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Global behaviour of a heroin epidemic model with distributed delays

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ABSTRACT

In this paper, we study a heroin epidemic model with distributed time delays. The basic reproduction number $\mathcal{R}_0$ for the model is identified and the threshold property of $\mathcal{R}_0$ is established. It is shown that drug-free equilibrium is globally asymptotically stable if $\mathcal{R}_0 < 1$. When $\mathcal{R}_0 > 1$, there is a disease endemic equilibrium which is locally asymptotically stable, it is proved that the disease is uniformly persistent in the population, and explicit formulae are obtained by which the eventual lower bound of the drug user individuals can be computed.

1. Introduction

Over the past two decades, China has faced a dramatic increase in illicit drug abuse accompanying rapid economic reform and development [1]. In 2000, heroin was the first choice among drug users (rising from 83.4% in 1993 to 95.9% in 2000), and its most frequent routes of delivery were intravenous injection (25%) and inhalation [2]. In addition to their deleterious somatic and psychological effects, heroin abuse and dependence constitute one of the most important modes of transmitting human immunodeficiency virus (HIV) and the Hepatitis C virus (HCV) [3–5].

Drug abuse and dependence are gaining increasing attention from politicians and the medical community in China due to their major social and public health implications [6,7]. Treatment of heroin users or users of other drugs such as crack cocaine is a costly procedure and is a major burden on the health system of any country. Likewise, treatment of individuals with alcohol problems is also a major issue. Thus more progress needs to be made towards reducing harmful drinking and its impact as a contributor to ill health and inequalities. Mathematical modelling is a means to provide a general insight for how classes of drug takers behave, and as such, could hopefully becomes a useful device to aid specialist teams in devising treatment strategies. While social problems such as alcohol and drug use have been referred to in terms of epidemics, little has been published on the application of mathematical modelling methods to such problems.

Recently, an ordinary differential equation (ODE) compartmental model for heroin epidemics was formulated by White and Comiskey [8]. In this model the population is assumed to be of constant size, and is divided into three compartments depending on disease status, namely susceptibles, heroin users and heroin users in treatment. Assuming standard incidence, a basic reproduction number R_0 is identified. Sensitivity analysis is performed on R_0 and it is then used to examine the stability of the system. A condition under which a backward bifurcation may exist is found, as are conditions that permit the existence of one or more endemic equilibria. Furthermore, this ODE model was revisited by Mulone and Straughan [9], the authors proved that the positive equilibrium of the White and Comiskey [8] model is stable.

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Our aim is to formulate a delayed three compartmental model for heroin epidemics. We allow for a relapse distribution, and assume that the relapse time is not a constant, thus leads to a delay differential equation.

In Section 2, we formulate our SU_1U_2 model for heroin epidemics and some basic results are given. The basic reproduction number $\mathcal{R}_0$ is calculated and the drug-free equilibrium is shown to be globally asymptotically stable if $\mathcal{R}_0 < 1$ in Section 3. If $\mathcal{R}_0 > 1$, we obtain the local stability of a positive (endemic) equilibrium (in Section 4), and we show the permanence of the disease (in Section 5). We conclude with some discussions in Section 6.

2. Model formulation

White and Comiskey [8] have produced an interesting model for the dynamics of heroin users. Their model is based on the equations

$$\begin{cases} \dot{S} = \Lambda - \dfrac{\beta_1 U_1 S}{N} - \mu S, \\ \dot{U}_1 = \dfrac{\beta_1 U_1 S}{N} - pU_1 + \dfrac{\beta_3 U_1 U_2}{N} - (\mu + \delta_1)U_1, \\ \dot{U}_2 = pU_1 - \dfrac{\beta_3 U_1 U_2}{N} - (\mu + \delta_2)U_2. \end{cases} \tag{2.1}$$

Here $S, U_1, U_2, N(=S+U_1+U_2)$ are the number of susceptibles in the population, the numbers of drug users not in treatment, the number of drug users in treatment, and the total population size, respectively.

The quantities Λ, μ, δ_1, δ_2, β_1, β_3, p are as follows:

Λ: The number of individuals in the general population entering the susceptible population.

μ: The natural death rate of the general population.

δ_1: A removal rate that includes drug-related deaths of users not in treatment and a spontaneous recovery rate; individuals not in treatment who stop using drugs but are no longer susceptible.

δ_2: A removal rate that includes drug-related deaths of users in treatment and a rate of successful "care" that corresponds to recovery to a drug-free life and immunity to drug addiction for the duration of the modelling time period.

β_1: The probability of becoming a drug user.

β_3: The probability of a drug user in treatment relapsing to untreated use.

p: The probability of drug users who enter treatment.

The assumptions of the model are clearly stated in [8]. Among these assumptions the population is assumed to be of constant size, i.e.,

$$\Lambda = \mu S + (\mu + \delta_1)U_1 + (\mu + \delta_2)U_2. \tag{2.2}$$

In the present work, we consider the delay effect in those returning to untreated drug taking from a treatment programme. Relapse to frequent heroin use is related to many psychological and behavioural factors, such as perceived stress, negative affects, positive outcome expectancies about substance use, coping behaviours, etc. Having a drug-using partner or having no partner were also significantly associated with a higher risk of relapse. So the time needed to return to untreated drug varies according to drug users' different temporal, social, and physical contexts. In order to make the model more realistic, we assume that this delay is not the same for the whole drug users in treatment, but it is a distributed parameter over the interval $[0, \tau]$, where τ is the limit superior of the delay.

With these assumptions, we obtain the following delay differential equation

$$\begin{cases} \dot{S} = \Lambda - \beta S U_1 - \mu S, \\ \dot{U}_1 = \beta S U_1 - pU_1 + \displaystyle\int_0^\tau f(s) p U_1(t-s) \mathrm{e}^{-(\mu+\delta_2)s} \mathrm{d}s - (\mu + \delta_1)U_1, \\ \dot{U}_2 = pU_1 - (\mu + \delta_2)U_2 - \displaystyle\int_0^\tau f(s) p U_1(t-s) \mathrm{e}^{-(\mu+\delta_2)s} \mathrm{d}s. \end{cases} \tag{2.3}$$

Here, the drug user incidence is modelled using mass action incidence. β is the probability of becoming a drug user. $\int_0^\tau f(s)\mathrm{d}s = 1, f$ is non-negative and continuous, is the distribution function of delay s.

The first two terms in the right-hand side of the third equation in (2.3) are easy to interpret. They are, respectively, conversion of drug users not in treatment to drug users in treatment via treatment and the death rate of drug users in treatment. The last term $\int_0^\tau f(s)pU_1(t-s)\mathrm{e}^{-(\mu+\delta_2)s}\mathrm{d}s = \int_{t-\tau}^t f(t-\xi)pU_1(\xi)\mathrm{e}^{-(\mu+\delta_2)(t-\xi)}\mathrm{d}\xi$ in the third equation in (2.3) tells us the rate at which the drug users in treatment relapse to untreated use. At time t, the individuals in treatment have each acquired treatment at a time $\xi \in (t-\tau, t)$ with the rate $pU_1(\xi)$. The probability that the individual will survive from becoming treated at time ξ until relapsing to drug user at time t is

$$\mathrm{e}^{-(\mu+\delta_2)(t-\xi)}.$$

Then ξ running from $t-\tau$ to t totals up the contributions from all possible times at which drug users in treatment might have relapsed to the untreated use.

The initial conditions of (2.3) take the form of

$$S(\theta) = \phi_1(\theta), \qquad U_1(\theta) = \phi_2(\theta), \qquad U_2(\theta) = \phi_3(\theta), \quad -\tau \le \theta \le 0, \tag{2.4}$$

where $\phi = (\phi_1, \phi_2, \phi_3) \in C([-\tau, 0], \mathbb{R}^3_+)$, the space of continuous functions mapping $[-\tau, 0]$ into $\mathbb{R}^3_+$. For biological reasons, we further assume that $\phi_i(0) > 0$, $i = 1, 2, 3$. And for the continuity of the solutions to system (2.3), in this paper, we require

$$U_2(0) = \int_0^\tau \int_{-s}^0 f(s) p U_1(x) e^{(\mu+\delta_2)x} dx ds. \tag{2.5}$$

By the third equation of system (2.3), the initial conditions (2.5), we have

$$U_2(t) = \int_0^\tau \int_{t-s}^t f(s) p U_1(x) e^{-(\mu+\delta_2)(t-x)} dx ds. \tag{2.6}$$

Lemma 2.1. *Assume $(S(t), U_1(t), U_2(t))$ is the solution of system (2.3), then it follows that $S(t) > 0$, $U_1(t) > 0$, $U_2(t) > 0$ for all finite $t \ge 0$.*

Proof. On the face $S(t) = 0$, $\dot{S}(t) = \Lambda > 0$, then $S(t) > 0$ for all $t \ge 0$. Assume there is a $t_1 > 0$ such that $U_1(t) > 0$ for $t \in [0, t_1)$ and $U_1(t_1) = 0$.

Let

$$h(t) = \int_0^\tau f(s) p U_1(t-s) e^{-(\mu+\delta_2)s} ds.$$

By the choice of t_1, $h(t_1) \ge 0$. Denote

$$a(t) = \beta S(t) - (p + \mu + \delta_1).$$

Using an integrating factor for (2.3) gives

$$U_1(t_1) = e^{\int_0^{t_1} a(s) ds} \left[U_1(0) + \int_0^{t_1} h(s) e^{-\int_0^s a(\xi) d\xi} ds \right] > 0.$$

This implies that such a $t_1 > 0$ cannot exist, and thus, $U_1(t) > 0$ for all finite $t \ge 0$. Using (2.6), we also have that $U_2(t) > 0$ for all finite $t \ge 0$, proving Lemma 2.1. □

Let

$$D = \left\{ (S, U_1, U_2) : S \ge 0, U_1 \ge 0, U_2 \ge 0, S + U_1 + U_2 \le \frac{\Lambda}{\mu} \right\}.$$

Lemma 2.2. *Let $(S(t), U_1(t), U_2(t))$ be the solution of (2.3) with initial condition in D, then the solution exists for $t \ge 0$ and remains in D.*

Proof. Non-negativity of $(S(t), U_1(t), U_2(t))$ follows from Lemma 2.1. The rate of change of the total population, obtained by adding all the equations in (2.3), is given by $\frac{dN}{dt} = \Lambda - \mu N - \delta_1 U_1 - \delta_2 U_2$, which implies that $N(t) \le (N(0) - \frac{\Lambda}{\mu}) e^{-\mu t} + \frac{\Lambda}{\mu} \le \frac{\Lambda}{\mu}$, it follows that $S(t)$, $U_1(t)$ and $U_2(t)$ are bounded. Therefore, the solution exists for all $t \ge 0$ and remains in D. □

3. Drug-free equilibrium

Since $U_2(t)$ is completely determined by $U_1(t)$, thus the following system can be separated from system (2.3):

$$\begin{cases} \dot{S} = \Lambda - \beta S U_1 - \mu S, \\ \dot{U}_1 = \beta S U_1 - p U_1 + \displaystyle\int_0^\tau f(s) p U_1(t-s) e^{-(\mu+\delta_2)s} ds - (\mu + \delta_1) U_1. \end{cases} \tag{3.1}$$

In the present paper, our main purpose is to study the global dynamics of our system (3.1). It is clear that the model has the drug-free equilibrium (DFE) $E_0 = (\frac{\Lambda}{\mu}, 0)$.

Let

$$\hat{f} = \int_0^\tau f(s) e^{-(\mu+\delta_2)s} ds \le 1 \tag{3.2}$$

and define

$$\mathcal{R}_0 = \frac{\beta\frac{\Lambda}{\mu}}{p+\mu+\delta_1-p\hat{f}}. \tag{3.3}$$

To interpret formula (3.3) for $\mathcal{R}_0$, note that the average time in the drug users not in treatment class on the first pass is $\frac{1}{p+\mu+\delta_1}$ and the probability of surviving this class is $\frac{p}{p+\mu+\delta_1}$. Since $\hat{f}$ is the probability of surviving the drug users in treatment class, thus, the total average time in the drug users not in treatment class (on multiple passes) is

$$\frac{1}{p+\mu+\delta_1}\left[1+\frac{p\hat{f}}{p+\mu+\delta_1}+\frac{p^2\hat{f}^2}{(p+\mu+\delta_1)^2}+\cdots\right]=\frac{1}{p+\mu+\delta_1-p\hat{f}}.$$

Multiplying this by $\beta\frac{\Lambda}{\mu}$ gives $\mathcal{R}_0$, which is the average number of new drug users produced by one drug users not in treatment introduced into a susceptible population [10]. Thus, $\mathcal{R}_0$ is the basic reproduction number, and acts as a threshold as is shown in the following result.

Theorem 3.1. *The system (3.1) always has the drug-free equilibrium $E_0 = (\frac{\Lambda}{\mu}, 0)$. If $\mathcal{R}_0 < 1$, then it is globally asymptotically stable; if $\mathcal{R}_0 > 1$, then it is unstable.*

Proof. The characteristic equation of system (3.1) at E_0 is

$$(z+\mu)\left[z-\frac{\beta\Lambda}{\mu}+p+\mu+\delta_1-p\int_0^\tau f(s)\mathrm{e}^{-(z+\mu+\delta_2)s}\mathrm{d}s\right]=0.$$

Hence, one characteristic root is $z=-\mu<0$, the others are the roots of

$$g(z)=z-\frac{\beta\Lambda}{\mu}+p+\mu+\delta_1-p\int_0^\tau f(s)\mathrm{e}^{-(z+\mu+\delta_2)s}\mathrm{d}s=0. \tag{3.4}$$

(i) Assume that $\mathcal{R}_0=\frac{\beta\frac{\Lambda}{\mu}}{p+\mu+\delta_1-p\hat{f}}>1$; then $g(0)=p+\mu+\delta_1-p\hat{f}-\beta\frac{\Lambda}{\mu}<0$, and $g(+\infty)=+\infty$. Hence $g(z)$ has at least one positive root and E_0 is unstable.

(ii) Assume now that $\mathcal{R}_0=\frac{\beta\frac{\Lambda}{\mu}}{p+\mu+\delta_1-p\hat{f}}<1$. Taking $z=u+\mathrm{i}v$ with $u, v\in\mathbb{R}$ in (3.4) and assuming that $u\geq 0$ gives

$$\left|u+p+\mu+\delta_1-\beta\frac{\Lambda}{\mu}+\mathrm{i}v\right|\leq|p\hat{f}|.$$

Thus, $(u+p+\mu+\delta_1-\beta\frac{\Lambda}{\mu})^2+v^2\leq p^2\hat{f}^2$ implying that $(u+p+\mu+\delta_1-\beta\frac{\Lambda}{\mu})^2-p^2\hat{f}^2\leq -v^2$ which is impossible if $p+\mu+\delta_1-\beta\frac{\Lambda}{\mu}-p\hat{f}>0$ (equivalently $\mathcal{R}_0<1$). Thus, if $\mathcal{R}_0<1$, then $u<0$ and the DFE is locally asymptotically stable.

To complete the proof of Theorem 3.1, we only need to show that E_0 is globally attractive under the condition $\mathcal{R}_0<1$. Consider the Lyapunov function $V_1(U_1(t))=\frac{1}{2}U_1^2(t)$. Then for those values of $t\geq\tau$ such that $V_1(U_1(t+s))\leq V_1(U_1(t))$ for $s\in[-\tau,0]$, the derivative of $V_1(U_1(t))$ along (3.1) is estimated as below:

$$\begin{aligned}
\dot{V}_1 &= \beta S(t)U_1^2(t)-(p+\mu+\delta_1)U_1^2(t)+U_1(t)\int_0^\tau f(s)pU_1(t-s)\mathrm{e}^{-(\mu+\delta_2)s}\mathrm{d}s\\
&\leq \beta S(t)U_1^2(t)-(p+\mu+\delta_1)U_1^2(t)+\frac{p}{2}\int_0^\tau f(s)[U_1^2(t)+U_1^2(t-s)]\mathrm{e}^{-(\mu+\delta_2)s}\mathrm{d}s\\
&\leq \beta\frac{\Lambda}{\mu}U_1^2(t)-(p+\mu+\delta_1)U_1^2(t)+pU_1^2(t)\int_0^\tau f(s)\mathrm{e}^{-(\mu+\delta_2)s}\mathrm{d}s\\
&= \beta\frac{\Lambda}{\mu}U_1^2(t)-(p+\mu+\delta_1)U_1^2(t)+p\hat{f}U_1^2(t)\\
&= -\beta\frac{\Lambda}{\mu}\left[\frac{1}{\mathcal{R}_0}-1\right]U_1^2(t).
\end{aligned} \tag{3.5}$$

Now by the assumption that $\mathcal{R}_0<1$ and a Lyapunov–Razumikhin type theorem (see, e.g., Bélair [11]), we conclude that $U_1(t)\to 0$ as $t\to\infty$. By system (3.1), it follows that $S(t)\to\frac{\Lambda}{\mu}$ as $t\to\infty$, proving Theorem 3.1. □

4. Endemic equilibrium

When $\mathcal{R}_0 > 1$, the DFE becomes unstable (from Theorem 3.1) and there exists an endemic equilibrium (EE) given by $E^* = (S^*, U_1^*) = (\frac{\Lambda}{\mu\mathcal{R}_0}, \frac{\mu(\mathcal{R}_0-1)}{\beta})$.

Local stability of the unique endemic equilibrium is now investigated. This is governed by the Jacobian matrix in S, U_1 variables from (3.1) with $S = S^*$ and $U_1 = U_1^*$. This leads to the following equation in the variable z given by

$$\begin{vmatrix} z + \beta U_1^* + \mu & \beta S^* \\ -\beta U_1^* & z - \beta S^* + p + \mu + \delta_1 - p\int_0^\tau f(s)\mathrm{e}^{-(z+\mu+\delta_2)s}\mathrm{d}s \end{vmatrix} = 0,$$

which can be written as

$$h_\tau(z) = z^2 + \left(p\hat{f} + \frac{\Lambda}{S^*} - p\int_0^\tau f(s)\mathrm{e}^{-(z+\mu+\delta_2)s}\mathrm{d}s\right)z + \frac{\Lambda}{S^*}\left(p\hat{f} - p\int_0^\tau f(s)\mathrm{e}^{-(z+\mu+\delta_2)s}\mathrm{d}s\right) + \beta^2 S^* U_1^* = 0. \tag{4.1}$$

Setting $z = 0$, gives

$$h_\tau(0) = \beta^2 S^* U_1^* > 0.$$

Setting $\tau = 0$, gives

$$h_0(z) = z^2 + \frac{\Lambda}{S^*}z + \beta^2 S^* U_1^*,$$

this equation has all coefficients positive, and so both roots of the polynomial have negative real parts. Therefore as $\tau = 0$, Eq. (4.1) is stable. Instability can occur for $\tau > 0$ only by roots crossing the finite imaginary axis. Without loss of generality, assume $z = \mathrm{i}y$, $y > 0$ be a root of (4.1). Then we have

$$\begin{aligned} &-y^2 + \left[p\hat{f} + \frac{\Lambda}{S^*} - p\int_0^\tau f(s)\mathrm{e}^{-(\mu+\delta_2)s}(\cos(ys) - \mathrm{i}\sin(ys))\mathrm{d}s\right]yi \\ &+\frac{\Lambda}{S^*}\left[p\hat{f} - p\int_0^\tau f(s)\mathrm{e}^{-(\mu+\delta_2)s}(\cos(ys) - \mathrm{i}\sin(ys))\mathrm{d}s\right] + \beta^2 S^* U_1^* = 0. \end{aligned}$$

Separating the real and imaginary parts gives

$$\begin{cases} \displaystyle\int_0^\tau pf(s)\mathrm{e}^{-(\mu+\delta_2)s}\left[y\sin(ys) + \frac{\Lambda}{S^*}\cos(ys)\right]\mathrm{d}s = -y^2 + p\frac{\Lambda}{S^*}\hat{f} + \beta^2 S^* U_1^*, \\ \displaystyle\int_0^\tau pf(s)\mathrm{e}^{-(\mu+\delta_2)s}\left[y\cos(ys) - \frac{\Lambda}{S^*}\sin(ys)\right]\mathrm{d}s = \left(p\hat{f} + \frac{\Lambda}{S^*}\right)y. \end{cases} \tag{4.2}$$

Multiplying the first equation by $\frac{\Lambda}{S^*}$ and the second equation by y, then adding them together gives

$$\left[\left(\frac{\Lambda}{S^*}\right)^2 + y^2\right]p\int_0^\tau f(s)\mathrm{e}^{-(\mu+\delta_2)s}\cos(ys)\mathrm{d}s = \left[\left(\frac{\Lambda}{S^*}\right)^2 + y^2\right]p\hat{f} + \Lambda\beta^2 U_1^*. \tag{4.3}$$

Since $\int_0^\tau f(s)\mathrm{e}^{-(\mu+\delta_2)s}\cos(ys)\mathrm{d}s \le \int_0^\tau f(s)\mathrm{e}^{-(\mu+\delta_2)s}\mathrm{d}s = \hat{f}$, then (4.3) does not hold and no pure imaginary root $z = \mathrm{i}y$ can exist. It follows that all roots of (4.1) have negative real parts, and the endemic equilibrium is locally asymptotically stable.

Theorem 4.1. *If $\mathcal{R}_0 > 1$, then the endemic equilibrium E^* is locally asymptotically stable.*

5. Permanence

We now consider the issue of disease persistence.

Theorem 5.1. *$\mathcal{R}_0 = \frac{\beta\frac{\Lambda}{\mu}}{p+\mu+\delta_1-p\hat{f}} > 1$, then there exists an $\epsilon > 0$ such that every solution $(S(t), U_1(t))$ of system (3.1) satisfies*

$$\liminf_{t\to\infty} S(t) \ge \epsilon, \qquad \liminf_{t\to\infty} U_1(t) \ge \epsilon.$$

Proof. Consider a positive root $(S(t), U_1(t))$ of (3.1), and then define $V_2(t) = U_1(t) + \int_0^\tau\int_{t-s}^t f(s)pU_1(\xi)\mathrm{e}^{-(\mu+\delta_2)s}\mathrm{d}\xi\mathrm{d}s$. By (3.1), we have

$$\dot{V}_2 = \beta S(t)U_1(t) - (p+\mu+\delta_1-p\hat{f})U_1(t) = (p+\mu+\delta_1-p\hat{f})\left[\frac{\mathcal{R}_0}{\frac{\Lambda}{\mu}}S(t) - 1\right]U_1(t). \tag{5.1}$$

Since $\mathcal{R}_0 > 1$, we have $\bar{U} = \frac{\mu\mathcal{R}_0}{\beta}(1 - \frac{1}{\mathcal{R}_0}) > 0$. We then claim that for any $t_0 > 0$, it is impossible that $U_1(t) \le \frac{\bar{U}}{2}$ for all $t \ge t_0$. Suppose the contrary. Then there is a $t_0 > 0$ such that $U_1(t) \le \frac{\bar{U}}{2}$ for all $t \ge t_0$. By the first equation of (3.1), for $t \ge t_0$,

$$\dot{S}(t) \ge \Lambda - \left(\beta\frac{\bar{U}}{2} + \mu\right) S(t),$$

it follows that

$$\begin{aligned} S(t) &\ge S(t_0)\mathrm{e}^{-(\beta\frac{\bar{U}}{2}+\mu)(t-t_0)} + \frac{\Lambda}{(\beta\frac{\bar{U}}{2}+\mu)}(1 - \mathrm{e}^{-(\beta\frac{\bar{U}}{2}+\mu)(t-t_0)}) \\ &> \frac{\Lambda}{(\beta\frac{\bar{U}}{2}+\mu)}(1 - \mathrm{e}^{-(\beta\frac{\bar{U}}{2}+\mu)(t-t_0)}) \\ &= \frac{2\Lambda}{\mu(\mathcal{R}_0+1)}(1 - \mathrm{e}^{-\frac{\mu(\mathcal{R}_0+1)}{2}(t-t_0)}). \end{aligned} \tag{5.2}$$

We can choose a $T_1 > 0$ such that

$$\frac{1}{4}\left(1 - \frac{1}{\mathcal{R}_0}\right) = \mathrm{e}^{-\frac{\mu(\mathcal{R}_0+1)}{2}T_1},$$

which implies that

$$S(t) > \frac{(3\mathcal{R}_0+1)\Lambda}{2\mu\mathcal{R}_0(\mathcal{R}_0+1)} \triangleq \bar{S}, \quad \text{for } t \ge t_0 + T_1. \tag{5.3}$$

Then by (5.1), we have

$$\dot{V}_2 > (p + \mu + \delta_1 - p\hat{f})\left[\frac{\mathcal{R}_0}{\frac{\Lambda}{\mu}}\bar{S} - 1\right] U_1(t), \quad \text{for } t \ge t_0 + T_1. \tag{5.4}$$

Set

$$\underline{U} = \min_{\theta\in[-\tau,0]} U_1(t_0 + T_1 + \tau + \theta).$$

We will show that $U_1(t) \ge \underline{U}$ for all $t \ge t_0 + T_1$. Otherwise, there is a $T_2 \ge 0$ such that $U_1(t) \ge \underline{U}$ for all $t_0 + T_1 \le t \le t_0 + T_1 + \tau + T_2$, $U_1(t_0 + T_1 + \tau + T_2) = \underline{U}$, and $\dot{U}_1(t_0 + T_1 + \tau + T_2) \le 0$. However, the second equation of (3.1) and (5.3) imply, that for $t = t_0 + T_1 + \tau + T_2$,

$$\begin{aligned} \dot{U}_1 &\ge \beta S\underline{U} - (p + \mu + \delta_1)\underline{U} + \int_0^\tau f(s)p\underline{U}\mathrm{e}^{-(\mu+\delta_2)s}\mathrm{d}s \\ &= [\beta S - (p + \mu + \delta_1) + p\hat{f}]\underline{U} \\ &> [\beta\bar{S} - (p + \mu + \delta_1) + p\hat{f}]\underline{U} \\ &= \frac{\beta\Lambda(\mathcal{R}_0 - 1)}{2\mu\mathcal{R}_0(\mathcal{R}_0+1)}\underline{U} > 0, \end{aligned} \tag{5.5}$$

a contradiction. Thus, $U_1(t) \ge \underline{U}$ for all $t \ge t_0 + T_1$. Eq. (5.4) leads to

$$\dot{V}_2 > (p + \mu + \delta_1 - p\hat{f})\frac{\mathcal{R}_0 - 1}{2(\mathcal{R}_0+1)}\underline{U}, \quad \text{for } t \ge t_0 + T_1, \tag{5.6}$$

which implies that $V_2(t) \to \infty$ as $t \to \infty$. This contradicts with $V_2(t) \le \frac{\Lambda}{\mu}(1 + p\tau\hat{f})$. Hence, the claim is proved.

By the claim, we are left to consider two possibilities.

(i) First, $U_1(t) \ge \frac{\bar{U}}{2}$ for all large t.

(ii) $U_1(t)$ oscillates about $\frac{\bar{U}}{2}$ for all large t.

Define

$$\tilde{U} = \frac{\bar{U}}{2}\mathrm{e}^{-(p+\mu+\delta_1)(T_1+\tau)}. \tag{5.7}$$

We will show that $U_1(t) \geq \tilde{U}$ for all large t. The conclusion is clear for case (i). For case (ii), let t_1 and t_2 satisfy

$$U_1(t_1) = U_2(t_2) = \frac{\bar{U}}{2},$$
$$U_1(t) < \frac{\bar{U}}{2} \quad \text{for } t_1 < t < t_2.$$

If $t_2 - t_1 \leq T_1 + \tau$, since $\dot{U}_1(t) > -(p + \mu + \delta_1)U_1(t)$, it follows that $U_1(t) \geq \tilde{U}$ for $t_1 \leq t \leq t_2$. If $t_2 - t_1 \geq T_1 + \tau$, again we obtain $U_1(t) \geq \tilde{U}$ for $t_1 \leq t \leq t_1 + T_1 + \tau$. Then, proceeding exactly as the proof for above claim, we see that $U_1(t) \geq \tilde{U}$ for $t_1 + T_1 + \tau \leq t \leq t_2$. Thus, $U_1(t) \geq \tilde{U}$ for $t \in [t_1, t_2]$. By the arbitrariness of the interval $[t_1, t_2]$, we conclude that $U_1(t) \geq \tilde{U}$ for all large t in the second case. Based on our above discussions, the choices of T_1 and $\tilde{U}$ are independent of the positive solution, and we actually have proved that any positive solution of (3.1) satisfies $U_2(t) > \tilde{U}$ for all large t. The proof is complete. □

Corollary 5.1. *If $\mathcal{R}_0 > 1$, then system (3.1) is permanent.*

Proof. By (3.1) and Lemma 2.2, we have $\dot{S}(t) \geq \Lambda - (\beta\frac{\Lambda}{\mu} + \mu)S(t)$ for all $t \geq 0$, it follows that $S(t) \geq \frac{\Lambda}{2(\beta\frac{\Lambda}{\mu}+\mu)}$ for large t, which is independent of initial values. Then by Theorem 5.1 and Lemma 2.2, we conclude that system (3.1) is permanent. □

6. Discussions

In this paper, we have modified the White and Comiskey heroin epidemic model, we take the mass action incidence and delete the restriction (2.2), which means that the total population is not a constant, we include a delay effect in those returning to untreated drug taking from a treatment programme, and finally developed a delay SU_1U_2 model. We have then shown that the model is well-posed. We have also shown that the basic reproduction number characterizes the disease transmission dynamics: if $\mathcal{R}_0 < 1$, there exists only the drug-free equilibrium which is globally asymptotically stable; and if $\mathcal{R}_0 > 1$ then there is a disease endemic equilibrium and the disease persists.

To examine the sensitivity of $\mathcal{R}_0$ to its parameters, we choose to focus on one of two parameters: either p, the proportion of users who enter treatment or β, the probability of an individual becoming a drug user. Following Arriola and Hyman [12], the normalized forward sensitivity index with respect to β and p are calculated:

$$\frac{\frac{\partial \mathcal{R}_0}{\mathcal{R}_0}}{\frac{\partial \beta}{\beta}} = \frac{\beta}{\mathcal{R}_0}\frac{\partial \mathcal{R}_0}{\partial \beta} = \beta\left(\frac{p + \mu + \delta_1 - p\hat{f}}{\beta\frac{\Lambda}{\mu}}\right)\left(\frac{\frac{\Lambda}{\mu}}{p + \mu + \delta_1 - p\hat{f}}\right) = 1,$$
$$\frac{\frac{\partial \mathcal{R}_0}{\mathcal{R}_0}}{\frac{\partial p}{p}} = \frac{p}{\mathcal{R}_0}\frac{\partial \mathcal{R}_0}{\partial p} = \frac{-p(1-\hat{f})}{p + \mu + \delta_1 - p\hat{f}}.$$

Thus, it is concluded that $\mathcal{R}_0$ is most sensitive to changes in β. An increase in β will bring about an increase of the same proportion in $\mathcal{R}_0$ (equally, a decrease in β will bring about an equivalent decrease in $\mathcal{R}_0$; they are directly proportional). While p has an inversely proportional relationship with $\mathcal{R}_0$; an increase in p will bring about a decrease in $\mathcal{R}_0$, however, the size of the decrease will be proportionally smaller. Given $\mathcal{R}_0$'s sensitivity to β and in the knowledge that a treatment cycle exists (individuals who enter treatment are likely to relapse and re-enter treatment), it seems sensible to focus efforts on the reduction of β. In other words, this sensitivity analysis tells us that prevention is better than cure; efforts to increase prevention are more effective in controlling the spread of habitual drug use than efforts to increase the numbers of individuals accessing treatment. Also $\frac{\partial \mathcal{R}_0}{\partial \hat{f}} = \frac{\beta\frac{\Lambda}{\mu}p}{(p+\mu+\delta_1-p\hat{f})^2} > 0$, then as $\hat{f}$ increases, $\mathcal{R}_0$ increases. Since $\hat{f}$ is the probability leaving the treatment class and then entering the untreated class, then long time treatment is beneficial to control the spread of habitual drug use.

The aim of this model is to identify parameters of interest for study in the drug-using career, with a view to informing and assisting policy-maker in targeting prevention and treatment resources for maximum effectiveness.

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