A mathematical model for the Cannabis epidemic in a South African province with a non-linear incidence rate

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Abstract

A deterministic mathematical model for the dynamics of cannabis use in a South Africa metropolis of Durban is designed and analysed. The threshold parameter $\mathcal{R}_0$, i.e., the basic reproduction number, is determined and used in the analysis of the model. It is shown that the model has multiple cannabis persistent equilibria. For a certain range of $\mathcal{R}_0$, the locally asymptotically stable cannabis-free equilibrium co-exists with the locally asymptotically stable cannabis persistent equilibrium which indicates the model exhibits backward bifurcation phenomenon due to double exposure to cannabis sources and re-addiction in the population. In this case, the cannabis consumption will remain endemic in the population even though the basic reproduction number is less than unit. In the absence of double exposure and re-addiction, it is shown that the cannabis-free equilibrium point is globally asymptotically stable (GAS) for $\mathcal{R}_0 < 1$, while the cannabis persistent equilibrium point is GAS for $\mathcal{R}_0 > 1$. The model fitting to the available data is used to estimate the parameters involved in the model. Sensitivity analysis of the model, using the parameters relevant to cannabis transmission, is given. Numerical experiments are given to support the theoretical analysis of the model.

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Keywords: Cannabis-free equilibrium, cannabis persistent equilibrium, backward bifurcation, locally asymptotically stable, globally asymptotically stable.

1 Introduction

Cannabis, commonly known as marijuana, is a psychoactive drug from the cannabis plant. Modern use primarily include recreational, medicinal drug and as part of religious or spiritual rites. Since the early 20th century, cannabis has been subject to legal restrictions with the possession, use and sale of cannabis preparations containing psychoactive cannabinoids currently illegal in most countries of the world. In the Western world, cannabis is the most frequently detected drug in the blood specimen taken from people suspected of driving under the influence of drugs, [22]. The United Nations deems it the most-used illicit drug in the world [20, 21].

Cannabis is often consumed for its psychoactive and physiological effect. The common effects of cannabis use are euphoria and anxiety. The most robust cognitive effects are on memory loss, altered time perception, impaired driving ability and decrease in performance in school resulting in lower level of education. See for example [23] for a review on the effects of memory loss in cannabis users. The common physical and psychiatric are chronic inflammation of the respiratory tract, cancer of the respiratory tract, precipitation of clinically overt schizophrenia, acute anxiety or panic and increasing risk of depression and suicide [11, 14]. The onset of most of these mental effects is within minutes and can last for hours depending on the amount used. Long term effects may include addiction.

There has been a dramatic increase in treatment demand for drugs in South Africa. According to the survey made from 1999 to 2001 in Durban, cannabis addiction among health centre visitors oscillated between $20 - 30\%$. The patients using cannabis increased from 10 to 26 patients from the second half of 1996 to 2002. Among these patients, more than 50% were under the age of 20, [7, 5].

It is against this background and the implication of cannabis abuse to public health that we propose a mathematical approach to study the prevalence of the cannabis epidemic in Durban using the available rehabilitation data. Similar efforts can also be found in [5, 24].

The threshold parameter $\mathcal{R}_0$, the basic reproduction number is determined and used in the analysis of the model. It is shown that the model has multiple cannabis persistent equilibria. For a certain range of $\mathcal{R}_0$, the locally asymptotically stable cannabis-free equilibrium co-exists with the locally asymptotically stable cannabis persistent equilibrium which indicates the model may exhibit backward bifurcation phenomenon. In this case, the cannabis consumption will remain endemic in the population even though the basic reproduction number is less than unity. The system of resulting ordinary differential equations are solved using MatLab's stiff solver, *ode45*. Numerical simulations are provided to support the theoretical analysis of the model.

The rest of the paper is arranged in the following order. The cannabis model is formulated in the next section. The mathematical analysis of the model is presented in Section 3. In Section 4, the numerical results of the model which includes the parameter estimation using data collected from 1996 to 2011 and the sensitivity analysis of the model are given. Finally, the concluding remarks on our findings are discussed Section 5.

2 Model formulation

In this section, we give a detailed mathematical formulation of cannabis epidemic model in a population. The population under consideration is classified into four disjoint compartments or classes as indicated in Fig. 1. The susceptible individuals to cannabis are denoted by S. The exposed and addicted individuals to cannabis are represented by A. Individuals under treatment or rehabilitation and individuals completely free from cannabis addiction are denoted by T and R, respectively. The total population N under consideration is given by

$$N = S + A + T + R.$$

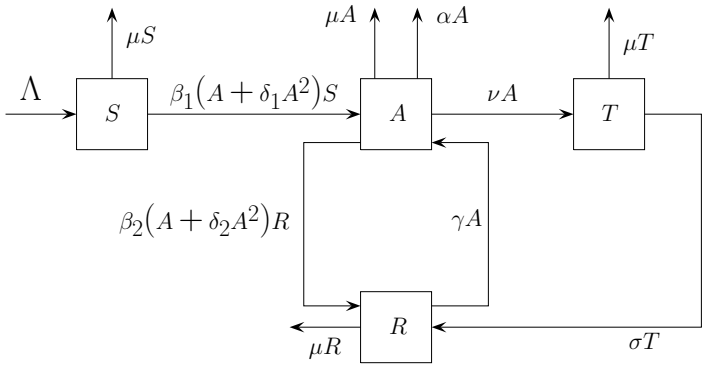


Figure 1: Schematic diagram of the model.

The recruitment of new cannabis users is assumed to be due to the contact rate that depends on an increase likelihood of being a cannabis user from double exposer to cannabis users [4]. More precisely, the number of individuals leaving the susceptible compartment and the recovered compartment to the cannabis users compartment are $\beta_1(1+\delta_1 A)AS$ and

$\beta_2(1+\delta_2 A)AS$, respectively. In both cases, the force of infection is due to double exposures to the cannabis source over a short time interval. Mathematical models formulated based on incidence rate with double exposure can also be found in [2, 3, 6, 18]. Moreover, we assume:

1. Relapse is only after recovery from treatment. The rate of defaulting once in treatment is assumed to be very low.
2. Relapse is through double exposure.
3. Self recover for the addicted individuals.
4. Homogenous mixing.
5. Cannabis addiction leads to additional mortality.
6. Inpatient rehabilitation/treatment.

The rate of movement of individuals from one compartment to another compartment is illustrated in Fig. 1. The description of parameters involved in the model formulation are given in Table 1. The values of all parameters are nonnegative.

Parameter	**Description**
Λ	Recruitment rate into S
μ	Natural death rate
β_1	Contact rate to spread the habit in class S
β_2	Contact rate to spread the habit in class R
δ_1	Rate of cannabis exposer for individuals in S
δ_2	Rate of cannabis exposer for individuals in R
α	Death rate induced by high cannabis consumption in A
ν	Rate of transfer for individuals from A to T
σ	Rate of transfer for individuals from T to R

Table 1: Parametric description

Mathematically, the flow diagram given in Fig. 1 is equivalent to the following system of equations.

$$\frac{dS}{dt} = \Lambda - \beta_1(A+\delta_1 A^2)S - \mu S, \tag{1}$$

$$\frac{dA}{dt} = \beta_1(A+\delta_1 A^2)S + \beta_2(A+\delta_2 A^2)R - (\mu+\alpha+\nu+\gamma)A, \tag{2}$$

$$\frac{dT}{dt} = \nu A - (\mu+\sigma)T, \tag{3}$$

$$\frac{dR}{dt} = \sigma T + \gamma A - \beta_2(A+\delta_2 A^2)R - \mu R. \tag{4}$$

If we add the equations from (1) – (4), we obtain the conservation law

$$\frac{dN}{dt} = \Lambda - \mu N - \alpha A. \tag{5}$$

From Eq. (5), we get the inequality

$$\Lambda - (\mu + \alpha)N \leq \frac{dN}{dt} \leq \Lambda - \mu N.$$

By Gronwall inequality, we obtain

$$0 \leq N \leq \frac{\Lambda}{\mu}. \tag{6}$$

Thus the model is biologically feasible on the positive cone

$$\Omega = \left\{ (S, A, T, R) \in \mathbb{R}^4_+ : 0 \leq S + A + T + R = N \leq \frac{\Lambda}{\mu} \right\}.$$

We assume that the system (1)-(4) is appended with the following initial condition:

$$S(0) = S_0 \geq 0,\ A(0) = A_0 \geq 0,\ T(0) = T_0 \geq 0 \quad \text{and} \quad R(0) = R_0 \geq 0.$$

Theorem 2.1. *The system (1) – (4) defines a dynamical system on* Ω.

Proof. The proof of the theorem is provided in two steps.

First, we want to show that Ω is positively invariant set. More precisely, we need to show that no trajectory leaves Ω by crossing one of its faces (see [5]). Let us assume that a trajectory crosses one of the faces at certain time given below.

- t_1 : $S(t_1) = 0,\ \dfrac{dS}{dt}(t_1) < 0,\quad S(t) > 0,\quad A(t) > 0,\quad T(t) > 0$ and $R(t) > 0$ for $0 < t < t_1$, or
- t_2 : $A(t_2) = 0,\ \dfrac{dA}{dt}(t_2) < 0,\quad S(t) > 0,\quad A(t) > 0,\quad T(t) > 0$ and $R(t) > 0$ for $0 < t < t_2$, or
- t_3 : $T(t_3) = 0,\ \dfrac{dT}{dt}(t_3) < 0,\quad S(t) > 0,\quad A(t) > 0,\quad T(t) > 0$ and $R(t) > 0$ for $0 < t < t_3$, or
- t_4 : $R(t_4) = 0,\ \dfrac{dR}{dt}(t_4) < 0,\quad S(t) > 0,\quad A(t) > 0,\quad T(t) > 0$ and $R(t) > 0$ for $0 < t < t_4$.

In the first case, from Eq. (1), we obtain $\frac{dS}{dt}(t_1) = \Lambda > 0$, which is a contradiction. Thus, S remains positive. In the second case, using Eq. (2), we have $\dfrac{dA}{dt}(t_2) = 0$, which is also a contradiction with our assumption and hence, A remains positive. In the third and fourth cases, we have $\dfrac{dT}{dt}(t_3) = \nu A(t_3) > 0$ (see (3)), and $\dfrac{dR}{dt}(t_4) = \sigma T(t_4) + \gamma A(t_4) > 0$ (see (4)), respectively. These are contradictions to our assumptions as well. Therefore, in all cases, for any positive initial data in Ω, S, A, T and R remain positive and stay in Ω.

Secondly, the total population $N(t)$ at time t satisfies Eq. (6).

Combining the two steps, the result in Theorem 2.1 follows from the classical theory of dynamical systems [17]. □

3 Equilibrium points and their stability

The equilibrium solutions of (1) – (5) are investigated as solutions of the system

$$\begin{aligned}
\Lambda - \beta_1(A + \delta_1 A^2)S - \mu S &= 0, && (7)\\
\beta_1(A + \delta_1 A^2)S + \beta_2(A + \delta_2 A^2)R - (\mu + \alpha + \nu + \gamma)A &= 0, && (8)\\
\nu A - (\mu + \sigma)T &= 0, && (9)\\
\sigma T + \gamma A - \beta_2(A + \delta_2 A^2)R - \mu R &= 0. && (10)
\end{aligned}$$

From Eq. (8), we either have

$$A = 0 \quad \text{or} \quad \beta_1(1 + \delta_1 A)S + \beta_2(1 + \delta_2 A)R - (\mu + \alpha + \nu + \gamma) = 0. \tag{11}$$

If $A = 0$, then from (7) and (9) – (10), we obtain

$$S = \frac{\Lambda}{\mu}, \quad T = 0, \quad \text{and} \quad R = 0,$$

respectively. Hence,

$$E_0 = (S, A, T, R) = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right), \tag{12}$$

which is called the cannabis-free equilibrium point.

The so called basic reproduction number, the average number of secondary cases produced by a cannabis user during his/her cannabis use life time in a population, denoted by $\mathcal{R}_0$ is determined by using the next generation matrix method [1, 8]. In this approach, we get

(taking the intiated compartment to be A),

$$F = \beta_1(A + \delta_1 A^2)S + \beta_2(A + \delta_2 A^2)R \quad \text{and} \quad V = (\mu + \alpha + \nu + \gamma)A.$$

The Jacobian of F and V are given by

$$J_F = \beta_1(1 + 2\delta_1 A)S + \beta_2(1 + 2\delta_2 A)R \quad \text{and} \quad J_V = \mu + \alpha + \nu + \gamma,$$

respectively. Thus

$$J_F(E_0) = \frac{\beta_1 \Lambda}{\mu} \quad \text{and} \quad J_V(E_0) = \mu + \alpha + \nu + \gamma.$$

Numerically, $\mathcal{R}_0$ is defined as the spectral radius of $K = J_F.(J_V)^{-1}$ or

$$\mathcal{R}_0 = \frac{\beta_1 \Lambda}{\mu(\mu + \alpha + \nu + \gamma)}. \tag{13}$$

Theorem 3.1. *The cannabis-free equilibrium E_0 is locally asymptotically stable (LAS) for $\mathcal{R}_0 < 1$ and unstable when $\mathcal{R}_0 > 1$.*

Proof. The result is obtained by Hartman-Grobman Theorem [17]. The Jacobian matrix of the system (1)-(4) at E_0 is

$$J(E_0) = \begin{pmatrix} -\mu & \frac{-\beta_1 \Lambda}{\mu} & 0 & 0 \\ 0 & \frac{\beta_1 \Lambda}{\mu} - (\mu + \alpha + \nu + \gamma) & 0 & 0 \\ 0 & \nu & -(\mu + \sigma) & 0 \\ 0 & \gamma & \sigma & -\mu \end{pmatrix}.$$

To find the eigenvalues r of $J(E_0)$, we solve the equation

$$\det(rI - J(E_0)) = 0,$$

where I is the 4×4 identity matrix. This equation can be written as

$$\begin{vmatrix} r+\mu & \dfrac{\beta_1\Lambda}{\mu} & 0 & 0 \\ 0 & r-\left(\dfrac{\beta_1\Lambda}{\mu}-(\mu+\alpha+\nu+\gamma)\right) & 0 & 0 \\ 0 & -\nu & r+(\mu+\sigma) & 0 \\ 0 & -\gamma & -\sigma & r+\mu \end{vmatrix} = 0$$

or equivalently

$$(r+\mu)^2\left[r-\left(\frac{\beta_1\Lambda}{\mu}-(\mu+\alpha+\nu+\gamma)\right)\right](r+(\mu+\sigma))=0.$$

Hence, $r_1=-\mu$ (with multiplicity 2), $r_2=-(\mu+\sigma)$ and $r_3=\dfrac{\beta_1\Lambda}{\mu}-(\mu+\alpha+\nu+\gamma)$ are the eigenvalues with negative real part if $r_3=\frac{\beta_1\Lambda}{\mu}-(\mu+\alpha+\nu+\gamma)<0$. This is true if $\mathcal{R}_0=\dfrac{\beta_1\Lambda}{\mu(\mu+\alpha+\nu+\gamma)}<1$. Therefore, E_0 is LAS if $\mathcal{R}_0<1$ and unstable when $\mathcal{R}_0>1$. This completes the proof of the theorem. □

3.1 Existence of backward bifurcation

Before investigating the global asymptotic stability of the cannabis-free equilibrium, it is instructive to determine the number of cannabis persistent equilibrium for (1) – (4). For $A>0$ and if we assume that $E^*=(S^*,A^*,T^*,R^*)$ be a cannabis persistent equilibrium, then from Eq. (9), we obtain

$$T^*=\Psi_1 A^*, \tag{14}$$

where

$$\Psi_1=\frac{\nu}{\mu+\sigma}.$$

From Eq. (10), we have

$$R^*=\frac{\Psi_2 A^*}{\mu+\beta_2(1+\delta_2 A^*)A^*}, \tag{15}$$

where,

$$\Psi_2=\frac{\nu\sigma+\gamma(\mu+\sigma)}{\mu+\sigma}=\sigma\Psi_1+\gamma.$$

Moreover, from Eq. (7) and Eq. (11), we get

$$S^* = \frac{\Lambda}{\mu + \beta_1(1+\delta_1 A^*)A^*} \tag{16}$$

and

$$\beta_1(1+\delta_1 A^*)S^* + \beta_2(1+\delta_2 A^*)R^* - Q = 0, \tag{17}$$

respectively, where,

$$Q = \mu + \alpha + \gamma + \nu.$$

After plugging (15) and (16) into (17), we obtain the following expression

$$\beta_1(1+\delta_1 A^*)\frac{\Lambda}{\mu + \beta_1(1+\delta_1 A^*)A^*} + \beta_2(1+\delta_2 A^*)\frac{\Psi_2 A^*}{\mu + \beta_2(1+\delta_2 A^*)A^*} - Q = 0, \tag{18}$$

or equivalently

$$g(A) = b_4 A^4 + b_3 A^3 + b_2 A^2 + b_1 A + b_0 = 0, \tag{19}$$

where

$$\begin{aligned}
b_4 &= \beta_1\beta_2\delta_1\delta_2(Q - \Psi_2) > 0,\\
b_3 &= \beta_1\beta_2(\delta_1+\delta_2)(Q-\Psi_2) - \Lambda\beta_1\beta_2\delta_1\delta_2,\\
b_2 &= Q\beta_1\beta_2 + Q\mu\beta_1(\delta_1+\delta_2) - \Lambda\beta_1\beta_2(\delta_1+\delta_2) - \beta_1\beta_2\Psi_2 - \mu\beta_2\delta_2\Psi_2,\\
b_1 &= Q\mu(\beta_1+\beta_2) - \Lambda\beta_1\beta_2 - \Lambda\mu\beta_1\delta_1 - \mu\beta_2\Psi_2,\\
b_0 &= Q\mu^2 - \Lambda\mu\beta_1 = Q\mu^2(1-\mathcal{R}_0).
\end{aligned}$$

The positive roots of Eq. (19) are the cannabis persistent equilibrium points.

Remark 3.2. *From (19), we infer the following points.*

1. *Notice that* $b_4 > 0$ *as* $Q - \Psi_2 > 0$.
2. *The coefficient* $b_3 > 0$ *if* $(\delta_1+\delta_2)(Q-\Psi_2) > \Lambda\delta_1\delta_2$.
3. *The sign of* b_0 *is dependend on the value of* $\mathcal{R}_0$. *The relation is summarized in the following form*

$$b_0 \begin{cases} > 0, & \text{if} \quad \mathcal{R}_0 < 1 \\ < 0, & \text{if} \quad \mathcal{R}_0 > 1. \end{cases}$$

cases	b_4	b_3	b_2	b_1	b_0	$\mathcal{R}_0$	No of sign changes	No of possible equilibrium
1	+	+	+	+	+	<1	0	0
	+	+	+	+	-	>1	1	1
2	+	+	+	-	+	<1	2	0, 2
	+	+	+	-	-	>1	1	1
3	+	+	-	+	+	<1	2	0, 2
	+	+	-	+	-	>1	3	1, 3
4	+	-	+	+	+	<1	2	0, 2
	+	-	+	+	-	>1	3	1, 3
5	+	-	-	+	+	<1	2	0, 2
	+	-	-	+	-	>1	3	1, 3
6	+	-	+	-	+	<1	4	0, 2, 4
	+	-	+	-	-	>1	3	1, 3
7	+	+	-	-	+	<1	2	0, 2
	+	+	-	-	-	>1	1	1
8	+	-	-	-	+	<1	2	0, 2
	+	-	-	-	-	>1	1	1

Table 2: Number of possible positive roots of $g(A)$.

By applying Descartes' rule of signs [9] on Eq. (19), the various possibilities for the roots of $g(A)$ are given in Table 2. Based on the existence of the different possible positive roots, we have the following result.

Theorem 3.3. *The model (1)-(4)*

1. *has a unique cannabis persistent equilibrium if cases 1, 2, 7 and 8 are satisfied and* $\mathcal{R}_0 > 1$.

2. *could have more than one cannabis persistent equilibrium if cases 3, 4, 5 and 6 are satisfied and* $\mathcal{R}_0 > 1$.

3. *could have multiple cannabis persistent equilibria if cases* $2-8$ *are satisfied and* $\mathcal{R}_0 < 1$.

4. *has no cannabis persistent equilibrium if case 1 is satisfied and* $\mathcal{R}_0 < 1$.

Theorem 3.3 (3) shows the co-existence of cannabis-free equilibrium and cannabis persistent equilibrium, which indicates the system (1)-(4) can undergo backward bifurcation phenomenon for $\mathcal{R}_0 < 1$. In this case, the cannabis problem will stay in the population even though the basic reproduction is less than unity. By using (21), a schematic diagram of backward bifurcation is given in Figure 2.

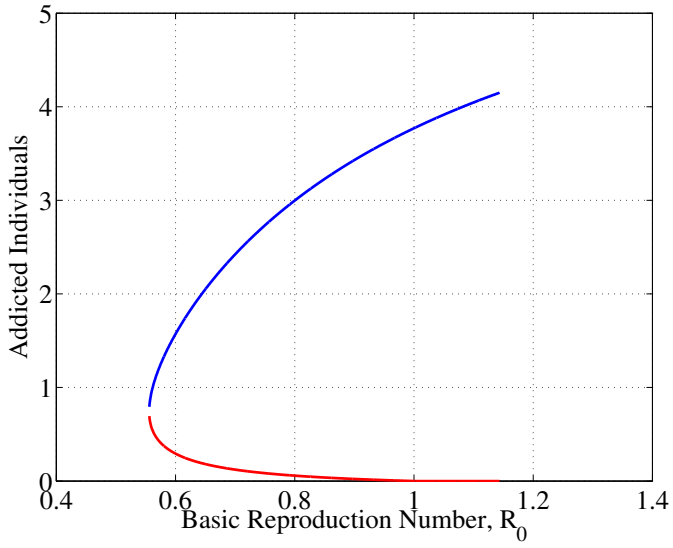


Figure 2: Backward bifurcation

3.2 Non-existence of backward bifurcation

If there is no double exposure (i.e., $\delta_1 = \delta_2 = 0$) and relapse (i.e., $\beta_2 = 0$) in the cannabis dynamics, then from (19), we obtain

$$g(A) = b_1 A + b_0 = 0, \tag{20}$$

where

$$\begin{aligned} b_1 &= \mu Q \beta_1, \\ b_0 &= Q\mu^2 - \Lambda\mu\beta_1 = Q\mu^2(1 - \mathcal{R}_0). \end{aligned}$$

Then from (20), we infer that the model will have only cannabis-free equilibrium for $\mathcal{R}_0 < 1$ and unique cannabis persistent equilibrium for $\mathcal{R}_0 > 1$. It is important to observe that if there is no double exposure (i.e., $\delta_1 = \delta_2 = 0$) and there is relapse (i.e., $\beta_2 \neq 0$), then (19) reduces to

$$g(A) = b_2 A^2 + b_1 A + b_0 = 0, \tag{21}$$

where

$$\begin{aligned} b_2 &= \beta_1\beta_2(Q-\Psi_2) > 0, \\ b_1 &= \mu Q\beta_1 - \mu Q\beta_2\left(-1+\mathcal{R}_0+\frac{\Psi_2}{Q}\right), \\ b_0 &= Q\mu^2 - \Lambda\mu\beta_1 = Q\mu^2(1-\mathcal{R}_0). \end{aligned}$$

Then the model still has a backward bifurcation when $b_1 < 0$ and $\mathcal{R}_0 < 1$. Therefore, to have a model without a backward bifurcation, we need also to avoid relapse. Avoiding relapse may be achieved through the introduction of educational programs that lead to individuals staying clean after rehabilitation. Hence, in the absence of double exposure and relapse, we claim the following two results.

Theorem 3.4. *Considering the model (1)-(4) in the absence of relapse and double exposure, the cannabis-free equilibrium is globally asymptotically stable (GAS) whenever* $\mathcal{R}_0 \leq 1$.

Proof. To prove the global stability of the cannabis-free equilibrium, we use LaSalle Invariance Principle [10].

We consider the function

$$V : \Omega \to \mathbf{R},\ V(E) = A,$$

where $E = (S, A, T, R)$. It is clear that V is positive definite (i. e. $V(E_0) = 0$ and $V(E) > 0$ for $E_0 \neq E \in \Omega$). Denote by $f(S, A, T, R)$ the vector-function in the right-side of (1)-(4) with $\delta_1 = \delta_2 = \beta_2 = 0$ and by $\dot{V}$ the directional derivative of V in the direction of $f(S, A, T, R)$. Then we obtain

$$\begin{aligned} \dot{V} &= \nabla V.f(S,A,T,R), \\ &= (0,1,0,0).f(S,A,T,R), \\ &= (\beta_1 S - (\mu+\alpha+\nu+\gamma))A \\ &\leq (\beta_1\frac{\Lambda}{\mu} - (\mu+\alpha+\nu+\gamma))A, \quad \text{because} \quad S \leq \frac{\Lambda}{\mu} \\ &= (\mu+\alpha+\nu+\gamma)(\mathcal{R}_0-1)A. \end{aligned}$$

Thus, $\dot{V} \leq 0$ on Ω if $\mathcal{R}_0 \leq 1$. Hence, V is a Lyapunov function for E_0 on Ω. Furthermore,

$$\dot{V} = 0 \Leftrightarrow E = E_0.$$

Hence, the largest invariant set contained in $\mathcal{M} = \left\{E \in \Omega : \dot{V} = 0\right\}$ is $\{E_0\}$, i. e., $E(t) \to E_0$

as $t \to \infty$. Therefore, we conclude by LaSalle Invariance Principle [10] that the cannabis-free equilibrium E_0 of the model with $\delta_1 = \delta_2 = \beta_2 = 0$ is GAS on Ω for $\mathcal{R}_0 \leq 1$. This completes the proof of the theorem. □

The global asymptotic stability of the cannabis-free equilibrium point guaranteed by Theorem 3.4 is illustrated in Fig. 3.

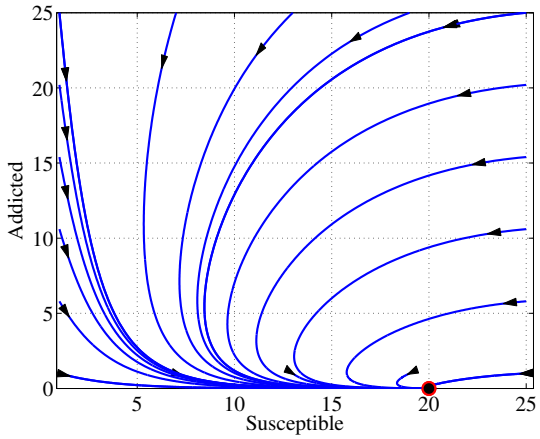


Figure 3: Numerical simulations supporting the GAS of the cannabis-free equilibrium.

Theorem 3.5. *Considering the model (1)-(4) with $\delta_1 = \delta_2 = \beta_2 = 0$, the unique cannabis persistent equilibrium E^* guaranteed by (20) is GAS whenever $\mathcal{R}_0 > 1$.*

Proof. We prove this theorem by using the LaSalle Invariance Principle [10] with the Lyapunov function defined on

$$\Omega_0 = \Big\{E = (S, A, T, R) \in \Omega : S, A, T, R > 0\Big\},$$

such that

$$V(E) = \left[S - S^* - S^* \ln\left(\frac{S}{S^*}\right)\right] + \left[A - A^* - A^* \ln\left(\frac{A}{A^*}\right)\right]. \tag{22}$$

It is possible to show that V is positive definite, i.e., $V(E^*) = 0$ and $V(E) > 0$ for $E^* \neq E \in \Omega_0$. The directional derivative of V along a solution of (1)-(4) is

$$\begin{aligned} \dot{V} &= \left(1 - \frac{S^*}{S}\right)\dot{S} + \left(1 - \frac{A^*}{A}\right)\dot{A}, \\ &= \left(1 - \frac{S^*}{S}\right)\left[\Lambda - (\beta_1 A + \mu)S\right] + \left(1 - \frac{A^*}{A}\right)\left[\beta_1 S - (\mu + \alpha + \nu + \gamma)\right] A. \end{aligned} \tag{23}$$

At the endemic equilibrium, we obtain

$$\Lambda = (\beta_1 A^* + \mu)S^* \quad \text{and} \quad \beta_1 S^* = \mu + \alpha + \nu + \gamma. \tag{24}$$

Plunging (24) into (23) gives

$$\dot{V} = \left(1 - \frac{S^*}{S}\right)\left[(\beta_1 A^* + \mu)S^* - (\beta_1 A + \mu)S\right] + \left(1 - \frac{A^*}{A}\right)\left[\beta_1 S - \beta_1 S^*\right] A. \tag{25}$$

Further simplifications of (25) give

$$\begin{aligned}
\dot{V} &= -\mu\frac{(S-S^*)^2}{S} + \beta_1 A^* S^* \left(1 - \frac{A}{A^*}\frac{S}{S^*}\right)\left(1 - \frac{S^*}{S}\right) + \beta_1 A^* S^* \left(1 - \frac{A}{A^*}\right)\left(1 - \frac{S}{S^*}\right), \\
&\leq -\mu\frac{(S-S^*)^2}{S} + \beta_1 A^* S^* \left(1 - \frac{S^*}{S}\right) + \beta_1 A^* S^* \left(1 - \frac{S}{S^*}\right), \\
&= -\mu\frac{(S-S^*)^2}{S} + \beta_1 A^* S^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right).
\end{aligned}$$

By using the arithmetic-geometric mean inequality (i.e. $a_1 + a_2 + \cdots + a_n \geq n\sqrt[n]{a_1 a_2 \ldots a_n}$), we infer that

$$\dot{V}(E) \leq 0 \quad \text{for all} \quad E \in \Omega_0.$$

Furthermore

$$\dot{V} = 0 \Leftrightarrow E = E^*.$$

Thus, the largest invariant subset contained in the set

$$\mathcal{M} = \left\{E \in \Omega_0 : \dot{V} = 0\right\}$$

is the set $\{E^*\}$. Hence, by LaSalle Invariance Principle, the endemic equilibrium is GAS for $\mathcal{R}_0 > 1$. □

The global asymptotic stability of the cannabis persistent equilibrium is depicted in Figure 4.

4 Application of the model

In this section we apply the proposed model to the available data. A sensitivity analysis and numerical simulations will also be provided.

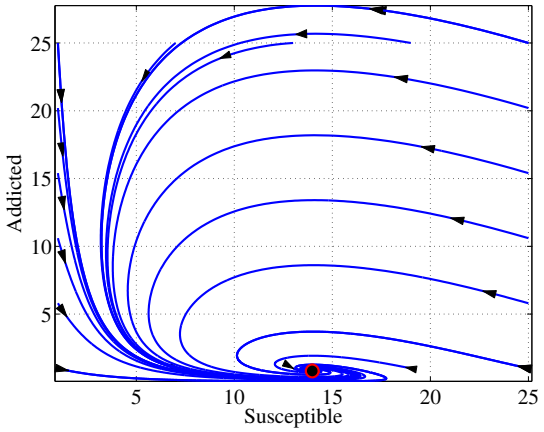


Figure 4: The GAS of the cannabis persistent equilibrium for $\mathcal{R}_0 = 1.7298$.

4.1 Parameter estimation

KwaZulu Natal has 10.27 million of inhabitants [16]. This province is the second largest province in South Africa. Its population has increased from 8.5 million in 1996 to 10.27 million in 2011. The growth is due to migration from other provinces. As an application of the system (1)−(4), we fit the model to data from the South African Community Epidemiology Network on Drug Use (SACENDU) [15]. We model the cannabis epidemic as from 1996 to 2013, due to the availability of documented data. The table below shows the data of individuals seeking treatment for cannabis as their primary substance of abuse at specialised treatment centres in Durban and KwaZulu Natal Province respectively. The data was collected from 1996 to 2013 on a six month interval by SACENDU.

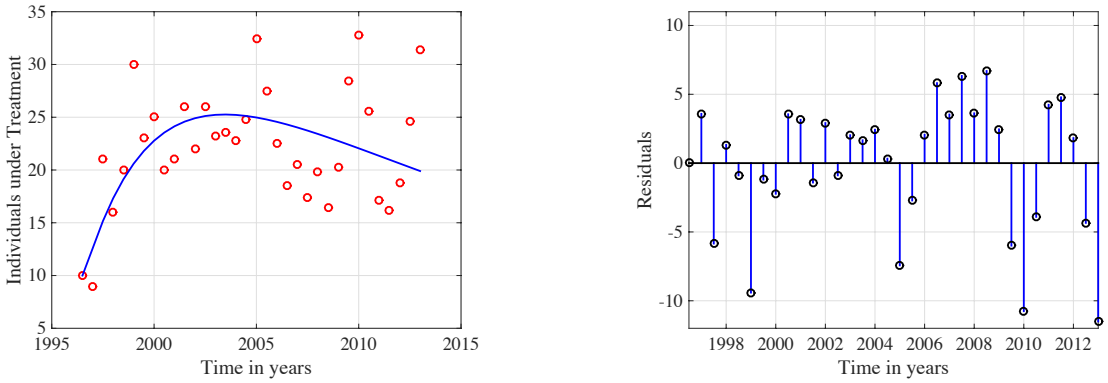
Year	96b	97a	97b	98a	98b	99a	99b	00a	00b	01a	01b	02a	02b
Users	10	9	21	16	20	30	23	25	20	21	26	22	26

Year	03a	03b	04a	04b	05a	05b	06a	06b	07a	07b	08a	08b	09a
Users	23.2	23.6	22.8	24.8	32.4	27.5	22.5	18.5	20.5	17.4	19.8	16.4	20.3

Year	09b	10a	10b	11a	11b	12a	12b	13a
Users	28.4	32.8	25.6	17.1	16.2	18.8	24.6	31.5

Table 3: Primary Cannabis abuse for the period of 1996b to 2013a in %

In Figure 5 (a) we show a representation of the proposed model fitted to the data in Table 3 for individual seeking treatment for Cannabis as their primary substance. To support the fitting, we plot the residuals in Figure 5 (b). It is clear that the model fits well for the corresponding parameters given in Table 4.



(a). Data fitting to the model. (b). Distribution of residuals.

Figure 5: Illustration of the data fitting to the model.

Parameter	Value	Source
Λ	0.0400	[13]
μ	0.0200	[13]
α	0.0300	[13]
γ	0.0110	[13]
β_1	0.121	Fitting
β_2	0.0443	Fitting
δ_1	0.164	Fitting
δ_2	0.822	Fitting
ν	0.0789	Fitting
σ	0.172	Fitting

Table 4: Parameter values used in the simulations

4.2 Sensitivity analysis

The basic reproduction number $\mathcal{R}_0$ is an important quantity that depends on the parameters involved in the system of differential equations (1)-(4). In this section, we would like to know how $\mathcal{R}_0$ responds to the changes in the parameters. The change in the value of $\mathcal{R}_0$ with respect to a changes in the values of the parameters is measured by the derivative of this quantity with respect to that parameter. Mathematically, the sensitivity of $\mathcal{R}_0$ with respect

to a parameter p is given by [12],

$$\gamma_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p}. \tag{26}$$

A much more powerful tool is the normalized sensitivity index of $\mathcal{R}_0$, which gives the change in the value of $\mathcal{R}_0$ with respect to the change in the parameter p and is given by

$$\mathcal{E}_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p}\frac{p}{\mathcal{R}_0} = \frac{\triangle \mathcal{R}_0 \%}{\triangle p \%}. \tag{27}$$

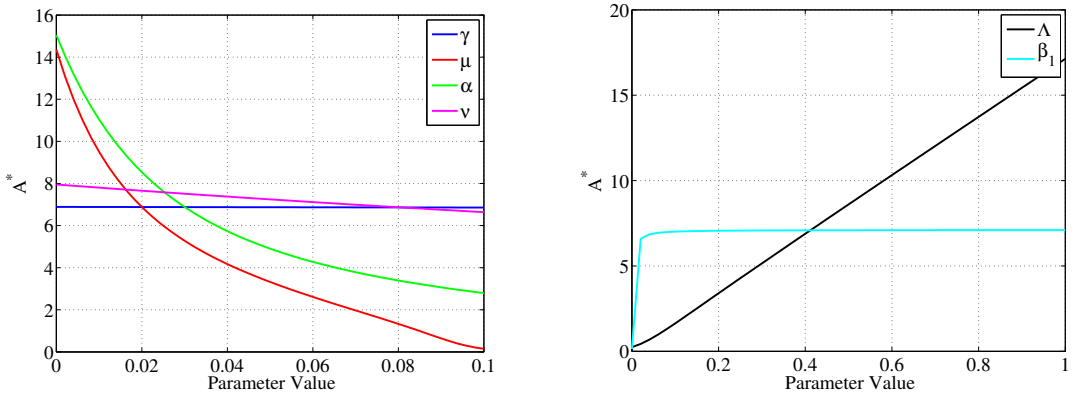
Hence, we infer that if p changes by $y\%$, then $\mathcal{R}_0$ will change by $\mathcal{E}_p^{\mathcal{R}_0} y\%$. The sensitivity index of $\mathcal{R}_0$ with respect to the parameter p is positive if $\mathcal{R}_0$ is increasing with respect to p and negative if $\mathcal{R}_0$ is decreasing with respect to p. This analysis helps us to know the sensitive parameters for the control strategy of the epidemic. The calculation of sensitive index of $\mathcal{R}_0$ at the baseline parameter values of the model is given in Table 5.

Parameter	Baseline Value	Sensitivity index	Source
Λ	0.0400	1.0000	[13]
β_1	0.1210	1.0000	Fitting
μ	0.0200	-1.1430	[13]
α	0.0300	-0.2144	[13]
ν	0.0789	-0.5640	Fitting
γ	0.0110	-0.0786	[13]

Table 5: Table for the sensitivity index of $\mathcal{R}_0(= 1.7298)$ with respect to each parameter in (13).

The identification of the key parameters for the cannabis transmission is crucial in designing effective control strategies. Hence, by using the reproduction number $\mathcal{R}_0$ as the response function, the table can be used to propose effective control strategies to avoid direct and indirect contacts with the potential cannabis sources. In Table 5, the negative sign indicates that $\mathcal{R}_0$ is decreasing when the corresponding parameter is increasing. In a similar way, a positive sign indicates that $\mathcal{R}_0$ increases when the corresponding parameter is increased.

The cannabis persistent equilibrium A^* decreases as the γ, μ, α and ν increase is presented in Figure 6 (a) while Figure 6 (b) explains that cannabis persistent equilibrium A^* increases as Λ and β_1 increase.



(a) (b)

Figure 6: (a): Sensitivity analysis with respect to γ, μ, α and ν. (b): Sensitivity analysis with respect to Λ and β_1.

5 Conclusion

Addiction to alcohol and heroin in a population are studied in [4] and [13], respectively. In this work, we presented the mathematical analysis of cannabis epidemic model in the population. When there is double exposure to the cannabis source and a possibility of re-addiction of cannabis in the population, the classical control strategy $\mathcal{R}_0 < 1$ is not sufficient. Due to the existence of backward bifurcation phenomena, cannabis epidemic can persist in the population. The mathematical analysis confirmed that the cannabis epidemic dies out from the population whenever there is no double exposure to the cannabis source and re-addiction of cannabis for $\mathcal{R}_0 < 1$. In this case, the cannabis-free endemic equilibrium is globally asymptotically stable for $\mathcal{R}_0 < 1$. Moreover, in the absence of backward bifurcation, it is proved that the cannabis persistent equilibrium point is globally asymptotically stable for $\mathcal{R}_0 > 1$. We also fitted the model to data on rehabilitation with the objective of using the model parameters that give the best fit to obtain the incidence curve. The sensitivity index of $\mathcal{R}_0$ with respect to the parameters involved in the model is discussed. The index helps the policy makers to identify the key parameters such as Λ and β_1 which contribute for the increment of $\mathcal{R}_0$ in the population in oder to propose the right control strategies. Whenever these parameters increase, the basic reproduction number $\mathcal{R}_0$ also increases correspondingly. The other information for the policy makers is increasing μ, α, ν and γ result in a decrease in $\mathcal{R}_0$.

This work offers many opportunities for improvement and extensions of the proposed model.

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