Table 1 Primary 'tik' abuse for the period 1997a to 2010a (%). Source: Plüddemann et al. (2010)

Year	97a	97b	98a	98b	99a	99b	00a	00b	01a	01b	02a	02b	03b
% 'tik' use	0.0	0.1	0.0	0.1	0.1	0.1	0.2	0.1	0.1	0.3	0.3	0.8	2.3
Year	04a	04b	05a	05b	06a	06b	07a	07b	08a	08b	09a	09b	10a
% 'tik' use	10.7	19.3	26.1	34.7	37.2	42.3	40.7	36.1	35.8	35.1	40.6	35.5	33.6

We thus assume that the growth of the density of drugs in supply chains is directly proportional to the number of drug users present at any time t. We argue here that, as the number of drug users increase, the demand for drugs from the supply chains increases. This is borne out by the rapid increase in availability of 'tik' in a short space of time, as seen in Table 1.

Furthermore, we shall assume that $\alpha_2 = \phi\alpha_1$, where $\phi > 1$, due to the greater demand for drugs by heavy 'tik' users. The removal rate of drug-supply chains can be modelled by a function $f(D)$. This function can take several forms, depending on the assumptions. We suggest a function in which policing is proportional to the number of drug-supply chains. We thus have

$$f(D) = \nu D.$$

Since demand increases with supply and supply increases with demand, the result is potentially a feedback loop. The function $f(D)$ provides a damping on this loop. We can define $\frac{1}{\nu}$ as the duration that drugs spend in circulation in the supply chain. It is important to assume that D is large enough to be modelled deterministically. The compartment D represents the density of drugs in the supply chain with units of kilograms per square kilometre. The population density $N(t)$ has units of individuals per square kilometre. The description above translates into the five-state model depicted by Fig. 1. The division between the left- and right-hand sides of Fig. 1 separate initiation and 'tik' use patterns with the latter having data available.

The dynamical system representing the schematic diagram is given by

$$\begin{aligned}
\dot{S} &= \mu N - (\lambda_u + \lambda_s)S - \mu S,\\
\dot{U}_l &= (\lambda_u + \lambda_s)S + \rho U_h + r_3 Q - (\mu + k + \theta_1)U_l,\\
\dot{U}_h &= kU_l + r_1 U_r + r_2 Q - (\mu + \sigma + \rho)U_h,\\
\dot{U}_r &= \sigma U_h - (\mu + r_1 + \theta_2)U_r,\\
\dot{Q} &= \theta_1 U_l + \theta_2 U_r - (\mu + r_2 + r_3)Q,\\
\dot{D} &= \alpha_1(U_l + \phi U_h) - \nu D,
\end{aligned} \tag{2}$$

where λ_u and λ_s are as defined in (1).

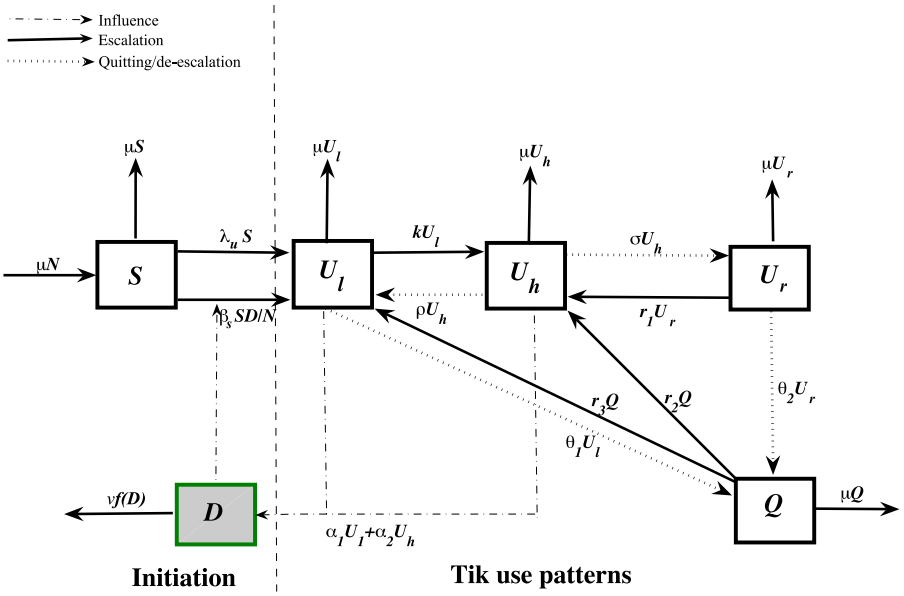

Fig. 1 A compartmental representation of the epidemic of 'tik' use

It is helpful to re-scale system (2) so that we have dimensionless variables. We let

$$s = \frac{S}{N}, \quad v = \frac{U_l}{N}, \quad w = \frac{U_h}{N}, \quad x = \frac{U_r}{N}, \quad y = \frac{Q}{N}, \quad z = \frac{\alpha_1}{\nu N} D.$$

We thus have the following re-scaled system

$$\begin{aligned}
\dot{s} &= \mu - \beta_u(v + \eta w)s - \hat{\beta}_s z s - \mu s, \\
\dot{v} &= \beta_u(v + \eta w)s + \hat{\beta}_s z s + \rho w + r_3 y - (\mu + k + \theta_1)v, \\
\dot{w} &= kv + r_1 x + r_2 y - (\mu + \sigma + \rho)w, \\
\dot{x} &= \sigma w - (\mu + r_1 + \theta_2)x, \\
\dot{y} &= \theta_1 v + \theta_2 x - (\mu + r_2 + r_3)y, \\
\dot{z} &= \nu(v + \phi w - z),
\end{aligned} \tag{3}$$

where $\hat{\beta}_s = \beta_s \alpha_1 / \nu$. The transmission parameter $\hat{\beta}_s$ contains the supply-chain-to-person transmission, β_s, and the person-to-supply-chain contact rate, α_1. It is thus important to note that $\hat{\beta}_s$ represents the entire person-supply-chain-person transmission cycle.

The feasible region of system (3) is given by the following set:

$$\mathcal{G} = \{s, v, w, x, y, z \geq 0 : s + v + w + x + y = 1\}. \tag{4}$$

3 Analysis

3.1 Long-Term Behaviour

It is always imperative to establish the long-term behaviour of solutions to any given dynamical system. For any $\epsilon > 0$, we define

$$\mathcal{G}_{z^*} = \left\{(s, v, w, x, y, z) \in \mathcal{G} : z^* \leq 1 + \phi + \epsilon\right\}. \tag{5}$$

We now prove that, for all $t > 0$, the solutions of system (3) exist and lie in $\mathcal{G}_{z^*}$.

Lemma 1 *Let $\mathcal{G}$ and $\mathcal{G}_{z^*}$ be as defined in (4) and (5), respectively. If $X(t)$ denotes the solution set to system (3) with initial conditions $X(0) \in \mathcal{G}$, then $X(t) \in \mathcal{G}$ for all $t > 0$. Furthermore, there exists a $T_\epsilon > 0$ such that, for all $t > T_\epsilon$, $X(t) \in \mathcal{G}_{Z^*}$.*

Proof To prove that solutions starting in $\mathcal{G}$ remain in $\mathcal{G}$, we let $n = s + v + w + x + y$. Differentiating n, we have

$$\dot{n} = \dot{s} + \dot{v} + \dot{w} + \dot{x} + \dot{y} = \mu(1 - n),$$

with $n = 1$ as the steady state. Note that $n(t) = 1 - (1 - n_0)e^{-\mu t}$ for n_0 a constant. It can be easily shown that $n(0) = 1$, so that $s(t) + v(t) + w(t) + x(t) + y(t) = 1$. Consider system (3) when at least one of the phase variables is zero. If $X_i \in X = 0$ then $\dot{X}_i \geq 0$ by a direct computation of the variables in system (3). So the trajectories of system (3) do not leave through $\partial\mathcal{G}$, the boundary of $\mathcal{G}$ for $t \geq 0$.

Considering the last equation of system (3), the largest value $v + \phi w$ can be is $1 + \phi$, since $v \leq 1$ and $w \leq 1$. Thus, for $\dot{z} < 0$, we need $z > 1 + \phi$. Hence, z is decreasing whenever $z > 1 + \phi$, so that z is bounded. Therefore, solutions to system (3) with initial conditions in $\mathcal{G}$ exist for all $t > 0$.

To prove that $X(t)$ is contained in $\mathcal{G}_{z^*}$, it is important to note that $\dot{z} < 0$ for $z = 1 + \phi + \epsilon$. This means that the solutions starting from $z_0 > 1 + \phi + \epsilon$ enter $\mathcal{G}_{z^*}$. Whenever $z < 1 + \phi + \epsilon$,

$$\dot{z} < \nu\big[1 + \phi - (1 + \phi + \epsilon)\big] = -\nu\epsilon,$$

so that $\dot{z} < -\nu\epsilon$. With $z_0 > 1 + \phi + \epsilon$, we have $z(t) < z_0 - \nu\epsilon t$ as long as z remains greater than $1 + \phi + \epsilon$. We now define

$$T_\epsilon = \frac{z_0 - (1 + \phi + \epsilon)}{\nu\epsilon}.$$

If the solution is outside $\mathcal{G}_{z^*}$ at T_ϵ, then $z(T_\epsilon) < z_0 - \epsilon\eta T_\epsilon = 1 + \phi + \epsilon$. This is a contradiction, so the solution must enter $\mathcal{G}_{z^*}$ before T_ϵ. □

3.2 The Reproduction Number

System (3) has a drug-free equilibrium given by

$$\mathcal{E}_0 = (1, 0, 0, 0, 0, 0).$$

The reproduction number, $\mathcal{R}_0$, is determined by the method of the next-generation matrix (van den Driessche and Watmough 2002). A reproduction number obtained this way determines the local stability of the drug-free equilibrium point for $\mathcal{R}_0 < 1$ and instability for $\mathcal{R}_0 > 1$ (Heffernan et al. 2005). Using the approach in van den Driessche and Watmough (2002), and adopting the matrix notations, the matrices for new infection terms and the transfer terms at the drug-free equilibrium are given by

$$F = \begin{pmatrix} \beta_u & \eta\beta_u & 0 & 0 & \hat{\beta}_s \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} Q_1 & -\rho & 0 & -r_3 & 0 \\ -k & Q_2 & -r_1 & -r_2 & 0 \\ 0 & -\sigma & Q_3 & 0 & 0 \\ -\theta_1 & 0 & -\theta_2 & Q_4 & 0 \\ -\nu & -\phi\nu & 0 & 0 & \nu \end{pmatrix},$$

where $Q_1 = \mu + k + \theta_1$, $Q_2 = \mu + \sigma + \rho$, $Q_3 = \mu + r_1 + \theta_2$ and $Q_4 = \mu + r_2 + r_3$.

The reproduction number is given by the spectral radius (the dominant eigenvalue) of the matrix FV^{-1}, denoted by $\varrho(FV^{-1})$. Thus,

$$\varrho\left(FV^{-1}\right) = \mathcal{R}_0 = R_1 + R_2 + R_3, \tag{6}$$

where

$$R_1 = \left(\frac{\beta_u}{Q_1}\right)\left(\frac{1 - (\Phi_1 + \Phi_3)}{1 - (\Phi_1 + \Phi_2 + \Phi_3 + \Phi_4)}\right),$$

$$R_2 = \left(\frac{\eta\beta_u}{Q_2}\right)\left(\frac{k}{Q_1} + \frac{r_2\theta_1}{Q_1Q_4}\right)\Pi,$$

$$R_3 = \left\{\left(\frac{\phi\hat{\beta}_s}{Q_2}\right)\left(\frac{k}{Q_1} + \frac{r_2\theta_1}{Q_1Q_4}\right) + \left(\frac{\hat{\beta}_s}{Q_1}\right)\left[1 - (\Phi_1 + \Phi_3)\right]\right\}\Pi,$$

with

$$\Pi = \frac{1}{1 - (\Phi_1 + \Phi_2 + \Phi_3 + \Phi_4 + \Phi_5(1 - \Phi_1) + \Phi_6)},$$

$$\Phi_1 = \frac{\sigma r_1}{Q_2Q_3}, \qquad \Phi_2 = \frac{k\rho}{Q_1Q_2}, \qquad \Phi_3 = \frac{\sigma r_2\theta_2}{Q_2Q_3Q_4},$$

$$\Phi_4 = \frac{\rho r_2\theta_1}{Q_1Q_2Q_4}, \qquad \Phi_5 = \frac{r_3\theta_1}{Q_1Q_4}, \qquad \Phi_6 = \frac{k\sigma r_3\theta_2}{Q_1Q_2Q_3Q_4}.$$

Note that $0 < \Phi_j < 1$ for all j and $\Pi, R_1, R_2, R_3 > 0$.

$\mathcal{R}_0$ is a sum of three terms representing the contribution of the light-drug users, hard-drug users, and the drug-supply chains to the generation of new initiates. We have carefully written the expression of the reproduction number so that the contribution of the supply chains to initiation can be determined. The reproduction number

is defined as the secondary number of initiates produced by one single initiated individual introduced into a wholly susceptible population. This definition is directly translated from epidemic models (Diekmann et al. 1990). In the context of this paper, $\mathcal{R}_0$ determines whether 'tik' use will persist or die out in the population.

Following van den Driessche and Watmough (2002, Theorem 2), we have the following result.

Theorem 1 *The drug-free equilibrium of system* (3) *is locally asymptotically stable whenever* $\mathcal{R}_0 < 1$ *and unstable otherwise.*

3.3 Global Stability of the Drug-Free Equilibrium

In this subsection, we prove the global stability of the drug-free equilibrium $\mathcal{E}_0$ when $\mathcal{R}_0 < 1$.

Theorem 2 *The drug-free equilibrium* $\mathcal{E}_0$ *of system* (3) *is globally asymptotically stable if* $\mathcal{R}_0 < 1$ *and unstable otherwise. The drug-free equilibrium* $\mathcal{E}_0$ *is the only equilibrium when* $\mathcal{R}_0 \leq 1$.

Proof Let

$$L = Av + Bw + Cx + Dy + Ez$$

be the Lyapunov function for some non-negative values of A, B, C, D, and E. The time derivative of L is given by

$$\begin{aligned}
\dot{L} &= A\dot{v} + B\dot{w} + C\dot{x} + D\dot{y} + E\dot{z} \\
&= A\big[\beta_u(v+\eta w)s + \hat{\beta}_s z s + \rho w + r_3 y - Q_1 v\big] + B[kv + r_1 x + r_2 y - Q_2 w] \\
&\quad + C[\sigma w - Q_3 x] + D[\theta_1 v + \theta_2 x - Q_4 y] + E\big[\nu(v + \phi w - z)\big] \\
&= (A\beta_u s + Bk + D\theta_1 + E\nu - AQ_1)v + (A\eta\beta_u s + A\rho + C\sigma + E\nu\phi - BQ_2)w \\
&\quad + (Br_1 + D\theta_2 - CQ_3)x + (Ar_3 y + Br_2 - DQ_4)y + (A\hat{\beta}_s s - E\nu)z \\
&\leq (A\beta_u + Bk + D\theta_1 + E\nu - AQ_1)v + (A\eta\beta_u + A\rho + C\sigma + E\nu\phi - BQ_2)w \\
&\quad + (Br_1 + D\theta_2 - CQ_3)x + (Ar_3 y + Br_2 - DQ_4)y + (A\hat{\beta}_s - E\nu)z.
\end{aligned}$$

We now evaluate the coefficients of the suitable Lyapunov function such that the coefficients of w, x, y, and z are equal to zero. We thus obtain

$$A = Q_2 Q_3 Q_4\big[1 - (\Phi_1 + \Phi_3)\big] > 0,$$

$$B = Q_3 Q_4(\eta\beta_u + \phi\hat{\beta}_s + \rho) + \rho r_3\theta_2,$$

$$C = (\eta\beta_u + \phi\hat{\beta}_s + \rho)(r_1 Q_4 + r_2\theta_2) + r_3\theta_2 Q_2,$$

$$D = Q_3 r_2(\eta\beta_u + \phi\hat{\beta}_s + \rho) + r_3 Q_2 Q_3(1 - \Phi_1) > 0,$$

$$E = Q_2 Q_3 Q_4 \hat{\beta}_s\big[1 - (\Phi_1 + \Phi_3)\big]/\nu > 0.$$

Using these coefficients, the time derivative of the Lyapunov function can be expressed as

$$\dot{L} \leq \left[\frac{Q_1[1 - (\Phi_1 + \Phi_2 + \Phi_3 + \Phi_4 + \Phi_5(1 - \Phi_1) + \Phi_6)]}{\hat{\beta}_s[1 - (\Phi_1 + \Phi_3)]}\right](\mathcal{R}_0 - 1)v.$$

Note that the quantity in square brackets is always positive.

Clearly, $\dot{L} \leq 0$ when $\mathcal{R}_0 \leq 1$, with equality if $\mathcal{R}_0 = 1$. Furthermore, $\dot{L} = 0$ if and only if $w = x = y = z = 0$. Therefore, the largest compact invariant set in $\{(s, v, w, x, y, z) \in \mathcal{G} : \dot{L} = 0\}$, when $\mathcal{R}_0 \leq 1$, is the singleton $\mathcal{E}_0$. Therefore, $\mathcal{E}_0$ is the only steady state when $\mathcal{R}_0 \leq 1$. LaSalle's invariance principle (LaSalle 1976) then implies that $\mathcal{E}_0$ is globally stable in $\mathcal{G}$ if $\mathcal{R}_0 < 1$. Using Lemma 5 in Magel and Ruan (2008), we observe that the Jacobian matrix evaluated at $\mathcal{E}_0$ has a positive eigenvalue whenever $\mathcal{R}_0 > 1$. The drug-free equilibrium is therefore unstable if $\mathcal{R}_0 > 1$. This completes the proof. □

This result has useful implications regarding the spread of the 'tik' epidemic. Irrespective of the initial state of the epidemic, as long as $\mathcal{R}_0 < 1$ the epidemic will clear from the population. Thus, interventions that target the reduction of $\mathcal{R}_0$ will be most desirable. As the reproduction number passes through $\mathcal{R}_0 = 1$, there is a change in stability. In fact, there is a transcritical bifurcation at $\mathcal{R}_0 = 1$ and hence $\mathcal{R}_0$ is a threshold. See Li et al. (2011) for more discussion.

Further analysis of the model is made by considering the slow and fast dynamics given in the next section.

4 Slow and Fast Dynamics

We assume that the parameters α_1, α_2, and ν are much smaller than the other parameters. This is because the number of supply chains is very small compared to the population they serve. We therefore rescale them such that

$$\alpha_1 = \varepsilon\tilde{\alpha}_1, \quad \alpha_2 = \varepsilon\tilde{\alpha}_2, \quad \text{and} \quad \nu = \varepsilon\tilde{\nu}, \tag{7}$$

where ε is a small positive parameter.

We use the geometric singular perturbation theory for differential equations (Fenichel 1979) to analyse the system. We therefore consider two timescales: the fast and slow dynamics. We consider the original time t as the fast timescale variable and the scaled time $\tau = \varepsilon t$ as the slow timescale, and then denote "$\cdot$" $= \frac{d}{dt}$ and "$'$" $= \frac{d}{d\tau}$. In our analysis, we use the re-scaled system (3), describing the drug-using population and the drug-supply chains, and transform it to a system with re-scaled parameters with respect to the slow and fast variables. The resulting system of equations for the

fast dynamics are

$$\begin{aligned}
\dot{s} &= \mu - \beta_u(v+\eta w)s - \hat{\beta}_s z s - \mu s,\\
\dot{v} &= \beta_u(v+\eta w)s + \hat{\beta}_s z s + \rho w + r_3 y - (\mu + k + \theta_1)v,\\
\dot{w} &= kv + r_1 x + r_2 y - (\mu + \sigma + \rho)w,\\
\dot{x} &= \sigma w - (\mu + r_1 + \theta_2)x,\\
\dot{y} &= \theta_1 v + \theta_2 x - (\mu + r_2 + r_3)y,\\
\dot{z} &= \varepsilon\tilde{\nu}(v + \phi w - z),
\end{aligned} \tag{8}$$

and for the slow dynamics are

$$\begin{aligned}
\varepsilon s' &= \mu - \beta_u(v+\eta w)s - \hat{\beta}_s z s - \mu s,\\
\varepsilon v' &= \beta_u(v+\eta w)s + \hat{\beta}_s z s + \rho w + r_3 y - (\mu + k + \theta_1)v,\\
\varepsilon w' &= kv + r_1 x + r_2 y - (\mu + \sigma + \rho)w,\\
\varepsilon x' &= \sigma w - (\mu + r_1 + \theta_2)x,\\
\varepsilon y' &= \theta_1 v + \theta_2 x - (\mu + r_2 + r_3)y,\\
z' &= \tilde{\nu}(v + \phi w - z).
\end{aligned} \tag{9}$$

Our interest is to investigate the dynamics of 'tik' use in the human population. We thus focus on the fast dynamics subsystem. To obtain some useful insights into the fast dynamics, we set $\varepsilon = 0$ in Eq. (8) and analyse the fast dynamics subsystem at equilibrium. During the fast dynamics, the change of supply chains over time is thus taken to be constant. The resulting system describes the dynamics of substance abuse for a given drug-supply chain. The equilibrium of the resulting system is given in the next subsection.

4.1 Existence of the Drug-Persistent Equilibrium for Fast Dynamics

To compute equilibria, we set $\varepsilon = 0$ and the left-hand side of system (8) to zero. From the fourth equation of (8),

$$x^* = \frac{\sigma}{Q_3} w^*.$$

The fifth equation of (8) gives

$$y^* = \frac{\theta_1}{Q_4} v^* + \frac{\theta_2 \sigma}{Q_3 Q_4} v^*.$$

The third equation of (8) results in

$$w^* = \xi v^*, \quad \text{where } \xi = \frac{kQ_4 + r_2\theta_1}{Q_2Q_4[1-(\Phi_1+\Phi_3)]} > 0.$$

Expressing all the other variables in terms of v^* gives, after some algebraic manipulations,

$$x^* = \frac{\sigma}{Q_3}\xi v^*, \quad y^* = \left(\frac{\theta_1}{Q_4} + \frac{\theta_2\sigma}{Q_3Q_4}\xi\right)v^* \quad \text{and} \quad z^* = (1+\phi\xi)v^*.$$

From the second equation of (8), we have either $v^* = 0$ or

$$s^* = Q_1\left[\frac{1-(\Phi_1+\Phi_2+\Phi_3+\Phi_4+\Phi_5(1-\Phi_1)+\Phi_6)}{[1-(\Phi_1+\Phi_3)][\beta_u(1+\eta\xi)+\hat{\beta}_s(1+\phi\xi)]}\right] = \frac{1}{\mathcal{R}_0} > 0.$$

The case v^*=0 gives the drug-free equilibrium, treated earlier.

Given the expression for s^*, from the first equation we can solve for v^* so that

$$v^* = \frac{\mu}{[\beta_u(1+\eta\xi)+\hat{\beta}_s(1+\phi\xi)]}(\mathcal{R}_0 - 1).$$

Therefore, we obtain a unique drug-persistent equilibrium given by $\mathcal{E}_1 = (s^*, v^*, w^*, x^*, y^*, z^*)$. We thus have the following theorem on the existence of the drug-persistent equilibrium.

Theorem 3 *If $\mathcal{R}_0 > 1$, the system (8) with fast dynamics has a unique drug-persistent equilibrium given by $\mathcal{E}_1$.*

The Center Manifold Theorem (CMT) can be used to prove local stability of the unique drug-persistent equilibrium. Using the fact that $w^* = \xi v^*$, the last equation of system (9) becomes

$$\frac{dz}{d\tau} = \tilde{\nu}v^*(1+\phi\xi) - \tilde{\nu}z. \tag{10}$$

The solution of z is given by

$$z = v^*(1+\phi\xi) + \tilde{C}e^{-\tilde{\nu}t}, \tag{11}$$

where $\tilde{C}$ is a constant.

If the initial drug-supply chain is denoted by z_0 at $t = 0$, then

$$z = v^*(1+\phi\xi) + \big(z_0 - v^*(1+\phi\xi)\big)e^{-\tilde{\nu}t}. \tag{12}$$

The drug-supply chains are bounded between the initial supply and the equilibrium state dependent on the endemic equilibrium. This result indicates that the resulting manifold is bounded and is therefore locally invariant. The exponential term in Eq. (12) indicates that the supply chains approach the steady state at a faster rate with high-level policing compared to relatively low levels of policing. The reduction

in supply chains reduces the probability that a susceptible individual will be initiated into drug use through supply-chain-to-person contact. This is further confirmed through numerical simulations via the analysis of the reproduction number as a function of policing. This result has implications in the fight against 'tik' abuse. Increased levels of policing yield positive effects, as they reduce the growth of the epidemic.

4.2 Global Stability of the Drug-Persistent Equilibrium

Theorem 4 *The drug-persistent equilibrium $\mathcal{E}_1$ is globally asymptotically stable whenever $\mathcal{R}_0$ is greater than unity.*

Proof We propose a suitable Lyapunov function $\mathcal{V}$ such that

$$\mathcal{V} = \left(s - s^* - s^* \ln \frac{s}{s^*}\right) + \mathcal{A}\left(v - v^* - v^* \ln \frac{v}{v^*}\right) + \mathcal{B}\left(w - w^* - w^* \ln \frac{w}{w^*}\right)$$
$$+ \mathcal{C}\left(x - x^* - x^* \ln \frac{x}{x^*}\right) + \mathcal{D}\left(y - y^* - y^* \ln \frac{y}{y^*}\right) + \mathbf{E}\left(z - z^* - z^* \ln \frac{z}{z^*}\right).$$

The constants $\mathcal{A}$, $\mathcal{B}$, $\mathcal{C}$, $\mathcal{D}$, and $\mathbf{E}$ are all positive. We note that, using the constructed Lyapunov function, the first partial derivatives with respect to any of state variables given by

$$\frac{\partial \mathcal{V}}{\partial s} = \left(1 - \frac{s^*}{s}\right), \qquad \frac{\partial \mathcal{V}}{\partial v} = \mathcal{A}\left(1 - \frac{v^*}{v}\right), \qquad \frac{\partial \mathcal{V}}{\partial w} = \mathcal{B}\left(1 - \frac{w^*}{w}\right),$$
$$\frac{\partial \mathcal{V}}{\partial x} = \mathcal{C}\left(1 - \frac{x^*}{x}\right), \qquad \frac{\partial \mathcal{V}}{\partial y} = \mathcal{D}\left(1 - \frac{y^*}{y}\right), \qquad \frac{\partial \mathcal{V}}{\partial z} = \mathbf{E}\left(1 - \frac{z^*}{z}\right),$$

are zero at the corresponding drug-persistent equilibrium point values. The second partial derivatives of $\mathcal{V}$ with respect to any of the state variables are given by

$$\frac{\partial^2 \mathcal{V}}{\partial s^2} = \frac{s^*}{s^2}, \qquad \frac{\partial^2 \mathcal{V}}{\partial v^2} = \mathcal{A}\frac{v^*}{v^2}, \qquad \frac{\partial^2 \mathcal{V}}{\partial w^2} = \mathcal{B}\frac{w^*}{w^2},$$
$$\frac{\partial^2 \mathcal{V}}{\partial x^2} = \mathcal{C}\frac{x^*}{x^2}, \qquad \frac{\partial^2 \mathcal{V}}{\partial y^2} = \mathcal{D}\frac{y^*}{y^2}, \qquad \frac{\partial^2 \mathcal{V}}{\partial z^2} = \mathbf{E}\frac{z^*}{z^2}.$$

The second partial derivatives are all positive, suggesting that the drug-persistent equilibrium states are the minimum points of each of the state variables. The time derivative of the Lyapunov function is given by

$$\dot{\mathcal{V}} = \left(1 - \frac{s^*}{s}\right)\dot{s} + \mathcal{A}\left(1 - \frac{v^*}{v}\right)\dot{v} + \mathcal{B}\left(1 - \frac{w^*}{w}\right)\dot{w} + \mathcal{C}\left(1 - \frac{x^*}{x}\right)\dot{x}$$
$$+ \mathcal{D}\left(1 - \frac{y^*}{y}\right)\dot{y} + \mathbf{E}\left(1 - \frac{z^*}{z}\right)\dot{z},$$
$$= \left(\mu - \beta_u(v + \eta w)s - \hat{\beta}_s z s - \mu s\right)\left(1 - \frac{s^*}{s}\right)$$

$$+\mathcal{A}\big(\beta_u(v+\eta w)s+\hat{\beta}_s zs+\rho w+r_3 y-Q_1 v\big)\left(1-\frac{v^*}{v}\right)$$
$$+\mathcal{B}(kv+r_1x+r_2y-Q_2w)\left(1-\frac{w^*}{w}\right)+\mathcal{C}(\sigma w-Q_3x)\left(1-\frac{x^*}{x}\right)$$
$$+\mathcal{D}(\theta_1 v+\theta_2 x-Q_4 y)\left(1-\frac{y^*}{y}\right)+\mathbf{E}\xi v(v+\phi w-z)\left(1-\frac{z^*}{z}\right).$$

We now use the system of Eq. (8) at the drug-persistent equilibrium to obtain

$$\begin{aligned}
\mu &= \beta_u\big(v^*+\eta w^*\big)s+\beta_s z^*s^*+\mu s^*,\\
Q_1 &= \frac{\beta_u(v^*+\eta w^*)s+\beta_s z^*s^*+\rho w^*+r_3y^*}{v^*},\\
Q_2 &= \frac{kv^*+r_1x^*+r_2y^*}{w^*},\\
Q_3 &= \frac{\sigma w^*}{x^*},\\
Q_4 &= \frac{\theta_1 v^*+\theta_2 x^*}{y^*},\\
1 &= \frac{v^*+\phi w^*}{z^*}.
\end{aligned} \tag{13}$$

We now substitute the terms in system (13) into the derivative of the Lyapunov function to obtain

$$\begin{aligned}
\dot{\mathcal{V}} = &\left(1-\frac{s^*}{s}\right)\left[\mu s^*\left(1-\frac{s}{s^*}\right)+\beta_u v^*s^*\left(1-\frac{sv}{s^*v^*}\right)+\beta_u\eta w^*s^*\left(1-\frac{ws}{w^*s^*}\right)\right.\\
&\left.+\hat{\beta}_s z^*s^*\left(1-\frac{zs}{z^*s^*}\right)\right]+\mathcal{A}\left(1-\frac{v^*}{v}\right)\left[-\beta_u s^*v^*\left(\frac{v}{v^*}-\frac{sv}{s^*v^*}\right)\right.\\
&-r_3y^*\left(\frac{v}{v^*}-\frac{y}{y^*}\right)-\beta_u\eta w^*s^*\left(\frac{v}{v^*}-\frac{sw}{s^*w^*}\right)-\hat{\beta}_s z^*s^*\left(\frac{v}{v^*}-\frac{zs}{z^*s^*}\right)\\
&\left.-\rho w^*\left(\frac{v}{v^*}-\frac{w}{w^*}\right)\right]+\mathcal{B}\left(1-\frac{w^*}{w}\right)\left[-kv^*\left(\frac{w}{w^*}-\frac{v}{v^*}\right)-r_1x^*\left(\frac{w}{w^*}-\frac{x}{x^*}\right)\right.\\
&\left.-r_2y^*\left(\frac{w}{w^*}-\frac{y}{y^*}\right)\right]+\mathcal{C}\left(1-\frac{x^*}{x}\right)\left[-\sigma w^*\left(\frac{x}{x^*}-\frac{w}{w^*}\right)\right]\\
&+\mathcal{D}\left(1-\frac{y^*}{y}\right)\left[-\theta_1 v^*\left(\frac{y}{y^*}-\frac{v}{v^*}\right)-\theta_2x^*\left(\frac{y}{y^*}-\frac{x}{x^*}\right)\right]\\
&+\mathbf{E}\xi v\left(1-\frac{z^*}{z}\right)\left[-v^*\left(\frac{z}{z^*}-\frac{v}{v^*}\right)-\phi w^*\left(\frac{z}{z^*}-\frac{w}{w^*}\right)\right].
\end{aligned}$$

Let

$$\frac{s}{s^*} = H, \qquad \frac{v}{v^*} = I, \qquad \frac{w}{w^*} = J, \qquad \frac{x}{x^*} = K, \qquad \frac{y}{y^*} = L, \qquad \frac{z}{z^*} = M.$$

The derivative of $\mathcal{V}$ with $\mathcal{A} = 1$ reduces to

$$\dot{\mathcal{V}} = -\mu s^* \frac{(1-H)^2}{H} + \mathcal{Q}(H, I, J, K, L, M),$$

where

$$\begin{aligned}
\mathcal{Q} = {} & \beta_u s^* v^* \left(2 - \frac{1}{H} - H\right) + \beta_u \eta w^* s^* \left(2 - \frac{1}{H} - \frac{JH}{I}\right) \\
& + \hat{\beta}_s z^* s^* \left(2 - \frac{1}{H} - \frac{MH}{I}\right) + \rho w^* \left(1 - \frac{J}{I}\right) + r_3 y^* \left(1 - \frac{L}{I}\right) \\
& + \mathcal{B} k v^* \left(1 - \frac{I}{J}\right) + \mathcal{B} r_1 x^* \left(1 - \frac{J}{J}\right) + \mathcal{B} r_2 y^* \left(1 - \frac{L}{J}\right) \\
& + \mathcal{C} \sigma w^* \left(1 - \frac{J}{K}\right) + \mathcal{D} \theta_1 v^* \left(1 - \frac{I}{L}\right) + \mathcal{D} \theta_2 x^* \left(1 - \frac{K}{L}\right) \\
& + \mathbf{E} \xi \nu v^* \left(1 - \frac{I}{M}\right) + \mathbf{E} \xi \nu \phi w^* \left(1 - \frac{J}{M}\right).
\end{aligned}$$

It is important to note that $\mathcal{Q}$ is obtained after setting the coefficients of I, J, K, L, and M to zero so that

$$\begin{aligned}
\mathcal{B} &= \frac{(\theta_1 v^* + \theta_2 x^*)(\beta_u \eta s^* + \phi \hat{\beta}_s s^* + \rho) w^*}{v^*[k(\theta_1 v^* + \theta_2 x^*) + r_2 \theta_1 y^* + r_3 \theta_1 y^*]}, \\
\mathcal{C} &= \left[\frac{\{r_1 x^* (\theta_1 v^* + \theta_2 x^*) + r_2 \theta_2 x^* y^*\} \mathcal{B} + r_3 \theta_2 x^* y^*}{\sigma w^* (\theta_1 v^* + \theta_2 x^*)} \right], \\
\mathcal{D} &= \frac{(r_2 + r_3) y^*}{\theta_1 v^* + \theta_2 x^*} \mathcal{B}, \\
\mathbf{E} &= \frac{\hat{\beta}_s s^*}{\xi \nu}.
\end{aligned} \tag{14}$$

Also note that the expressions $(2 - \frac{1}{H} - H)$, $(2 - \frac{1}{H} - \frac{JH}{I})$ and $(2 - \frac{1}{H} - \frac{MH}{I})$ are less than or equal to zero by the arithmetic-mean/geometric-mean inequality, with equality if and only if $H = 1$ and $J = M = I$. After some tedious algebraic manipulations of replacing the constants $\mathcal{B}, \mathcal{C}, \mathcal{D}$, and $\mathbf{E}$ with the relations (14), similar conclusions can be drawn from the remaining expression of $\mathcal{Q}$. This implies that $\mathcal{Q} \leq 0$ with equality only if $H = 1$ and $I = J = K = L = M$.

Therefore, $\mathcal{V} \leq 0$ with equality if and only if $s = s^*$. LaSalle's extension (LaSalle 1976) implies that the omega limit set of each solution lies in an invariant set con-

tained in

$$\mathcal{G} = \left\{(s, v, w, x, y, z) : s = s^*, \frac{v}{v^*} = \frac{w}{w^*} = \frac{x}{x^*} = \frac{y}{y^*} = \frac{z}{z^*}\right\}.$$

Since s must remain constant at s^*, $\dot{s}$ is zero. This implies that $\frac{v}{v^*} = \frac{w}{w^*} = \frac{x}{x^*} = \frac{y}{y^*} = \frac{z}{z^*} = 1$. Thus, the only invariant set contained in $\mathcal{G}$ is the singleton $\mathcal{E}_1$. This shows that each solution that intersects $\mathbb{R}^6{}_+$ tends to the endemic equilibrium $\mathcal{E}_1$. □

Global stability of the drug-persistent equilibrium has serious implications as regards the dynamics of 'tik' use. If the population is constant and $\mathcal{R}_0 > 1$, 'tik' use will always persist, irrespective of the initial conditions. It is thus important to reduce the reproduction number to below unity in order to control the 'tik' epidemic.

5 Numerical Simulations

5.1 Parameter Estimation

In this section, we estimate the model parameters used in our numerical simulations. The unprecedented increase in the use of 'tik' and other drugs in the Western Cape province of South Africa is associated with devastating social problems, including crime and violence, accidents and injury, and risky sexual behaviour (Morojele et al. 2009). Based on data from SACENDU (Plüddemann et al. 2010), there has been a general decrease in the prevalence of 'tik' abuse from 42.3 % in the second half of the year 2006 to 33.6 % in the first half of 2010. A similar trend (from 60.2–33.3 %) has been observed for individuals younger than 20 years who report methamphetamine as the primary substance of abuse at specialised treatment centres. Currently, there are up to 67 rehabilitation centres and 19 drug-counselling centres in the Western Cape.

Although there are many rehabilitation centres, not all of them may be participating in SACENDU's program of monitoring the trends of alcohol and drug abuse in the Western Cape. For example, between January and June 2010, 'tik' abuse by individuals who reported to specialist treatment centres participating in the program reduced from 36 % to 33 %. This data was collected from the 23 specialist centres that participated in the monitoring program during that time. In our view, it is likely that the reported figures could be underestimates of the actual problem. Although information on drugs reported as primary and secondary abused drugs (including methamphetamine) has been available, the actual amount of drug use attributed to light users or heavy users is not clearly known. This makes the task of ascertaining exact parameter values related to escalation of drug users challenging. In our modelling framework, we attribute the approximate time of 40 years (Burattini et al. 1998) that an individual may spend in the susceptible compartment, which is equivalent to the estimated mortality rate of 0.025 per year for sub-Saharan Africa. Plüddemann et al. (2004) established that the treatment demand trends for 'tik' as a primary or secondary drug of abuse in the Western Cape rose from less than 1 % in 2002 to more than 42 % in 2006.

Table 2 Parameter values and ranges used in numerical simulations. Note the two possible ranges for θ_1 described in Sect. 5.2. Some of the parameters are estimated from the literature

Parameter	Description	Range	Sample value
β_u	Person-to-person contact rate	0–1	0.090
β_s	Supply-chain-to-person contact rate	$0–2.08 \times 10^{-4}$	1.04×10^{-5}
η	Initiation by U_h relative to U_l	0–0.0053166	0.0026583
ν	Rate of removal of drug-supply chains	–	2.6927
k	Escalation of U_l to U_h	0–0.002	0.00100
ρ	Amelioration rate of heavy users	0–0.0019	0.0095
σ	Uptake into rehabilitation programs	0–0.25	0.0125
α_1	Escalation of supply due to light users	–	0.0250
α_2	Escalation of supply due to heavy users	–	0.018
r_1	Relapse rate of rehabilitants	0–0.0552	0.0276
r_2	Relapse rate of quitters to hard drug use	0–0.28172	0.14086
r_3	Relapse rate of quitters to light drug use	0–0.14086	0.07043
θ_1	Quitting rate of light-drug user	0–3, 1.8–3	0.06381
θ_2	Quitting rate of hard-drug user	0–0.1308	0.0654
μ	Natural mortality rate	0–0.04	0.02
ϕ	Measures difference in demand for drugs by U_l and U_h	0–3.1522	1.5776

We use the data in Table 1, on prevalence of 'tik' abuse as a primary substance of abuse, and use the least squares curve fit routine (lsqcurvefit) in Matlab with optimisation to estimate the parameter values.

5.2 Latin Hypercube Sampling

To examine the sensitivity of R_0 to variations in parameters, we used Latin hypercube sampling and partial rank correlation coefficients (PRCCs) with 1,000 simulations per run. Latin hypercube sampling is a statistical sampling method that allows for an efficient analysis of parameter variations across simultaneous uncertainty ranges in each parameter (Blower and Dowlatabadi 1994). PRCCs illustrate the degree of the effect that each parameter has on the outcome. Parameters with positive PRCCs will increase $\mathcal{R}_0$ when they are increased, whereas parameters with negative PRCCs will decrease $\mathcal{R}_0$ when they are increased.

To determine appropriate parameter ranges, we first estimated the sample value listed in the final column of Table 2. We initially ran the PRCC program with range $0–x$, where x was twice the sample value. From this, we determined that β_u and θ_1 were the two parameters with the most significant impact on $\mathcal{R}_0$. We then significantly extended the range of these parameters and re-ran the program.

Figure 2 illustrates the results for the range of parameters shown in Table 2, with $0 \leq \theta_1 \leq 3$. The upper value of θ_1 corresponds to an average of 6.67 months that light-drug users maintain their habit before quitting. That is, the range of θ_1 corresponds to light-drug users who maintain their habit any where between 6.67 months and the rest of their lives.

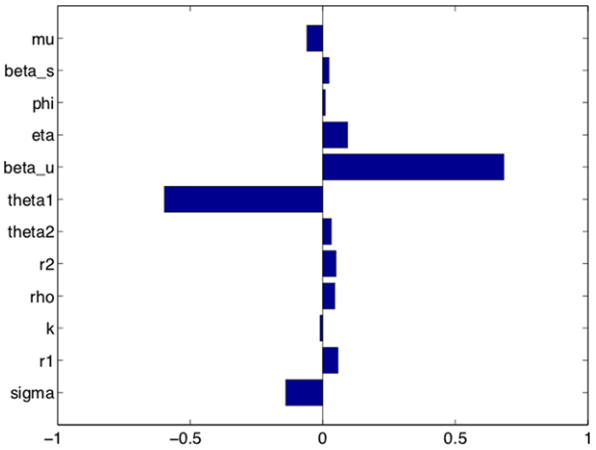

Fig. 2 Partial Rank Correlation Coefficients (PRCCs) for the full range of parameters from Table 2. The parameter with the greatest potential to make the epidemic worse when it is increased is β_u, while θ_1 is the parameter with the greatest potential to make the epidemic better when it is maximised

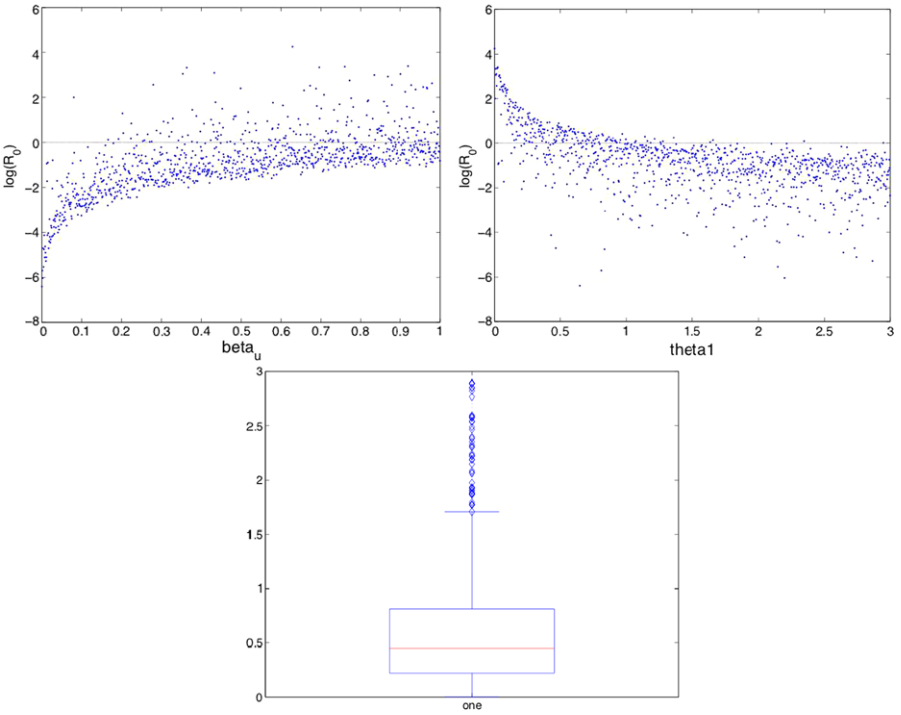

Fig. 3 Monte Carlo simulations for the two parameters with the greatest PRCC magnitude, using the values shown in Table 2 and with $0 \leq \theta_1 \leq 3$. 1,000 simulations per run were used

Figure 3 illustrates the variations in $\mathcal{R}_0$ against β_U and θ_1. All parameters are varied according to the ranges in Table 2, with $0 \leq \theta_1 \leq 3$. Also illustrated is the boxplot. Although the mean value of R_0 is less than 1, there are many simulations for which it is not, suggesting the epidemic will not always be controlled.

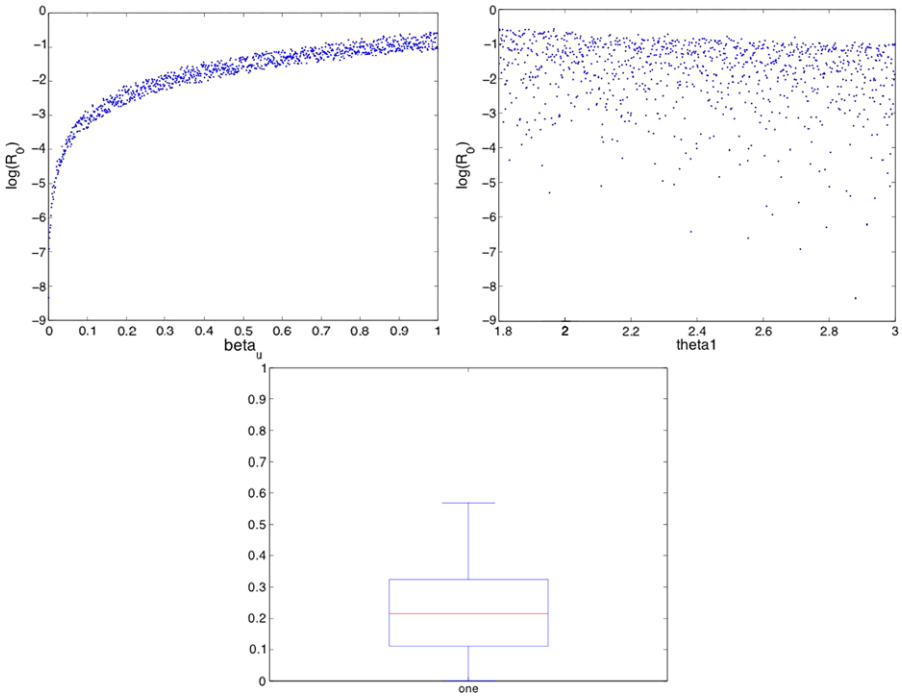

Fig. 4 Monte Carlo simulations for the two parameters with the greatest PRCC magnitude, using the values shown in Table 2 and with $1.8 \leq \theta_1 \leq 3$. 1,000 simulations per run were used

Given the potential of θ_1 to control the problem, we also examined the scenario where θ_1 was restricted to $1.8 \leq \theta_1 \leq 3$. This corresponds to a range of between 4 and 6.67 months of light drug use before quitting (since the average length of time a light-drug user is active corresponds to $\frac{1}{\theta_1}$). The results are illustrated in Fig. 4. In this case, the epidemic is entirely controlled.

Thus, Latin hypercube sampling first shows us which parameters have the greatest impact on the outcome and identifies the cutoff values for control. The value $\theta_1 = 1.8$ was determined from running 1,000 Monte Carlo simulations. Subsequently, a further 1,000 simulations were run with θ_1 restricted to the range $1.8 \leq \theta_1 \leq 3$ while all other parameters varied over their ranges. This shows that control can be achieved for this range of θ_1, even while all other parameters vary over their entire ranges. That is, θ_1 is not only the parameter which has the greatest effect on the outcome, but we can explicitly identify threshold values that occur independently of the other data.

5.3 Numerical Results

We fit the model system (3) to the data of individuals seeking treatment for 'tik' as a primary substance of abuse at specialised treatment centres. The least-squares curve fit is used to fit the model to data. Many parameters are known to lie within limits. Only a few parameters are known exactly and it is thus important to estimate the others. The estimation process attempts to find the best concordance between computed

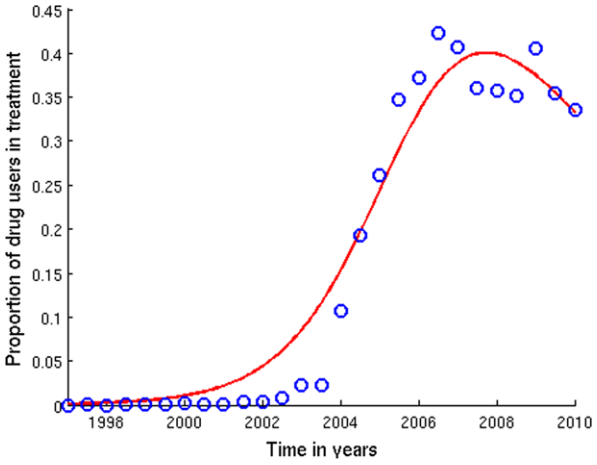

Fig. 5 Model system (3) fitted to data for individuals seeking treatment for 'tik' as a primary substance of abuse. *The blue circles* indicate the actual data and the solid line indicates the model fit to the data (Color figure online)

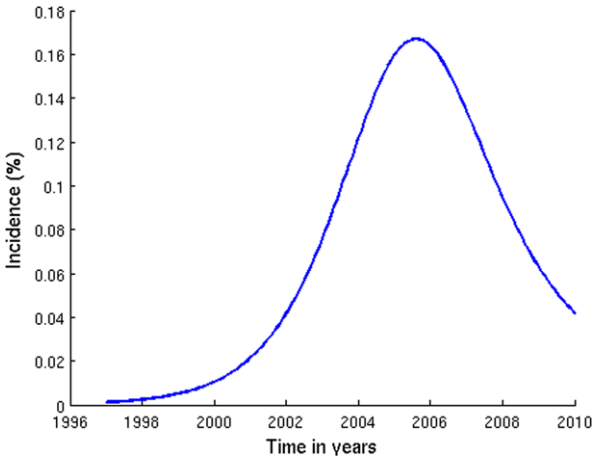

Fig. 6 Estimated incidence of 'tik' abuse as a primary substance of abuse in the Western Cape Province

and observed data. It can be carried out by trial and error or by the use of software programs designed to find parameters that give the best fit. Here, the fitting process involves the use of the least squares-curve fitting method. A Matlab code is used where unknown parameter values are given a lower and upper bound from which the set of parameter values that produce the best fit are obtained. Figure 5 shows that the number of drug users in treatment reached the peak between the second half (July–December) of 2006 and the first half (January–June) of 2009. Figure 5 demonstrates a good fit to the data from Table 1. Our estimated incidence, evaluated using the initiation function $(\lambda_u + \lambda_s)s$, is observed to have reached the peak between 2005 and 2007. See Fig. 6. The question of whether the incidence peaked in reality still remains unanswered, as no studies have been done to date to determine the incidence of 'tik' abuse in the Western Cape province of South Africa. Our results are indicative of a short-term, fast-growing 'tik' epidemic in which there is a significant increase in the number of users in a short period of time, followed by a significant slow down in the generation of new cases. This, however, does not translate into a similar pattern

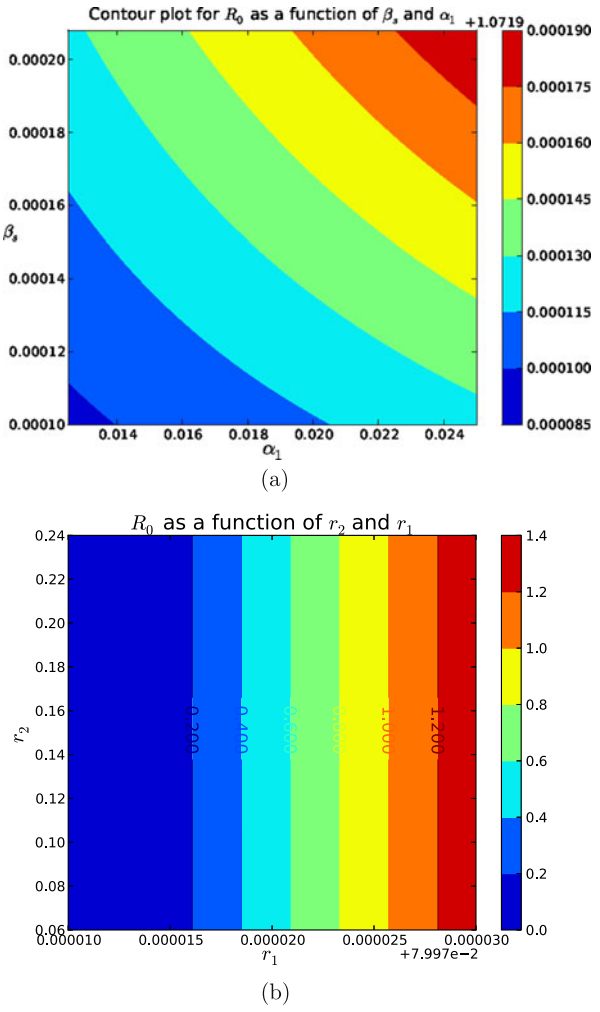

Fig. 7 Contour plot for $\mathcal{R}_0$ as a function of; (**a**) β_s and α_1, and (**b**) r_1 and r_2

with regards to the prevalence, since recovery from substance abuse is a difficult and expensive process. Thus, the number of drug users will remain significantly high over a long period of time.

We use the contour plots in Figs. 7 and 8 to ascertain the relationship between some selected pairs of parameters and $\mathcal{R}_0$. In Fig. 7(a), both β_s and α_1 increase the reproduction number. We observe that an amicable relationship exists between the two parameters: escalation of supply chains resulting from an increased number of light and heavy 'tik' users increases the likelihood of supply-chain-to-person interaction, which consequently results in initiation of more susceptible individuals into 'tik' use.

In Fig. 7(b), we observe a bigger increase in $\mathcal{R}_0$ with respect to an increase in r_2 relative to r_1. We argue here that the low contribution of r_1 to $\mathcal{R}_0$ relative to r_2 is due to the fact that r_1 simply results in cycling of 'tik' users between 'tik' using

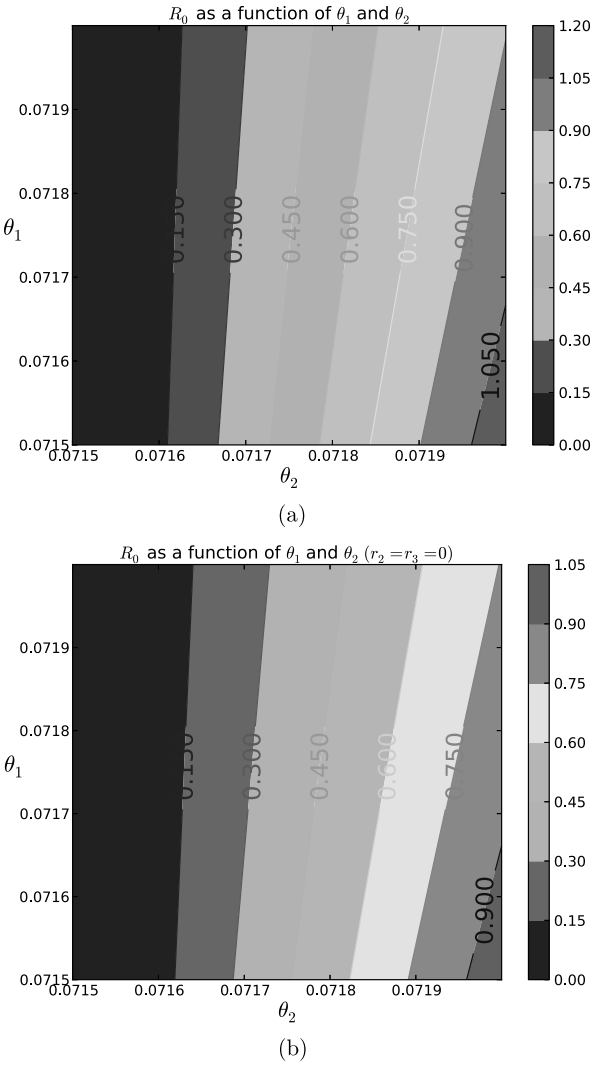

Fig. 8 Contour plot for $\mathcal{R}_0$ as a function of θ_1 and θ_2 (**a**) in presence of relapse for quitters (i.e. $r_2, r_3 \neq 0$) and (**b**) in absence of relapse for quitters (i.e. $r_2 = r_3 = 0$)

compartments U_h and U_r. The main outcome of this observation is that control efforts should aim at preventing quitters from getting re-initiated into drug use.

We also analysed the effect of the two quitting routes in the presence and absence of re-initiation of quitters. Figure 8(a) shows that, irrespective of the presence of re-initiation for quitters into 'tik' use, increasing θ_1 will reduce the prevalence of 'tik' use as opposed to the increase in θ_2. This observation is also in agreement with the PRCCs of θ_1 and θ_2. On the other hand, absence of relapse for quitters ($r_2 = r_3 = 0$) results in a reduction of $\mathcal{R}_0$; see Fig. 8(b). However, a similar trend as in the case with relapse of quitters is observed. The reduction in $\mathcal{R}_0$ indicates a reduction in the likelihood of susceptible individuals being initiated due to the reduction in the number of initiators, which is attributed to permanent quitting.

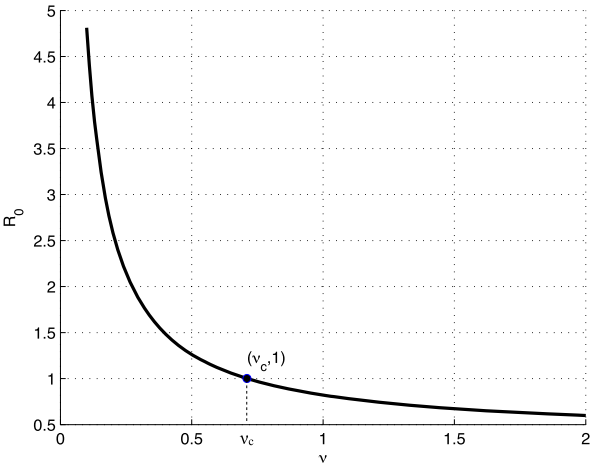

Fig. 9 The reproduction number as a function of policing for the following parameter values $\mu = 0.02$; $\beta_u = 0.1$; $\eta = 0.8$; $\rho = 0.2$; $k = 0.3$; $\theta_1 = 0.9$; $\theta_2 = 0.4$; $r_1 = 0.01$; $r_2 = 0.07$; $r_3 = 0.04$; $\sigma = 0.8$; $\alpha_1 = 0.6$; $\phi = 1.4$; $\beta_s = 0.1$

$\mathcal{R}_0$ exponentially decreases with the rate of policing (Fig. 9). Therefore, increasing the level of policing reduces the likelihood that a susceptible individual will be initiated into drug use through contact with supply chains. The reduction in the likelihood of initiation is due to the fact that policing increases the scarcity of abusable drugs through seizure of such drugs and incarceration of drug dealers, prevents aggressive marketing of illicit drugs, and legally penalizes identifiable (physiologically predisposed) drug users. It is important to note that, although increased policing may reduce incidence and consequently prevalence of 'tik' abuse, it does not lead to its extinction. This is partly explained by our reproduction number, which accounts for more than one route of initiation into 'tik' use. For this chosen set of parameter values (Fig. 9 caption), we can determine the critical rate of removal ν_c, obtained when $\mathcal{R}_0 = 1$. This is the rate of removal of drug-supply chains that leads to containment of the epidemic if other factors remain constant. In addition, the levelling off of $\mathcal{R}_0$ at high values of ν depicts a state when increasing policing does not significantly reduce the possibility of new initiations into drug use.

6 Discussion

In this paper, we used a 'tik'-abuse model that considers drug-supply chains in addition to person-to-person contact in a drug-use cycle to obtain qualitative results. We also fitted the model to data on rehabilitants with the objective of using the model parameters that give the best fit to obtain the incidence curve. Sensitivity of parameters was also considered. Latin hypercube sampling and partial rank correlation coefficients demonstrate that the two parameters with the greatest impact on the outcome are β_u, the person-to-person contact rate, and θ_1, the rate at which light-drug users quit. This suggests that control of 'tik' pivots around social intervention programs. Programs aimed at light-drug users that encourage them to quit will be significantly more effective than targeting hard-drug users, either in quitting or in rehabilitation. Similarly, the person-to-person contact rate (which is more dependent on light users)

may be reduced by social programs that raise awareness of the dangers of 'tik' use and discourage light users from recruiting others. It follows that efforts to manage the 'tik' epidemic will be significantly dependent on social programs. It is thus critical to assess the population-level impact of 'tik' use and to devote resources to education, awareness and quitting programs that are especially targeted to occasional users.

Acknowledgements F. Nyabadza and J.B.H. Njagarah acknowledge, with thanks, the support of the University of Stellenbosch. J.B.H. Njagarah appreciates with gratitude the support from the African Institute for Mathematical Sciences (AIMS) South Africa. R.J. Smith? is supported by an NSERC Discovery Grant, an Early Researcher Award and funding from MITACS. For citation purposes, please note that the question mark in "Smith?" is part of his name.

References

Blower, S. M., & Dowlatabadi, H. (1994). Sensitivity and uncertainty analysis of complex models of disease transmission: an HIV model, as an example. *Int. Stat. Rev.*, *2*, 229–243.

Burattini, M. N., Massad, E., & Coutinho, F. A. B. (1998). A mathematical model of the impact of crack-cocaine use on the prevalence of HIV/AIDS among drug users. *Math. Comput. Model.*, *28*, 21–29.

Diekmann, O., Heesterbeek, J. A. P., & Metz, J. A. J. (1990). On the definition and computation of the basic reproduction ratio R_0 in models of infectious diseases in heterogeneous populations. *J. Math. Biol.*, *28*, 503–522.

De Alarcon, R. (1969). The spread of a heroin abuse in a community. *Bull. Narc.*, *21*, 17–22.

Drug Library (1994). Substance use and transitions to abuse and addiction. Available from http://www.druglibrary.org/schaffer/library/studies/ota/ch5.htm.

Fenichel, N. (1979). Geometric singular perturbation theory for ordinary differential equations. *Journal of Differential Equations*, *31*, 53–98.

Heffernan, J. M., Smith, R. J., & Wahl, L. M. (2005). Perspectives on the basic reproductive ratio. *J. R. Soc. Interface*, *2*, 281–293.

Hunt, L. G., & Chambers, C. D. (1976). *The heroin epidemics*. New York: Spectrum Publications 1976.

Kapp, C. (2008). Crystal meth boom adds to South Africa's health challenges. *Lancet*, *371*, 193–194.

LaSalle, J. P. (1976). *CBMS-NSF regional conference series in applied mathematics: Vol. 25. The stability of dynamical systems*. Philadelphia: SIAM.

Li, J., Blakeley, D., & Smith? R. J. (2011). The Failure of R_0. *Comput. Math. Methods Med.*, *2011*, 527610.

Lineberry, T. W., & Bostwick, J. M. (2006). Methamphetamine abuse: a perfect storm of complications. *Mayo Clin. Proc.*, *81*, 77–84.

Mackintosh, D. R., & Stewart, G. T. (1979). A mathematical model of a heroin epidemic: implications for control policies. *J. Epidemiol. Community Health*, *33*, 299–304.

Magel, P. & Ruan, S. (Eds.) (2008). *Structured population models in biology and epidemiology*. Berlin: Springer.

Morojele, N. K., Parry, C. D. H., & Brook, J. S. (2009). Substance abuse and the young: taking action. *MRC-South Africa research brief*

Mulone, G., & Straughan, B. (2009). A note on heroin epidemics. *Math. Biosci.*, *218*, 138–141.

Nyabadza, F., & Hove-Musekwa, S. D. (2010). From heroin epidemics to methamphetamine epidemics: modelling substance abuse in a South African province. *Math. Biosci.*, *225*, 132–140.

Plüddemann, A., Dada, S., Parry, C., Bhana, A., Bachoo, S., Perreira, T., Nel, E., Mcweba, T., Gerber, W., & Freytag, K. (2010). Monitoring alcohol and drug abuse trends in South Africa (July 1996–June 2010). *SACENDU research brief*, *13*(2).

Plüddemann, A., Parry, C., Flisher, A. J., & Jordaan, E. (2004). The nature and extent of heroin use in Cape Town: Part 2—a community survey. Available from http://www.mrc.ac.za.

Rossi, C. (2004). Operational models for the epidemics of problematic drug use: the mover-stayer approach to heterogeneity. *Socio-Econ. Plan. Sci.*, *38*, 73–90.

Sharomi, O., & Gumel, A. B. (2008). Curtailing smoking dynamics: a mathematical modelling approach. *Appl. Math. Comput.*, *195*, 475–499.

van den Driessche, P., & Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibrium for compartmental models of disease transmission. *Math. Biosci.*, *180*, 29–48.

White, E., & Comiskey, C. (2007). Heroin epidemics, treatment and ODE modelling. *Math. Biosci.*, *208*, 312–324.