

Department of Mathematics and Statistics

Stability analysis of drinking epidemic models and investigation of optimal treatment strategy

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Declaration

To the best of my knowledge and belief, this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

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Abstract

In this research we first propose a more realistic drinking epidemic model, namely the SPARS (susceptible-periodic-alcoholic-recovered drinkers) model. The basic reproduction number, R_0 , is then derived, and then we study the dynamical behaviours of both drinking free equilibrium and drinking persistent equilibrium. The purpose is to determine long term optimal treatment and short period pulsing strategies for controlling the population of the periodic drinkers and alcoholics.

For long term optimal treatment, we show that an optimal control exists which minimizes the number of periodic and hazardous drinkers (alcoholics). The optimality is determined by using the Pontryagin Maximum Principle (PMP) and the dynamic behaviour has been revealed through numerical simulations by solving the underlying system of differential equations.

For short period pulsing strategy, we apply the pulse vaccination strategy (PVS) in the *SEIRS* epidemic model to our *SPARS* drinking epidemic model. Analytical results have been established for the stability of the periodic eradication solution and the persistent drinking for the *SPARS* model. The optimal pulse treatment strategy has also been derived.

List of publications during PhD candidature

- R.Thamchai and Y.H. Wu. "Stability Analysis and Optimal Treatment for the SPAR Drinking Epidemic Model", Proceedings of International Conference in Mathematics and Applications(ICMA - MU), 2011.
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CHAPTER 1

Introduction

1.1 Background

Control of alcohol drinking is an important problem in many countries since alcohol plays a significant role in our society and our economy. Alcohol also has dangerous effects on human body such as brain, heart, pancreas, liver and immune system, as well as evaluating to other dangers such as loss of performance, absenteeism in the workplace, drink-driving and harm to others, anti-social behavior, crime and family violence. Most drinkers try it for the first time as teenagers or even in childhood. There are many reasons why people start drinking alcohol, including the curiosity, sociability, ignorance, imitation from their parents or celebrities behavior. The explosion and spread of drinking has been studied for many years. The prediction about drinking can help scientists to evaluate vaccination or isolation plans and may have an important effect on the mortality rate of drinking epidemic. Drinking epidemic model is a tool which has been used to study the dynamic of the drinking spread, to predict the future and to simulate the outbreak, as well as evaluating the strategies to control drinking epidemic.

1.2 Objectives of the Thesis

The aim of this project is to construct a robust drinking epidemic model, and then study its dynamic properties and determine the optimal treatment strategy to control the growth of periodic drinkers and alcoholics. The specific objectives of this work are as follows.

(i) Establish a robust SPARS drinking epidemic model. As for the SEIRS epidemic model, there is a significant period of time during which the individual has been infected but is not yet infectious themselves. We model the drinking epidemic by considering the periodic drinkers (P) to be the

individual latent period which is in compartment E (for exposed), and the alcoholics (A) to be the infected (I).

- (ii) Study the basic reproduction number, R_0 , and analyze the stability of the equilibrium points of the *SPARS* model. The basic reproduction number concerns how many secondary drinkers resulted from the introduction of an individual drinker into the population of susceptible. The value of R_0 indicates whether an epidemic is possible. Sensitivity analysis will be performed on R_0 and the stability of the system will also be examined.
- (iii) Optimization is the strategy for controlling the number of individual drinkers. In our study, we will establish the optimal control problem of drinking epidemic, and show the existence of an optimal control and then derive the optimal system. The method used to determine the optimal strategy is the Pontryagin Maximum Principle (PMP).
- (iv) Investigate the properties of the model with pulse treatment. Since the process of vaccination is discontinuous or repeated applications, it can be described by impulsive differential equations. We call this kind of vaccination strategies pulse vaccination strategy (PVS). We will consider pulse treatment in the SPARS model, i.e. pulse vaccination strategy. We will also study the pulse effects by analyzing the local and global stability of equilibria.

1.3 Outline of the Thesis

In this thesis, various analytical and numerical results for the control of drinking epidemic are developed. The thesis is organized into five chapters.

Chapter 1 gives an overview of the research background and the objectives of the research.

Chapter 2 presents a literature review of the former work and results related to this work including the review of fundamental equations and prior research work in the field.

Chapter 3 presents the drinking epidemic model and analyze the basic reproduction number, R_0 , and the stability of equilibrium points. The Pontryagin Maximum Principle (PMP) is used to determine the optimal system. The existence of an optimal control is established, followed by derivation of the optimal system. Some numerical simulation results are also presented to demonstrate the dynamics of the drinking epidemic model and to verify the analytical results.

Chapter 4 establishes the drinking epidemic model with time delays and impulsive vaccination. The sufficient conditions are established for globally asymptotic stability of the drinking-free periodic solution and the permanence of the model. Various numerical simulations are also presented to demonstrate the system behaviour.

Chapter 5 summarizes the main results of this thesis and discusses further research.

CHAPTER 2

Literature Review

2.1 Overview

Epidemiology is concerned with the distribution of diseases in populations and the factors that influence the transmission of diseases. The epidemiologic approach helps to explain the transmission of communication diseases, such as cholera and measles [1]. Several epidemics models and associated theoretical studies are given in Bailey [2], Anderson and May [3], Murray [4], Brauer and Castillo-Chavez [5]. Although many social problems such as drug use [6, 7], zombie infection [8], smoking [9] and alcohol drinking [10–13] have been referred to in terms of epidemics, little has been published on the application of mathematical modeling methods to such problems.

In this research we will investigate the dynamics of drinking epidemics and the factors dominating the dynamics behave as well as the optimal control strategy. This work will include construction of mathematical models, investigation of the drinking epidemic treatment strategies, optimal control and the influences of impulsive vaccination. Hence, in this chapter, we will first review topics relevant to epidemic models in section 2.2. Then we will review the treatment strategies and optimal control in section 2.3, followed by work in vaccination in section 2.4. Finally, the review of previous work and results in drinking epidemic are represented in section 2.5.

2.2 Epidemic Model

2.2.1 Mathematical model

A mathematical model is an interpreted or idealized illustration of a system or process in mathematical terms, improvised to simplify calculation and prediction. The efficiency of a model depends on the fact that it allows for the perception and prediction of a phenomena without the work of performing the complex and expensive experiments [14].

Mathematical modeling of infectious diseases is a tool which has been used to study the mechanisms by which diseases spread, to predict the future course of an outbreak. It can be used to study the effects of a variety of strategies for disease eradication or control. A mathematical model for epidemics is in the form of a system of equations subject to a set of initial and boundary conditions. The structure and parameters involved in the equations are the main critical elements of a mathematical model. Study of the properties of the model is also as important as the model itself.

2.2.2 SIR and SEIR Model

Kermack and McKendrick developed the idea of threshold parameter in 1927, investigated and studied a basic SIR model [15]. In the model, all of the population in community initially are susceptible to the disease and the infected individual will have complete immunity after infection. The total population is divided into three distinct categories: susceptible individuals (S), infected individuals (I) and recovered individuals (R). The susceptible category is the healthy individuals who may catch the disease. The infected category consists of members who have the disease and may transmit it to others, and the recovered individuals are those who were infected but have developed immunity to the infection. The change of each of the individual categories is given in the flow chart below



Figure 2.1: Transfer diagram of the basic SIR model.

In the SIRS model, individuals recover with no immunity to the disease, that is, individuals are immediately susceptible once they have recovered. The dynamics of the SIR or SIRS have been widely analyzed [3,5,16].

There are many diseases for which individuals are not apparently infected because it need a period of time for incubation. Therefore, the *SIR* and *SIRS* models have been applied to study the transmission of diseases with a latent period. By the assumption that before becoming infected individual, a susceptible



Figure 2.2: Transfer diagram of the basic SIRS model.

individual may go through the latent period after catching the disease, the resulting models are of *SEIR* or *SEIRS* types, respectively, depending on whether the recovered individual has the permanent immunity or not. Many studies have been carried out for the *SEIR* and *SEIRS* model [17–19]. The state transfer diagrams of the *SEIR* and *SEIRS* models are shown respectively in Figures 2.3 and 2.4.



Figure 2.3: Transfer diagram of the basic *SEIR* model.



Figure 2.4: Transfer diagram of the basic SEIRS model.

2.3 Optimal Control

Optimal control theory has found application in many fields, including economics, finance, management, process control bioengineering and biological sciences. It can be used to control an object to influence its behaviour so as to achieve a desired goal with the constrains. In aerospace engineering, for example, optimal control techniques can be applied to object correlation, fuel usage, spacecraft characterization etc. Another example is to determine the optimal percentage of population which should be vaccinated to minimize the number of infected people and the cost of vaccination.

Optimal control is a powerful method for solving dynamic optimization problems, when the problems are expressed in continuous time. The primary method for optimal control was developed by Pontryagin et al. [20]. In this section, we focus on review of optimal control theory of ordinary differential equations (ODEs).

Lenhart and Workman [21] considered u(t) as the control and x(t) as the state. The state variable is governed by a differential equation involving the control variable:

$$x'(t) = g(t, x(t), u(t)).$$
(2.1)

An optimal control problem consists of finding piecewise continuous control u(t)and the associated state variable x(t) to maximize(minimize) the given objective functional,

$$J(u) = \max_{u} (\min_{u}) \int_{t_{0}}^{t_{1}} f(t, x(t), u(t)) dt,$$

subject to $x'(t) = g(t, x(t), u(t)),$
 $x(t_{0}) = x_{0} \text{ and } x(t_{1}) \text{ free.}$ (2.2)

Such a maximizing(minimizing) control is called an optimal control. By $x(t_1)$ free, it means that the value of $x(t_1)$ is unrestricted; f and g are continuous differentiable functions in all three arguments. Thus, the control(s) will always be piecewise continuous and the associated states will always be piecewise differentiable.

The principal technique for an optimal control problem is to solve a set of "necessary conditions" that an optimal control and corresponding state must satisfy. The necessary conditions are generated from the Hamiltonian H, which is defined as follows;

$$H(t, x, u, \lambda) = f(t, x, u) + \lambda g(t, x, u)$$
(2.3)

Since, we want to maximize(minimize) H with respect to u at u^* , and the neces-

sary conditions can be written in terms of the Hamiltonian:

$$\frac{\partial H}{\partial u}$$
 at $u^* \Rightarrow f_u + \lambda g_u = 0$ (optimality condition), (2.4)

$$\lambda' = -\frac{\partial H}{\partial x} \Rightarrow -(f_x + \lambda g_x)$$
 (adjoint equation), (2.5)

$$0 \qquad (transversality condition), \qquad (2.6)$$

where the dynamics of the state equation is

 $\lambda(t_1) =$

$$x' = g(t, x, u) = \frac{\partial H}{\partial \lambda}, x(t_0) = x_0.$$
(2.7)

Therefore, we can solve the optimal control problem by the following scheme;

- (i) Form the Hamiltonian for the problem.
- (ii) Set up the adjoint differential equations, transversality boundary conditions and optimality conditions. Now there are three unknowns, u^* , x^* and λ .
- (iii) Eliminate u^* by using the optimality equation $H_u = 0$, that is, solve u^* in terms of x^* and λ .
- (iv) Solve two differential equations for x^* and λ with two boundary conditions, substituting u^* in the differential equations with the expression for the optimal control from the previous step.
- (v) After finding the optimal state and adjoint, solve the optimal control.

Application of control theory to epidemics is a very important field, and the study of epidemic models is strongly related to the evaluation of different control strategies: screening and educational campaigns [22], the vaccination campaign [23], and resource allocation [24]. A comprehensive survey of control theory applied to epidemiology was performed by Wickwire [25]. Many different models with different objective functions have been proposed [9,26–29]. A major difficulty in applying control methods to practical epidemiology problems is the commonly made assumption that one has total knowledge of the state of the epidemics [30].

Zaman et al. [9] studied the stability of the equilibria for an SIR model. In order to achieve control of the disease, they considered a control problem associated with the SIR model. Some of the susceptible populations is vaccinated in this model. They presented the existence of an optimal control for the control problem and then conducted numerical simulations by using the Runge-Kutta fourth order procedure. Finally, they studied a real example to show the efficiency of the optimal control.

Wiraningsih et al. [31] formulated a *SEIR* model for rabies between dogs and human with vaccination effect. The basic reproduction number for this model is derived, and the strategies for optimal distribution of vaccine to minimize the cost of the control and the spread of the diseases is analyzed (minimize the infected classes and maximize the susceptible classes). The optimality system is derived by optimal control theory of the differential equation system and is then illustrated by numerical results.

2.4 Impulsive Vaccination

The theory of impulsive differential equations has been extensively applied to study evolution processes with a short term perturbation. Many processes and phenomena in the real world exhibit impulsive effects particularly in mechanics, control theory, pharmacokinetics, epidemiology, population dynamics, economics, ecology [32–36].

2.4.1 Impulsive Differential Equations

Consider an evolution process [36] described by

(i) a system of differential equations

$$x' = f(t, x), \tag{2.8}$$

where $f: R_+ \times \Omega \to R^n, \Omega \in R^n$ is an open set and R_+ , the non-negative real line;

- (ii) the sets $M(t), N(t) \in \Omega$ for each $t \in R_+$;
- (iii) the operator $A(t): M(t) \to N(t)$ for each $t \in R_+$.

Let $x(t) = x(t, t_0, x_0)$ be any solution of (2.8) with initial value (t_0, x_0) . The process goes as follows: the point $P_t = (t, x(t))$ starts at the initial point $P_{t_0} = (t_0, x_0)$ and moves along the curve $\{(t, x) : t \ge t_0, x = x(t)\}$ until $t_1 > t > 0$, at which the point P_t meets the set M(t). At $t = t_1$, the operator A(t) transfers the point to $P_{t_1^+} = (t_1, x_1^+) \in N(t_1)$, where $x_1^+ = A(t_1)x(t_1)$. Then the point P_t continues its motion along the curve with $x(t) = x(t, t_1, x_1^+)$ as the solution of (2.8) starting at $P_{t_1} = (t_1, x_1^+)$ until it hits the set M(t) again, at the next moment $t_2 > t_1$. Then, once again the point $P_{t_2} = (t_2, x(t_2))$ is transferred to the point $P_{t_2^+} = (t_2, x_2^+) \in N(t_2)$, where $x_2^+ = A(t)x(t_2)$. As before, the point P_t continues to move forward with $x(t) = x(t, t_2, x_2^+)$ as the solution of (2.8) starting at (t_2, x_2^+) . Thus the evolution process continues forward as long as the solution of (2.8) exists.

We shall call the set of relations (i), (ii) and (iii), that characterize the above mentioned evolution process, an impulsive differential system. The curve described by the point P_t is called the integral curve, and the function x = x(t)that defines this curve, a solution of the system.

Solutions of an impulsive differential system have the following three types: (a) A continuous function, if the integral curve does not intersect the set M(t) or hits it at fixed points of the operator A(t).

(b) A piecewise continuous function having a finite number of discontinuities of the first kind if the integral curve meets M(t) at a finite number of points that are not the fixed points of the operator A(t).

(c) A piecewise continuous function having a countable number of discontinuities of the first kind if the integral curve encounters M(t) at a countable number of points that are not the fixed points of the operator A(t).

2.4.2 Comparison Theorem

From [36], the theory of differential inequalities are essential in dynamics of differential equations. The corresponding theory of impulsive inequalities is equally useful in the investigation of impulsive differential equations.

To introduce the comparison principle of impulsive differential equations, we firstly give the definition of extremal solutions of

$$u'(t) = g(t, u), t \neq \tau_k,$$

 $u(t_k^+) = \psi(u(t_k)), t = \tau_k,$ (2.9)
 $u(t_0) = u_0,$

where $g \in C[R_+ \times R, R]$ and $\psi_k : R \to R$.

Definition 2.1. [36] Let $r(t) = r(t, t_0, u_0)$ be a solution of (2.9) on $[t_0, t_0 + a)$. A function r(t) is said to be the maximal solution of (2.9), if for any solution $u(t) = u(t, t_0, u_0)$ of (2.9) in $[t_0, t_0 + a)$, the inequality

$$u(t) \le r(t), \quad t \in [t_0, t_0 + a)$$
 (2.10)

holds. A minimal solution $\rho(t)$ may be defined similarly by reversing the (2.10).

Definition 2.2. [36] Let $V : R_+ \times r^n \to R_+$. V is said to belong to class V_0 if V satisfies:

(1) V is continuous on $(t_{k-1}, t_k] \times R^n$ and $\lim_{(t,y)\to(t_k^+,x)} V(t,y) = V(t_k^+,x)$ for every $x \in R^n, k \in N$;

(2) V is locally Lipschitz continuous with respect to x.

Definition 2.3. [36] Let $V \in V_0$, for $(t, x) \in (t_{k-1}, t_k] \times \mathbb{R}^n$. Define

$$D^{+}V(t,x) = \lim_{h \to 0^{+}} \sup \frac{1}{h} [V(t+h,x+hf(t,x)) - V(t,x)], \qquad (2.11)$$

and

$$D_{-}V(t,x) = \lim_{h \to 0^{-}} \inf \frac{1}{h} [V(t+h,x+hf(t,x)) - V(t,x)].$$
(2.12)

If the impulsive differential equation (2.9) and

$$\frac{dx}{dt} = f(t, x), \qquad t \neq \tau_k,
\Delta x = I_k(x), \qquad t = \tau_k,
x(t_0^+) = x_0, \qquad t_0 \ge 0,$$
(2.13)

satisfy the conditions:

(1) $0 < t_1 < t_2 < ...,$ and $t_k \to \infty$ as $k \to \infty$; (2) $f : R_+ \times R^n \to R^n$ is continuous on $(t_{k-1}, t_k] \times R^n$ and

$$\lim_{(t,y)\to(t_k^+,x)}f(t,y)=f(t_k^+,x)$$

for every $x \in \mathbb{R}^n, k \in N$; (3) $I_k : \mathbb{R}^n \to \mathbb{R}^n$; (4) $g : \mathbb{R}_+ \times \mathbb{R}_+ \to \mathbb{R}$ is continuous on $(t_{k-1}, t_k] \times \mathbb{R}^n$ and

$$\lim_{(t,y)\to(t_k^+,x)}g(t,y)=f(t_k^+,x)$$

for every $x \in R_+, k \in N$; then the following comparison principle holds.

Theorem2.4. [36] Let $V : R_+ \times r^n \to R_+, V \in V_0$. Suppose that (1)g : $R_+ \times R_+ \to R$ and satisfies the above conditions(4), and $\psi_k : R \to R$ is nondecreasing and for each k = 1, 2, ...,

$$D^+V(t,x) \le g(t,V(t,x)), \qquad t \ne \tau_k,$$

$$V(t,x+I_k(x)) \le \psi_k(V(t,x)), \qquad t = \tau_k.$$
(2.14)

(2) $r(t) = r(t, t_0, u_0)$ is the maximal solution of (2.9) existing on $[t_0, \infty)$. Then $V(t_0^+, x_0) \leq u_0$ implies that

$$V(t, x(t)) \le r(t), \qquad t > t_0,$$

where $x(t) = x(t, t_0, x_0)$ is any solution of (2.13) on $[t_0, \infty)$.

In recent years, pulse vaccination, repeated application of vaccine is gaining prominence as a strategy for eliminating a variety of epidemics. Pulse vaccination strategy (PVS) consists of periodical repetitions of impulsive vaccinations in population differently from the traditional constant continuous vaccination. Many SIR and SEIR epidemic models with pulse vaccination were extensively studied.

Zeng et al. [37] studied the impulsive control on an SIR epidemic model and got the conditions on which epidemic-elimination solution is globally asymptotically stable and the conditions of bounded system. The differential susceptibility SIR epidemic model with stage structure and pulse vaccination is introduced by Zhang et al. [38]. Their work give some sufficient conditions for the globally attractivity of an infection-free periodic solution and the permanence of infected individual. Shi et al. [39] considered including the impulsive vaccination affects on the original SIR system. Li and Yang [40] investigated two epidemic models with continuous and impulsive vaccination strategies. The associated basic reproduction numbers were given and they compared the effect of control measures on the spread of infection for the continuous and pulse vaccination strategies.

The application of PVS to *SEIR* models was discussed on d'Onofrio's work [41,42]. The author established the criteria for determining the space of vaccination parameters and the regions of local asymptotic stability (LAS). Furthermore, the author studied analytically the global asymptotic stability (GAS) of the eradication solutions in some cases and established the criterion which guarantees the LAS of the eradication solutions.

2.5 Previous Work on Drinking Epidemic

The definition of alcoholism varies significantly between the medical community and the treatment programs, such as Alcoholics Anonymous, which have been set up to help alcoholics to recover. Even within the medical community there is much debate about whether or not alcoholism should be considered as a disease. It was only recently that epidemiology began to be applied to the study of this kind of social problems. Since the beginning of this century, this area of mathematics has started to become more prominent in the study of this type of problems and other social phenomena, crime [43], drug abuse [6] and even the spread of urban legends [44].

A simple SIR model for alcoholism is suggested by Sanchez et al. [10] in which the population is divided into the following drinking classes: occasional and moderate drinkers (S), problem drinkers (D), and temporarily recovered (R). It is assumed that the population size remains constant, N. New recruits join the population as occasional and moderate drinkers (S) and have homogeneous mixing with the rest of the members of the population. A diagram of the various rates affecting the three groups of individuals is represented in Figure 2.5 below.



Figure 2.5: Transfer diagram of Sanchez and his collaborators model.

The governing system of equations is

$$\frac{dS}{dt} = \mu N - \beta \frac{SD}{N} - \mu S,$$

$$\frac{dD}{dt} = \beta \frac{SD}{N} + \rho \frac{RD}{N} - (\mu + \phi)D,$$

$$\frac{dR}{dt} = \phi D - \rho \frac{RD}{N} - \mu R,$$

$$S + D + R = N$$
(2.15)

The non - dimensionalized system of (2.15) is as follows:

$$s' = \mu - \beta sd - \mu s,$$

$$d' = \beta sd + \rho rd - (\mu + \phi)d,$$

$$r' = \phi d - \rho rd - \mu r,$$

$$s + d + r = 1$$
(2.16)

where $s = \frac{S}{N}, d = \frac{D}{N}$ and $r = \frac{R}{N}$.

The parameters of this model are defined as follows:

- μ : the birth and death rate.
- β : the rate of recruitment to alcoholism due to encounters between occasional and moderate drinkers and problem drinkers.
- p: the rate at which recovered drinkers relapse to alcoholism.
- ϕ : the rate of recovery.

The model's basic reproduction number (R_0) , which gives the average number of secondary drinker generated by the problem drinker in the population of moderate drinkers, has been computed. For this model, the reproductive number with recovery via treatment is $R_0 = \frac{\beta}{\mu + \phi}$, where β is a measure of the influence of problem drinkers on the susceptible individual and $\frac{1}{\mu + \phi}$ represents the average time a problem drinker spends on the drinking class D [10].

Their results are not typical in epidemic models because the outcomes depend not only on the value of R_0 but on the size of the initial population of problem drinkers. Especially, $R_0 < 1$ does not guarantee the eradication of drinking communities.

The results in this work also indicate that ineffective treatment programs with high relapse rates may develop the spread of alcoholism, because they create a group of recovered drinkers who could easily relapse. High relapse rates will occur when treatment programs have only short-term positive effects. From Witkiewitz's research indicate that within the first year most of drinkers whose receive treatment relapse to the lighter drinking [45]. An effective treatment strategy for controlling the spread of alcoholism is to limit the amount of time a recovered alcoholic spends in places where drinking occurs.

Benedict studied how alcoholism spreads, and how alcoholics relapse in [11]. At a standing-room-only talk at the 2006 Joint SMB - SIAM Conference on the Life Sciences in Raleigh, North Carolina, Fabio Sanchez of Cornell University presented a model for the spread of alcoholic drinking based on epidemiological models of infectious diseases. By further developing Sanchez and his collaborators' model [10], the researcher investigate how the drinking problem spread by alcoholics through social contacts among people with different drinking habits.

Newman [12] proposed the so-called SAR model which has similar parameters and a similar SIR structure to the Sanchez model. However, it accounts for not only recovered drinkers who relapse to occasional drinking but also those recovered drinkers who relapse to problem drinking. Newman's model also allows the birth rate and death rates to take different values, and also includes a relapse term from the recovered category to the susceptible class. Newman's model was further investigated by Benedict [11]. A diagram of the various rates affecting the three groups of individuals is shown in Figure 2.6.



Figure 2.6: Transfer diagram of Newman model.

The Newman model can be described mathematically as follows:

$$\frac{dS}{dt} = \mu N - \beta \frac{SA}{N} + \epsilon R - \gamma S,$$

$$\frac{dA}{dt} = \beta \frac{SA}{N} + \rho \frac{RA}{N} - \phi A - (\gamma + \delta)A,$$

$$\frac{dR}{dt} = \phi A - \rho \frac{RA}{N} - \epsilon R - (\gamma + \delta)R,$$

$$S + D + R = N$$
(2.17)

where

 μ is the birth rate;

- β is the rate of recruitment to alcoholism due to encounters between susceptible drinkers and alcoholics;
- ϵ is the rate at which recovered drinkers relapse to moderate drinkers;
- ρ is the rate at which recovered drinkers relapse to alcoholism;
- ϕ is the rate of recovery;
- γ is the natural death rate which is refer to any death rate not caused by alcohol;
- δ is the death rate related from drinking alcohol;
- S is the number of susceptible drinkers;
- A is the number of problem drinkers or alcoholics;
- R is the number of temporarily recovered drinkers;
- N is the number of total population.

This system (2.17) is subject to the following initial conditions

$$S(0) = S_0 \ge 0, \quad A(0) = A_0 \ge 0, \quad R(0) = R_0 \ge 0$$

where S_0 , A_0 and R_0 are constants. From (2.17), the total population N is defined by the following equation

$$\frac{dN}{dt} = \mu N - \delta(A+R) - \gamma N \tag{2.18}$$

Newman investigated the model and analyzed the basic reproduction number, R_0 , which give the average number of people who will become alcoholism by introducing one alcoholic in the compartment.

Manthey et al. [13] analyzed the dynamics of campus drinking by using an epidemiological model. They introduced a simple mathematical model capturing the dynamics of the campus drinking phenomenon, which is focused on a college campus and the student population is divided into three classes: non-drinkers (N), social drinkers (S) and problem drinkers (P). The student population is assumed to be constant. The interactions between these three categories of students are shown in Figure 2.7.

As the work in [13] focuses on students in a college campus for a relatively



Figure 2.7: Transfer diagram of Manthey's model.

short period of time only, their model does not include a recovered class and they also regard students who stop drinking as non-drinkers. Therefore, their model is a modified susceptible-infected-susceptible (SIS) model, and can be described mathematically as follows:

$$\frac{dN}{dt} = \eta - \eta N - \alpha NS - \kappa NP + \beta S + \epsilon P,
\frac{dS}{dt} = \sigma S - (\eta + \sigma)S + \alpha NS - \beta S - \gamma SP + \delta P,
\frac{dP}{dt} = \pi P - (\eta + \pi)P + \gamma SP + \kappa NP - \delta P - \epsilon P,
N + S + P = 1$$
(2.19)

where

 α is the transmission rate of non-drinkers to social drinkers;

 β is the recovery rate of social drinkers;

 γ is the transmission rate of social drinkers to problem drinkers;

 δ is the recovery rate of problem drinkers to social drinkers;

 ϵ is the recovery rate of problem drinkers to non-drinkers;

 η is the departure rate from campus environment;

 π is the entrance rate of problem drinkers;

 κ is the transmission rate of non-drinkers to problem drinkers;

 σ is the number of problem drinkers or alcoholics;

R is the entrance rate of social drinkers;

N is the entrance rate of problem drinkers.

The model suggests that the reproductive number is not sufficient to predict whether drinking behavior will persist on campus and that pattern of recruiting new members plays a significant role in minimizing the campus alcohol problem.

2.6 Concluding Remarks

Various mathematical models for drinking epidemics have been developed. However, existing models still have some limitations and modification are required in many aspects.

- (i) The model presented by Sanchez assumes that the population is constant. However in reality, this is not the case.
- (ii) Sanchez's model assumes that as people enter the population all of them are occasional or social drinkers. In the real world, there are many people who never try to have a drink.
- (iii) Sanchez's model assumes that an individual who enters the recovered drinking group maintains immunity indefinitely. However, realistically, a recov-

ered individual can relapse to the possible drinkers.

- (iv) Normally, we can classified the drinkers in two categories; occasional drinkers and problem drinkers or alcoholics group like as Manthey's model.
- (v) Manthey's model does not include a recovered class since they focus only on students in a college campus for a short period of time (about 6 years or less). To study the drinking epidemic not only in the college, one needs to consider the recovered drinkers.
- (vi) From the report [46], excessive alcohol use contributes to 88,000 deaths in the United States each year, including 1 in 10 deaths among working age adults. Excessive alcohol use includes binge drinking, heavy drinking. Then, the death rate related to alcohol drinking in the alcoholics group should not be equal to the death rate in other groups.

In this work, we will construct a more realistic drinking epidemic model and study its behaviour and the method for the control of the behaviour.

CHAPTER 3

Optimal Treatment for the Drinking Epidemic Model

3.1 General Overview

On the assumption that the spread of alcohol drinking follows a process similar to that of disease transmission, mathematical epidemiological modeling of the spread of alcohol drinking may give the conception on the evolution through the drinking career, from initiation or occasional drinking to usual drinking, treatment, relapse and final recovery. Benedict [11] described how alcoholism spreads, and how alcoholics relapse by determining the effects of reproduction numbers on the model dynamics and computing the equilibrium states of the model. Manthey et al. [13] analyzed the dynamics of campus drinking by using an epidemiological model. They introduced a basic drinking epidemic model to describe the dynamics of the campus drinking behavior and their research focused on students at a college campus. From their results, it can be concluded that the basic reproduction number is not sufficient to predict the behavior of drinking on this campus. There is persistence of drinking that produced from the new initiate drinking which is an interrupt to the reduction of the number of drinkers on the campus.

In this chapter, we develop a mathematical model for the control of alcohol drinking and then study its qualitative behavior. The rest of the chapter is organized as follows. In section 3.2, the *SPARS* drinking epidemic model is established, then an explicit expression for the basic reproduction number is derived, and then the equilibrium points are determined and their stability are investigated. In section 3.3, an optimal control problem for finding the optimal treatment (control) strategy is constructed, and then the Pontryagin Maximum Principle (PMP) is used to find the optimal solution. In section 3.4, numerical examples are given to validate the analytical results and to simulate the dynamic process of the movement of population among different groups. Finally, some conclusions are given in section 3.5.

3.2 Formulation and Analysis of the Drinking Epidemic Model

3.2.1 The SPARS Model

The model focuses on the population aged 16 and over. The population is divided into four classes: susceptible drinkers (S), periodic drinkers (P), alcoholics (A)and recovered drinkers (R). The total population is denoted by N with N = S + P + A + R. We assume that the recruitment rate is different from the death rate which indicates that the total population is not constant. The interactions between the four categories of population are shown in Figure 3.1.



Figure 3.1: Transfer diagram of the SPARS model.

The model presented in Figure 3.1 may be represented by the following system of equations:

$$\frac{dS(t)}{dt} = \mu N(t) - \alpha \frac{S(t)P(t)}{N(t)} - dS(t) + \eta R(t),$$

$$\frac{dP(t)}{dt} = \alpha \frac{S(t)P(t)}{N(t)} - \beta P(t) - (d + \varepsilon_1)P(t),$$

$$\frac{dA(t)}{dt} = \beta P(t) - \gamma A(t) - (d + \varepsilon_2)A(t),$$

$$\frac{dR(t)}{dt} = \gamma A(t) - \eta R(t) - (d + \varepsilon_3)R(t).$$
(3.1)

where

S(t) is the number of susceptible drinkers at time t,

P(t) is the number of occasional or periodic drinkers at time t,

- A(t) is the number of alcoholics or hazardous drinkers at time t,
- R(t) is the number of temporality recovered drinkers at time t,
- N(t) is size of the total population at time t,
- μ is the rate of the general population entering the susceptible population, that is, the demographic process of individuals reaching age 15 in the modeling time period,
- α is the contact rate between the susceptible and periodic drinkers,
- β is the proportion of becoming an alcoholic,
- γ is the proportion of hazardous drinkers who enter treatment,
- η is the rate at which recovered drinkers relapse to susceptible drinkers,
- d is the natural death rate of the general population,
- ε_1 is the death rate of occasional drinkers,
- ε_2 is the death rate of hazardous drinkers,
- ε_3 is the death rate of recovered drinkers.

We first find the equilibria of the *SPARS* model. By setting the RHS of the system (3.1) to zero, we get two equilibrium states, namely the drinking free state $E_0\left(\frac{\mu N}{d}, 0, 0, 0\right)$ and the endemic state $E_1\left(\frac{K_1N}{\alpha}, \Lambda K_2K_3N, \Lambda\beta K_3N, \Lambda\beta\gamma\right)$, where

$$K_{1} = (\beta + d + \varepsilon_{1})$$

$$K_{2} = (\gamma + d + \varepsilon_{2})$$

$$K_{3} = (\eta + d + \varepsilon_{3})$$

$$\Lambda = \frac{(\alpha \mu - K_{1}d)}{\alpha(K_{1}K_{2}K_{3} - \beta\gamma\eta)}.$$
(3.2)

It is easy to see that $K_1K_2K_3 - \beta\gamma\eta > 0$, and therefore, the endemic state E_1 occurs if and only if

$$\alpha \mu > K_1 d. \tag{3.3}$$

3.2.2 The Basic Reproduction Number

The number of secondary drinkers produced by a single drinking individual in the susceptible population is called the basic reproduction number, R_0 . The value of R_0 will indicates whether an epidemic is possible. Based on [47], the reproduction number can be determined as the spectral radius of the next generation matrix.

In the next generation matrix, the distinction between the drinkers and alcoholics compartments must be determined from the epidemiological interpretation of the model.

The drinking epidemic system (3.1) has a unique drinking free equilibrium $E_0(S_0, 0, 0, 0)$ with $S_0 = \frac{\mu N}{d}$. Taking the drinking compartments to be S and P gives

$$\begin{bmatrix} P'\\ A' \end{bmatrix} = \begin{bmatrix} \alpha \frac{S_0}{N} & 0\\ 0 & 0 \end{bmatrix} \begin{bmatrix} P\\ A \end{bmatrix} - \begin{bmatrix} \beta + d + \varepsilon_1 & 0\\ -\beta & \gamma + d + \varepsilon_2 \end{bmatrix} \begin{bmatrix} P\\ A \end{bmatrix}$$
$$= \begin{bmatrix} \frac{\alpha\mu}{d} & 0\\ 0 & 0 \end{bmatrix} \begin{bmatrix} P\\ A \end{bmatrix} - \begin{bmatrix} K_1 & 0\\ -\beta & K_2 \end{bmatrix} \begin{bmatrix} P\\ A \end{bmatrix}.$$
(3.4)

The next generation matrix can then be determined by $K = FV^{-1}$ where

$$F = \begin{bmatrix} \frac{\alpha\mu}{d} & 0\\ 0 & 0 \end{bmatrix} \quad , \quad V = \begin{bmatrix} K_1 & 0\\ -\beta & K_2 \end{bmatrix}.$$

Thus,

$$\mathbf{K} = FV^{-1} = \begin{bmatrix} \frac{\alpha\mu}{K_1d} & 0\\ 0 & 0 \end{bmatrix}$$
(3.5)

which has two eigenvalues $\lambda = 0$, $\frac{\alpha \mu}{K_1 d}$. Hence the basic reproduction number is

$$R_0 = \rho(\lambda) = \frac{\alpha \mu}{K_1 d}.$$
(3.6)

3.2.3 Stability of the equilibria

We now consider the stability of the two equilibrium states, namely the drinking free equilibrium state E_0 and the endemic state E_1 . For the system defined by (3.1), the Jacobian matrix is the 4 × 4 matrix given by

$$J = \begin{bmatrix} \frac{-\alpha P}{N} - d & \frac{-\alpha S}{N} & 0 & \eta \\ \frac{\alpha P}{N} & \frac{\alpha S}{N} - K_1 & 0 & 0 \\ 0 & \beta & -K_2 & 0 \\ 0 & 0 & \gamma & -K_3 \end{bmatrix}.$$
 (3.7)

At the drinking free equilibrium $E_0\left(\frac{\mu N}{d}, 0, 0, 0\right)$, the Jacobian matrix is

$$J_{0} = J\left(\frac{\mu N}{d}, 0, 0, 0\right) = \begin{bmatrix} -d & \frac{-\alpha\mu}{d} & 0 & \eta\\ 0 & \frac{\alpha\mu}{d} - K_{1} & 0 & 0\\ 0 & \beta & -K_{2} & 0\\ 0 & 0 & \gamma & -K_{3} \end{bmatrix}.$$
 (3.8)

By solving the characteristic equation det $(J_0 - \lambda I) = 0$, we obtain four eigenvalues

$$\lambda_{1} = -d,$$

$$\lambda_{2} = -K_{2},$$

$$\lambda_{3} = -K_{3},$$

$$\lambda_{4} = \frac{\alpha\mu - K_{1}d}{d}.$$
(3.9)

If $R_0 = \frac{\alpha \mu}{K_1 d} < 1$, i.e. $\alpha \mu < K_1 d$, then all the four eigenvalues are negative. Therefore, we conclude that the drinking free equilibrium is locally asymptotically stable if $R_0 < 1$, or unstable otherwise.

At the endemic state $E_1(\frac{K_1N}{\alpha}, \Lambda K_2K_3N, \Lambda\beta K_3N, \Lambda\beta\gamma)$, the Jacobian is

$$J_{1} = J(\frac{K_{1}N}{\alpha}, \Lambda K_{2}K_{3}N, \Lambda\beta K_{3}N, \Lambda\beta\gamma)$$

$$= \begin{bmatrix} -\alpha K_{2}K_{3}\Lambda - d & -k_{1} & 0 & \eta \\ \alpha K_{2}K_{3}\Lambda & 0 & 0 & 0 \\ 0 & \beta & -K_{2} & 0 \\ 0 & 0 & \gamma & -K_{3} \end{bmatrix}.$$
(3.10)

The characteristic equation of J_1 is

$$\lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4 = 0 \tag{3.11}$$

where

$$a_{1} = d + K_{2} + K_{3} + \alpha K_{2} K_{3} \Lambda,$$

$$a_{2} = K_{2} K_{3} + (\alpha K_{2} K_{3} \Lambda + d) (K_{2} + K_{3}) + \alpha K_{1} K_{2} K_{3} \Lambda,$$

$$a_{3} = K_{2} K_{3} (d + \alpha \Lambda (K_{1} K_{2} + K_{2} K_{3} + K_{1} K_{3})),$$

$$a_{4} = \alpha K_{2} K_{3} \Lambda (K_{1} K_{2} K_{3} - \eta \beta \gamma).$$
(3.12)

By the Routh-Hurwitz conditions [48], the equilibrium state is asymptotically stable if

$$a_1 > 0,$$

 $a_3 > 0,$
 $a_4 > 0$
 $a_1a_2a_3 > a_3^2 + a_1^2a_4.$
(3.13)

From (3.2), we can see that $K_1 > 0, K_2 > 0$ and $K_3 > 0$. Then, it is not difficult to verify the validity of the above inequalities. Thus, for $R_0 > 1$ there exists an unique positive equilibrium E_1 of the drinking epidemic model, which is always locally asymptotically stable.

3.3 Optimal Control

For the optimal control problem, we let the control variables $u_1(t)$ be the education campaign level used to control drinking in a community and $u_2(t)$ be the level of treatment in the form of drinking.

The objective is to minimize the numbers of both occasional and hazardous drinkers with minimum control. Hence, the optimal control problem can be constructed as follows

$$OCP: \qquad J(u_1, u_2) = \int_0^T \left[\delta_1 P(t) + \delta_2 A(t) + \frac{1}{2} \left(\xi_1 u_1^2(t) + \xi_2 u_2^2(t) \right) \right] dt,$$
(3.14)

subject to

$$\frac{dS(t)}{dt} = \mu N(t) - \alpha \frac{S(t)P(t)}{N(t)} - dS(t) + \eta R(t),
\frac{dP(t)}{dt} = \alpha \frac{S(t)P(t)}{N(t)} - (\beta + d + \varepsilon_1)P(t) - u_1(t)P(t),
\frac{dA(t)}{dt} = \beta P(t) - (\gamma + d + \varepsilon_2)A(t) - u_2(t)A(t),
\frac{dR(t)}{dt} = \gamma A(t) - (\eta + d + \varepsilon_3)R(t) + u_1(t)P(t) + u_2(t)A(t),$$
(3.15)

with initial conditions

$$S(0) = S_s \quad , P(0) = P_s \quad , A(0) = A_s \quad , R(0) = R_s.$$
(3.16)

Here δ_i and ξ_i for i = 1, 2 are weight factors (positive constants) representing drinker's level of acceptance of the control campaign. Let P(t) and A(t) be state variables with control variables $u_1(t)$ and $u_2(t)$. Then we can rewrite the system (3.15) in the following form:

$$\phi' = B\phi + F(\phi) := G(\phi), \qquad (3.17)$$

where

$$\phi = \begin{bmatrix} S(t) \\ P(t) \\ A(t) \\ R(t) \end{bmatrix},$$

$$B = \begin{bmatrix} -d & 0 & 0 & \eta \\ 0 & -(\beta + d + \varepsilon_1 + u_1(t)) & 0 & 0 \\ 0 & \beta & -(\gamma + d + \varepsilon_2 + u_2(t)) & 0 \\ 0 & u_1(t) & \gamma + u_2(t) & -(\eta + d + \varepsilon_3) \end{bmatrix},$$
$$F(\phi) = \begin{bmatrix} \mu N - \alpha \frac{SP}{N} \\ \alpha \frac{SP}{N} \\ 0 \\ 0 \end{bmatrix}.$$

Obviously (3.17) is a non-linear system with bounded coefficients. From the non-linear term of the right hand side of (3.17), we have

$$F(\phi_1) - F(\phi_2) = \begin{bmatrix} \mu N_1 - \alpha \frac{S_1 P_1}{N_1} \\ \alpha \frac{S_1 P_1}{N_1} \\ 0 \\ 0 \end{bmatrix} - \begin{bmatrix} \mu N_2 - \alpha \frac{S_2 P_2}{N_2} \\ \alpha \frac{S_2 P_2}{N_2} \\ 0 \\ 0 \end{bmatrix}$$
(3.18)

and thus

$$\begin{aligned} F(\phi_{1}) - F(\phi_{2})| &= \left| \left(\mu N_{1} - \alpha \frac{S_{1}P_{1}}{N_{1}} \right) - \left(\mu N_{2} - \alpha \frac{S_{2}P_{2}}{N_{2}} \right) \right| \\ &+ \left| \alpha \frac{S_{1}P_{1}}{N_{1}} - \alpha \frac{S_{2}P_{2}}{N_{2}} \right| \\ &\leq \mu \left| N_{1} - N_{2} \right| + \left| \alpha \frac{S_{2}P_{2}}{N_{2}} - \alpha \frac{S_{1}P_{1}}{N_{1}} \right| + \left| \alpha \frac{S_{1}P_{1}}{N_{1}} - \alpha \frac{S_{2}P_{2}}{N_{2}} \right| \\ &\leq \mu \left| N_{1} - N_{2} \right| + 2 \left| \alpha \frac{S_{1}P_{1}}{N_{1}} - \alpha \frac{S_{2}P_{2}}{N_{2}} \right| \\ &\leq \mu \left| N_{1} - N_{2} \right| + 2\alpha \left| \frac{S_{1}P_{1}N_{2} - S_{2}P_{2}N_{1}}{N_{1}N_{2}} \right| \\ &\leq \mu \left| N_{1} - N_{2} \right| + 2\alpha \left| \frac{S_{1}P_{1}N_{2} - S_{2}P_{2}N_{1}}{N_{1}N_{2}} \right| \\ &= \mu \left| N_{1} - N_{2} \right| + 2\alpha \left| \frac{(S_{1}N_{2} + S_{2}N_{1})}{2} (P_{1} - P_{2}) \right| \\ &+ \frac{(P_{2}N_{2} + P_{1}N_{1})}{2} (S_{1} - S_{2}) + \frac{(S_{2}P_{2} + S_{1}P_{1})}{2} (N_{2} - N_{1}) \right| \\ &\leq \mu \left| N_{1} - N_{2} \right| + \alpha \left| S_{1}N_{2} + S_{2}N_{1} \right| \left| P_{1} - P_{2} \right| \\ &+ \alpha \left| P_{2}N_{2} + P_{1}N_{1} \right| \left| S_{1} - S_{2} \right| + \alpha \left| S_{2}P_{2} + S_{1}P_{1} \right| \left| N_{2} - N_{1} \right| \\ &\leq M_{1} \left| S_{1} - S_{2} \right| + M_{2} \left| P_{1} - P_{2} \right| + M_{3} \left| N_{1} - N_{2} \right|, \end{aligned}$$

$$(3.19)$$

where

$$M_{1} = \alpha |P_{2}N_{2} + P_{1}N_{1}|$$
$$M_{2} = \alpha |S_{1}N_{2} + S_{2}N_{1}|$$
$$M_{3} = \mu + \alpha |S_{2}P_{2} + S_{1}P_{1}|.$$

Hence, we get

$$|G(\phi_1) - G(\phi_2)| \le L |\phi_1 - \phi_2| \tag{3.20}$$

where $L = \max \{M_1, M_2, M_3, ||B||\} < \infty$. Therefore, the function G is uniformly Lipchitz continuous [49]. From the definitions of the control $u_1(t), u_2(t)$ and the control on S(t), P(t), A(t) and R(t), we can conclude that the solution of system (3.20) exists [49], as described by the theorem below.

Theorem 3.1. Consider the optimal control problem OCP. There exists an optimal control $u^* = (u_1^*, u_2^*) \in U$ such that

$$\min_{(u_1, u_2) \in U} J(u_1, u_2) = J(u_1^*, u_2^*), \qquad (3.21)$$

with the state and control satisfying equations (3.15) and (3.16).

Proof. For the existence of an optimal control, based on [50], the following conditions must be satisfied.

(i) The set of controls and corresponding state variables are nonempty.

(ii) The control set U is convex and closed.

(iii) The RHS of the state system is bounded by a linear function in the state and the control variables.

(iv) The integrand of the objective functional is concave on U.

(v) There exist constants $c_1, c_2 > 0$ and $\sigma > 1$ such that the integrand, $L(P, A, u_1, u_2)$, of the objective functional satisfies

$$L(P, A, u_1, u_2) \ge c_2 + c_1 \left(|u_1|^2 + |u_2|^2 \right)^{\frac{1}{2}}.$$
 (3.22)

To verify all of these conditions, we use the result by Lukes [51] to give the existence of solutions of the state system (3.15) with bounded coefficients, which gives condition (i). The control set is closed and convex by definition, and thus satisfies condition (ii). Since our state system is bilinear in u_1 and u_2 , the RHS of the system (3.15) satisfies condition (iii), using the boundedness of the solutions.

In addition, the integrand of the objective functional (3.14) is convex on the control set U. We can also easily see that there exist a constant $\sigma > 1$ and $c_1, c_2 > 0$ since $\delta_1, \delta_2, \xi_1, \xi_2 > 0$, such that

$$\delta_1 P(t) + \delta_2 A(t) + \frac{1}{2} \left(\xi_1 u_1^2(t) + \xi_2 u_2^2(t) \right) \ge c_2 + c_1 \left(|u_1|^2 + |u_2|^2 \right)^{\frac{\sigma}{2}}, \quad (3.23)$$

which completes the proof for existence of the optimal control.

We can find an optimal solution of this optimal control problem by considering the Lagrangian and the Hamiltonian for the problem. The Lagrangian of the optimal control problem is given by

$$L(P, A, u_1, u_2) = \delta_1 P(t) + \delta_2 A(t) + \frac{1}{2} \left(\xi_1 u_1^2(t) + \xi_2 u_2^2(t) \right).$$
(3.24)

Applying Pontryagin's Maximum Principle (PMP), we form the Hamiltonian and derive the optimality system:

$$H(S, P, A, R, u_1, u_2, \lambda_1, \lambda_2, \lambda_3, \lambda_4) = L(P, A, u_1, u_2) + \lambda_1(t) \frac{dS(t)}{dt} + \lambda_2(t) \frac{dP(t)}{dt} + \lambda_3(t) \frac{dA(t)}{dt} + \lambda_4(t) \frac{dR(t)}{dt},$$
(3.25)

where $\lambda_1(t), \lambda_2(t), \lambda_3(t)$ and $\lambda_4(t)$ are the adjoint functions to be determined.

Theorem 3.2. If (u_1^*, u_2^*) is an optimal pair with corresponding states S^*, P^*, A^* and R^* , then there exist adjoint variables $\lambda_1(t), \lambda_2(t), \lambda_3(t)$ and $\lambda_4(t)$, which satisfy:

$$\begin{aligned} \lambda_{1}'(t) &= \frac{\alpha P(t)}{N(t)} \left(\lambda_{1}(t) - \lambda_{2}(t) \right) + d\lambda_{1}(t), \\ \lambda_{2}'(t) &= -\delta_{1} + \frac{\alpha S(t)}{N(t)} \left(\lambda_{1}(t) - \lambda_{2}(t) \right) \\ &+ \left(\beta + d + \varepsilon_{1} \right) \lambda_{2}(t) + u_{1}(t) \left(\lambda_{2}(t) - \lambda_{4}(t) \right) - \beta \lambda_{3}(t), \\ \lambda_{3}'(t) &= -\delta_{2} + \left(\gamma + d + \varepsilon_{2} \right) \lambda_{3}(t) - \gamma \lambda_{4}(t) + u_{2}(t) \left(\lambda_{3}(t) - \lambda_{4}(t) \right), \\ \lambda_{4}'(t) &= -\eta \lambda_{1}(t) + \left(\eta + d + \varepsilon_{3} \right) \lambda_{4}(t), \end{aligned}$$
(3.26)

and the transversality conditions (boundary conditions) are

$$\lambda_i(t_{final} = 0), i = 1, 2, 3, 4. \tag{3.27}$$

Furthermore we obtain

$$u_1^*(t) = \max\left\{\min\left\{\frac{(\lambda_2(t) - \lambda_4(t))}{\xi_1}P^*(t), \psi_1\right\}, 0\right\},$$
(3.28)

$$u_2^*(t) = \max\left\{\min\left\{\frac{(\lambda_3(t) - \lambda_4(t))}{\xi_2}A^*(t), \psi_2\right\}, 0\right\}.$$
 (3.29)

Proof. To consider the transversality conditions and the adjoint equations, the method in [21] is used. From the Hamiltonian (3.25), we obtain (3.26) from

$$\lambda_1'(t) = -\frac{\partial H}{\partial S} \quad , \ \lambda_2'(t) = -\frac{\partial H}{\partial P} \quad , \ \lambda_3'(t) = -\frac{\partial H}{\partial A} \quad , \ \lambda_4'(t) = -\frac{\partial H}{\partial R}. \tag{3.30}$$

Using the optimal conditions and the property of the control space U for the control variables u_1 and u_2 , we get

$$\frac{\partial H}{\partial u_1} = \xi_1 u_1(t) - (\lambda_2(t) - \lambda_4(t)) P^*(t),$$

$$\frac{\partial H}{\partial u_2} = \xi_2 u_2(t) - (\lambda_3(t) - \lambda_4(t)) A^*(t).$$
(3.31)

From the property of the control space, u_1^* and u_2^* are given by

$$u_{1}^{*}(t) = \begin{cases} 0 & \text{if } \frac{(\lambda_{2}(t) - \lambda_{4}(t)) P^{*}(t)}{\xi_{1}} \leqslant 0\\ \frac{(\lambda_{2}(t) - \lambda_{4}(t)) P^{*}(t)}{\xi_{1}} & \text{if } 0 < \frac{(\lambda_{2}(t) - \lambda_{4}(t)) P^{*}(t)}{\xi_{1}} < \psi_{1} \\ \psi_{1} & \text{if } \frac{(\lambda_{2}(t) - \lambda_{4}(t)) P^{*}(t)}{\xi_{1}} \geqslant \psi_{1} \end{cases}$$
(3.32)

and

$$u_{2}^{*}(t) = \begin{cases} 0 & \text{if } \frac{(\lambda_{3}(t) - \lambda_{4}(t)) A^{*}(t)}{\xi_{2}} \leqslant 0 \\ \frac{(\lambda_{3}(t) - \lambda_{4}(t)) A^{*}(t)}{\xi_{2}} & \text{if } 0 < \frac{(\lambda_{3}(t) - \lambda_{4}(t)) A^{*}(t)}{\xi_{2}} < \psi_{2} \\ \psi_{2} & \text{if } \frac{(\lambda_{3}(t) - \lambda_{4}(t)) A^{*}(t)}{\xi_{2}} \geqslant \psi_{2}. \end{cases}$$
(3.33)

These can be written in compact notation (3.28) and (3.29), respectively.

Therefore, the characterization of the optimal control $u^*(t) = (u_1^*(t), u_2^*(t))$ is defined by (3.32) and (3.33). The optimal control and the state are found by solving the optimality system, which consists of the state system (3.15), the adjoint system (3.26) and the boundary conditions (3.16) and (3.27). To solve the optimality system we use the initial and transversality conditions together with the characterization of the optimal control pair $(u_1^*(t), u_2^*(t))$. By substituting the value of $u_1^*(t)$ and $u_2^*(t)$ in the control system, we get the following system :
$$\begin{aligned} \frac{dS^{*}(t)}{dt} &= \mu N(t) - \alpha \frac{S^{*}(t)P^{*}(t)}{N^{*}(t)} - dS^{*}(t) + \eta R^{*}(t), \\ \frac{dP^{*}(t)}{dt} &= \alpha \frac{S^{*}(t)P^{*}(t)}{N^{*}(t)} \\ &- \left[\beta + d + \varepsilon_{1} - \max\left\{\min\left\{\frac{(\lambda_{2}(t) - \lambda_{4}(t))}{\xi_{1}}P^{*}(t), \psi_{1}\right\}, 0\right\}\right]P^{*}(t), \\ \frac{dA^{*}(t)}{dt} &= \beta P^{*}(t) \\ &- \left[\gamma + d + \varepsilon_{2} - \max\left\{\min\left\{\frac{(\lambda_{3}(t) - \lambda_{4}(t))}{\xi_{2}}A^{*}(t), \psi_{2}\right\}, 0\right\}\right]A^{*}(t), \\ \frac{dR^{*}(t)}{dt} &= \left[\gamma + \max\left\{\min\left\{\frac{(\lambda_{3}(t) - \lambda_{4}(t))}{\xi_{2}}A^{*}(t), \psi_{2}\right\}, 0\right\}\right]A^{*}(t) \\ &- (\eta + d + \varepsilon_{3})R^{*}(t) \\ &+ \max\left\{\min\left\{\frac{(\lambda_{2}(t) - \lambda_{4}(t))}{\xi_{1}}P^{*}(t), \psi_{1}\right\}, 0\right\}P^{*}(t), \end{aligned}$$
(3.34)

with the Hamiltonian,

$$H^{*}(S^{*}, P^{*}, A^{*}, R^{*}, u_{1}^{*}, u_{2}^{*}, \lambda_{1}, \lambda_{2}, \lambda_{3}, \lambda_{4}) = \delta_{1}P^{*}(t) + \delta_{2}A^{*}(t) + \frac{1}{2} \left[\xi_{1} \left(\max \left\{ \min \left\{ \frac{(\lambda_{2}(t) - \lambda_{4}(t))}{\xi_{1}} P^{*}(t), \psi_{1} \right\}, 0 \right\} \right)^{2} + \xi_{2} \left(\max \left\{ \min \left\{ \frac{(\lambda_{3}(t) - \lambda_{4}(t))}{\xi_{2}} P^{*}(t), \psi_{2} \right\}, 0 \right\} \right)^{2} \right] + \lambda_{1}(t) \frac{dS^{*}(t)}{dt} + \lambda_{2}(t) \frac{dP^{*}(t)}{dt} + \lambda_{3}(t) \frac{dA^{*}(t)}{dt} + \lambda_{4}(t) \frac{dR^{*}(t)}{dt}.$$

$$(3.35)$$

The optimal control and the corresponding states have been determined. Next we will show the numerical simulation that solve system (3.34) and Hamiltonian (3.35).

3.4 Numerical Simulations

A number of numerical simulations were carried out using MATLAB to illustrate the dynamics of the system. The parameter values used in the numerical simulations are : $\mu = 0.085$, $\alpha = 0.02$, $\beta = 0.01$, $\gamma = 0.001$, d = 0.075, $\eta = 0.001$, $\varepsilon_1 = 0.001$, $\varepsilon_2 = 0.01$ and $\varepsilon_3 = 0.002$. The percentages of initial individuals in susceptible, periodic, alcoholics and recovered classes are 50, 30, 15 and 5, respectively. The evolution of each class of population with time is shown in Figure 3.2. The results show that the drinking free state of the system is asymptotically stable, which is as expected from our analysis as $R_0 = \frac{\alpha\mu}{(\beta+d+\varepsilon_1)d} = 0.26 < 1$. Moreover, we considered another case in which the contact rate between the susceptible and periodic drinkers is $\alpha = 0.2$ which is given $R_0 > 1$. The evolution of each class of population in this case is shown in Figure 3.3. Obviously, the asymptotically stable endemic state has been captured in this case.

The optimal control problem for the *SPARS* model is solved numerically. We used an iterative method such as the Runge-Kutta fourth order scheme to solve this optimality system by using the method in [21]. The state variables S, P, Aand R are solved forward in time by using an initial guess of the control variables $u_1(t)$ and $u_2(t)$. Conversely, the adjoint variables, λ_i for i = 1, 2, 3, 4 are solved backwards in time. For the *SPARS* model presented in this work, the state system is given by (3.15). The adjoint system is given by (3.26) with the final time conditions given by (3.27) and the characterization of the optimal control by (3.28) and (3.29). The numerical results obtained are presented in Figure 3.4.

In Figure 3.4(a) and 3.4(e), we see that the number of susceptible drinkers and the total population, respectively, with control are greater than those without control, which can be caused by the education control that we put on the susceptible individual and the treatment control on the recovered drinkers for which this group could be relapse to susceptible group.

In Figure 3.4(b) and 3.4(c), we have plotted the periodic drinkers and alcoholics, respectively, with and without control. We see that in the first ten to fifteen days the number of population with and without control in both categories does not differ very much; but as time increases, the difference becomes substantial.

In Figure 3.4(d), the comparison of education control u_1^* , and the treatment control u_2^* , are plotted as a function of time in days.



Figure 3.2: The evolutions of the four classes of populations when $R_0 < 1$.



Figure 3.3: The evolutions of the four classes of populations when $R_0 > 1$.







Figure 3.4: Diagrams showing the effects of drinking control on the evolutions of the four classes of populations : (a) susceptible drinker; (b) periodic drinker; (c) alcoholic; (d) recovered drinker; (e) total population; (f) the optimal controls $u_1^*(t)$ and $u_2^*(t)$.

3.5 Concluding Remarks

An SPARS model has been proposed to describe the overall drinking population dynamics for the case in which the total population is not constant and the death rates for different population groups are different. The model is constructed taking into account the periodic drinkers compartment with bilinear incidence rate. Analysis of the model shows that there are two equilibria, drinking free state and endemic state. An explicit expression for the basic reproduction number, R_0 , has been derived and it has been shown that when $R_0 < 1$, that is $\alpha < \frac{(\beta+d+\varepsilon_1)d}{\mu}$, the drinking free equilibrium is locally asymptotically stable. The drinking endemic state has also been shown to be locally asymptotically stable for $R_0 > 1$. An optimal control problem has also been constructed to determine the optimal treatment strategies to minimize the number of drinkers and the resources for the control. The results show that the number of periodic drinkers and alcoholics decreases significantly in the optimal controlled system. It is found that the numerical results agree with the analytical results derived.

CHAPTER 4

Drinking Epidemic Model with Time Delays and Impulsive Vaccination

4.1 General Overview

The common method used for controlling the epidemic disease is vaccination. We normally adopt the vaccination to control or eradicate the spread. Vaccinations have many types. Constant vaccination and pulse vaccination are two main s-trategies [52]. Constant vaccination is a primary vaccination strategy that can protect the individual who received the vaccine. But this method of vaccination is not always sufficient for disease eradication and does not offer 100% protection, and some of individual get infected despite of vaccination [53]. Pulse vaccination strategy (PVS) is a method used to eliminate an epidemic disease by injection or vaccination repeated on a risk group over a defined age range [41,54]. Even though the effect of continuous vaccination strategy is better than impulsive vaccination strategy, the side effect of the cost and the material have potential harmful effects, especially for infants. So we prefer to the impulsive vaccination strategy as it is easier to be manipulated and it has the relatively low cost [52, 55–57].

The scientists at the University of Chile developed an experimental drug to cure alcoholism. If a person who has received the vaccine try to drink alcohol, they will almost immediately get severe nausea, accelerated heartbeat and discomfort, according to the Daily Mail [58]. The shot is effective for about six months to a year and works by speeding up the hangover process.

In recent years, many epidemic models with time delay were largely studied in [59–63]. Some of the research literature on *SEIR* or *SEIRS* epidemic models are established by ODEs [17, 64–67]. Impulsive differential equations and time delay are introduced to describe the dynamics of epidemic disease [68–75], and most of these research literature are on *SEIRS* model. Meng et al. [76] proposed and analyzed the dynamic behaviors of an *SEIRS* epidemic model with pulse vaccination and two time delays under the condition of nonlinear incidence rate. Using the stroboscopic map, the authors determined the dynamics of the discrete system and presented the existence of an infection-free periodic solution. Whenever the period of impulsive effect is less than some critical value, the stability of the infection-free equilibrium is globally attractive. Moreover, they obtained the efficient conditions for the peristence of epidemic model with pulse vaccination.

An impulsive vaccination of the SEIR epidemic model with two time delays is formulated by Gao and his teamwork [77]. They obtained the infection-free periodic solution of the system. Moreover, they found that whenever the vaccination rate is greater than θ^* , the infected disease dies out, while if the vaccination rate is less than θ_* , the disease will be permanence.

In this chapter, an *SPARS* drinking epidemic model with two time delays and impulsive vaccination is investigated in section 4.2 including some lemmas that we will use for considering the stability of periodic solution. In section 4.3, the property of periodic solution is investigated, while the essential conditions for the permanence of the drinking is obtained in section 4.4. In section 4.5, numerical examples are given to validate the analytical results and to simulate the dynamic process of the movement of population among different groups, followed by concluding remarks in section 4.6.

4.2 Model Formulation and Lemmas

In this study, we set the *SPARS* drinking epidemic model with two time delays and impulsive vaccination by the following assumptions:

- (i) The total population(N) is partitioned into four classes, the susceptible drinkers(S), periodic drinkers(P), alcoholics(A) and recovered drinkers(R).
- (ii) The natural death rate is assumed to be the same positive constant d for all four categories, and the extra death rates taking into account the effect of drinking in the categories of periodic, alcoholic and recovered drinker are $\varepsilon_1, \varepsilon_2$ and ε_3 , respectively. We also assume that the influx of susceptible population from a constant recruitment is K.
- (iii) The contact rate α is defined as the expected number of contacts at which potentially drinking occurs between susceptible individual and others. The rate at which an occasional drinker becomes an alcoholic is β with the addict

period ω ; the alcoholics receive treatment with rate γ and the recovered drinkers relapse to susceptible drinkers with rate η in the period τ .

(iv) The proportion of successful vaccination, which is called pulse vaccination rate, is θ (0 < θ < 1), and the interpulse time or the time between two consecutive pulse vaccinations is T.

The *SPARS* drinking epidemic model with two time delays and impulsive vaccination is established as follows

$$S'(t) = K - \alpha \frac{S(t)P(t)}{N(t)} - dS(t) + \eta R(t - \tau)e^{-(d + \varepsilon_3)\tau}$$

$$P'(t) = \alpha \frac{S(t)P(t)}{N(t)} - \beta P(t - \omega)e^{-(d + \varepsilon_1)\omega} - (d + \varepsilon_1)P(t)$$

$$A'(t) = \beta P(t - \omega)e^{-(d + \varepsilon_1)\omega} - \gamma A(t) - (d + \varepsilon_2)A(t)$$

$$R'(t) = \gamma A(t) - \eta R(t - \tau)e^{-(d + \varepsilon_3)\tau} - (d + \varepsilon_3)R(t)$$

$$S(t^+) = (1 - \theta)S(t)$$

$$P(t^+) = P(t)$$

$$A(t^+) = A(t)$$

$$R(t^+) = R(t) + \theta S(t)$$

$$K(t^+) = R(t) + \theta S(t)$$

Note that in model (4.1), we consider the impulsive vaccination of the SPARS model with time delays and the influx of susceptible comes from the constant recruitment rate, K, which is different to the original SPARS model in (3.1) on which the population enter the susceptible population from the demographic process of individuals reaching age 15 in the modeling time period.

The total population size N(t) can be determined by

$$N'(t) = K - dN(t) - (\varepsilon_1 P(t) + \varepsilon_2 A(t) + \varepsilon_3 R(t))$$

$$N(t^+) = N(t)$$
(4.2)

Thus, the total population size may vary in time. From (4.2), we have

$$K - (d + \varepsilon_1 + \varepsilon_2 + \varepsilon_3)N(t) \leqslant N'(t) \leqslant K - dN(t)$$
(4.3)

It follows that

$$\frac{K}{d + \varepsilon_1 + \varepsilon_2 + \varepsilon_3} \leqslant \lim_{t \to \infty} \inf N(t) \leqslant \lim_{t \to \infty} \sup N(t) \leqslant \frac{K}{d}$$
(4.4)

In the following, some previous results which are to be used in establishing our main results, are given.

Lemma 4.1. [73] Consider the following equation:

$$x'(t) = a_1 x(t - \omega) - a_2 x(t)$$
(4.5)

where $a_1, a_2, \omega > 0$ for $-\omega \leq t \leq 0$. We have (i) If $a_1 < a_2$, then $\lim_{t \to \infty} x(t) = 0$ (ii) If $a_1 > a_2$, then $\lim_{t \to \infty} x(t) = \infty$ The proofs of case (i) and (ii) are given in Theorem 3.2.1 [78] and Lemma 2.1 [79], respectively.

Lemma 4.2. [73] Consider the following impulsive differential equation

$$u'(t) = a - bu(t), t \neq kT, k \in \mathbb{N}$$

$$u(t^+) = (1 - \theta)u(t), t = kT, k \in \mathbb{N}$$

$$(4.6)$$

where a > 0, b > 0 and $0 < \theta \le 1$. Then, there exists a unique periodic solution of system(4.6):

$$\tilde{u}(t) = \frac{a}{b} + \left(u^* - \frac{a}{b}\right) e^{-b(t-kT)}, kT < t \le (k+1)T$$
(4.7)

which is globally asymptotically stable, where $u^* = \frac{a(1-\theta)(1-e^{-bT})}{b(1-(1-\theta)e^{-bT})}$.

Lemma 4.3. [80] Consider the following impulsive differential equation

$$u'(t) = a - bu(t) - cu(t - T), t \neq kT, k \in \mathbb{N}$$

$$u(t^+) = (1 - \theta)u(t), t = kT, k \in \mathbb{N}$$

$$(4.8)$$

where a > 0, b > 0, c > 0 and $0 < \theta \leq 1$. Then there exists a unique periodic solution of system (4.8) which is globally asymptotically stable.

4.3 Drinking-Free Periodic Solution

Since A(t) = N(t) - (S(t) + P(t) + R(t)), we focus on the following equivalent model of (4.1);

$$S'(t) = K - \alpha \frac{S(t)P(t)}{N(t)} - dS(t) + \eta R(t - \tau)e^{-(d+\varepsilon_3)\tau}$$

$$P'(t) = \alpha \frac{S(t)P(t)}{N(t)} - \beta P(t - \omega)e^{-(d+\varepsilon_1)\omega} - (d + \varepsilon_1)P(t)$$

$$R'(t) = \gamma N(t) - \gamma S(t) - \gamma P(t) - \eta R(t - \tau)e^{-(d+\varepsilon_3)\tau}$$

$$-(\gamma + d + \varepsilon_3)R(t)$$

$$N'(t) = K - (d + \varepsilon_2)N(t) + \varepsilon_2 S(t) + (\varepsilon_2 - \varepsilon_1)P(t)$$

$$+(\varepsilon_2 - \varepsilon_3)R(t)$$

$$S(t^+) = (1 - \theta)S(t)$$

$$P(t^+) = P(t)$$

$$R(t^+) = R(t) + \theta S(t)$$

$$N(t^+) = N(t)$$

$$I = kT, k \in \mathbb{N}$$

$$R(t^+) = N(t)$$

In this section, we first analyse the system (4.9) by demonstrating the existence of a drinking-free periodic solution, in which periodic drinking individuals are permanently absent from the population, i.e. P(t) = 0 for all $t \ge 0$. Under this condition the dynamics of susceptible individuals, alcoholics, recovered individuals and total population must satisfy the following system :

$$S'(t) = K - dS(t) + \eta R(t - \tau) e^{-(d + \varepsilon_3)\tau} R'(t) = \gamma N(t) - \gamma S(t) - \eta R(t - \tau) e^{-(d + \varepsilon_3)\tau} - (\gamma + d + \varepsilon_3) R(t) N'(t) = K - (d + \varepsilon_2) N(t) + \varepsilon_2 S(t) + (\varepsilon_2 - \varepsilon_3) R(t) S(t^+) = (1 - \theta) S(t) R(t^+) = R(t) + \theta S(t) N(t^+) = N(t) t = kT, k \in \mathbb{N}$$
(4.10)

Since $\lim_{t\to\infty} N(t) \ge \frac{K}{d+\varepsilon_2}$ and $\frac{K}{d+\varepsilon_1+\varepsilon_2+\varepsilon_3} \le \lim_{t\to\infty} \inf N(t) \le \lim_{t\to\infty} \sup N(t) \le \frac{K}{d}$, we can say that $\lim_{t\to\infty} N(t) \le \frac{K}{d}$. If $P(t) \equiv 0$, it follows from the third and seventh equations of model(4.1) that $\lim_{t\to\infty} A(t) = 0$. Therefore we have the following limit system of (4.10)

$$R(t) = \frac{K}{d} - S(t) \tag{4.11}$$

and

$$S'(t) = K\left(1 + \frac{\eta e^{-(d+\varepsilon_3)\tau}}{d}\right) - dS(t) - \eta e^{-(d+\varepsilon_3)\tau}S(t-\tau), t \neq kT$$

$$S(t^+) = (1-\theta)S(t), t = kT$$

$$(4.12)$$

According to Lemma 4.2, we can see that if $d > \eta e^{-(d+\varepsilon_3)\tau}$, then the system (4.12) has a unique positive periodic solution with period T which is globally asymptotically stable. We denote this periodic solution by $\widetilde{S}(t)$. Therefore, the drinking-free periodic solution of system (4.10) is $\left(\widetilde{S}(t), 0, \frac{K}{d} - \widetilde{S}(t), \frac{K}{d}\right)$.

From the delayed SPARS drinking epidemic model (4.1), letting the drinking compartments to be P and A gives

$$\begin{bmatrix} P'\\ A' \end{bmatrix} = \begin{bmatrix} \frac{\alpha S^*}{N^*} & 0\\ 0 & 0 \end{bmatrix} \begin{bmatrix} P\\ A \end{bmatrix} - \begin{bmatrix} d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega} & 0\\ -\beta e^{-(d + \varepsilon_1)\omega} & \gamma + d + \varepsilon_2 \end{bmatrix} \begin{bmatrix} P\\ A \end{bmatrix}$$
(4.13)

The next generation matrix can then be determined by $L = FV^{-1}$ where

$$F = \begin{bmatrix} \frac{\alpha S^*}{N^*} & 0\\ 0 & 0 \end{bmatrix} \quad , V = \begin{bmatrix} d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega} & 0\\ -\beta e^{-(d + \varepsilon_1)\omega} & \gamma + d + \varepsilon_2 \end{bmatrix}.$$

Thus,

$$L = FV^{-1} = \begin{bmatrix} \frac{\alpha S^*}{(d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega})N^*} & 0\\ 0 & 0 \end{bmatrix}$$
(4.14)

which has two eigenvalues;

$$\lambda = 0 , \frac{\alpha S^*}{(d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega})N^*},$$

where $S^* = \frac{K(d+\eta e^{-(d+\varepsilon_3)\tau})(1-e^{-dT})}{d^2(1-(1-\theta)e^{-dT})}$ and $N^* = \frac{K}{d}$. Hence the basic reproduction number is

$$R^* = \frac{\alpha(d + \eta e^{-(d + \varepsilon_3)\tau})(1 - e^{-dT})}{d(d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega})(1 - (1 - \theta)e^{-dT})}.$$
(4.15)

Theorem 4.4. If $R^* < 1$, the drinking-free periodic solution (DFPS) $\left(\widetilde{S}(t), 0, \frac{K}{d} - \widetilde{S}(t), \frac{K}{d}\right)$ is globally attractive, where

$$R^* = \frac{\alpha(d + \eta e^{-(d+\varepsilon_3)\tau})(1 - e^{-dT})}{d(d + \varepsilon_1 + \beta e^{-(d+\varepsilon_1)\omega})(1 - (1 - \theta)e^{-dT})}$$
(4.16)

Proof. Since $R^* < 1$, we can choose $\epsilon_0 > 0$ small enough such that

$$\frac{\alpha d\Gamma}{K} < (d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega})$$
(4.17)

where $\Gamma = \frac{K(d+\eta e^{-(d+\varepsilon_3)\tau})(1-e^{-dT})}{d^2(1-(1-\theta)e^{-dT})} + \epsilon_0.$

From system (4.12), we consider the following comparison impulsive differential system :

$$X'(t) = K\left(1 + \frac{\eta e^{-(d+\varepsilon_3)\tau}}{d}\right) - dX(t), t \neq kT, k \in \mathbb{N}$$

$$X(t^+) = (1-\theta)X(t), t = kT, k \in \mathbb{N}.$$
(4.18)

By Lemma 4.2, we have a periodic solution of system (4.18) as follows

$$\widetilde{X}(t) = \xi + (X^* - \xi)e^{-d(t - k\tau)}, kT < t \le (k+1)T$$
(4.19)

which is globally asymptotically stable, where $\xi = K \frac{d + \eta e^{-(d + \varepsilon_3)\tau}}{d^2}$ and $X^* = \frac{\xi(1-\theta)(1-e^{-dT})}{(1-(1-\theta)e^{-dT})}$ for $k > k_1$.

Therfore,

$$S(t) < X(t) \leqslant \widetilde{X}(t) + \epsilon_0 \leqslant \frac{K(d + \eta e^{-(d + \varepsilon_3)\tau})(1 - e^{-dT})}{d^2(1 - (1 - \theta)e^{-dT})} + \epsilon_0 \triangleq \Gamma \qquad (4.20)$$

Further, from the second equation of system (4.27), we have

$$P'(t) = \alpha \frac{S(t)P(t)}{N(t)} - \beta P(t-\omega)e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1)P(t)$$

$$\leq \frac{\alpha d\Gamma}{K}P(t) - \beta P(t-\omega)e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1)P(t).$$
(4.21)

From (4.17), we have $\frac{\alpha d\Gamma}{K} < d + \varepsilon_1 + \beta e^{-(d+\varepsilon_1)\omega}$. Further, considering the following comparison differential system

$$y'(t) = \frac{\alpha d\Gamma}{K} y(t) - \beta y(t-\omega) e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1) y(t), \qquad (4.22)$$

we have, $\lim_{t\to\infty} y(t) = 0$. By the comparison theorem and nonnegativity of P(t), we get

$$\lim_{t \to \infty} P(t) = 0. \tag{4.23}$$

Then, for any sufficiently small $\epsilon_1 > 0$, there exists an integer k_2 such that for all $t > k_2T$,

$$P(t) < \epsilon_1. \tag{4.24}$$

From the third equation of system (4.1), for $t > k_3 T$ we have

$$A'(t) < \beta \epsilon_1 - (\gamma + d + \varepsilon_2)A(t).$$
(4.25)

Consider the comparison equation for $t > k_3 \tau$,

$$z'(t) = \beta \epsilon_1 - (\gamma + d + \varepsilon_2) z(t).$$
(4.26)

It is easy to see that $\lim_{t\to\infty} z(t) = \frac{\beta\epsilon_1}{\gamma+d+\epsilon_2}$. By the comparison theorem, there exists an integer $k_3 > k_2$ such that

$$A(t) < \frac{\beta \epsilon_1}{\gamma + d + \varepsilon_2}.\tag{4.27}$$

Therefore, in view of the equation for A(t) and considering that ϵ_1 is sufficiently small, it follows that

$$\lim_{t \to \infty} A(t) = 0. \tag{4.28}$$

For the total population, from system (4.2) and equations (4.24) and (4.27), we get that

$$N'(t) = K - dN(t) - (\varepsilon_1 P(t) + \varepsilon_2 A(t) + \varepsilon_3 R(t))$$

$$\leqslant K - dN(t) - (\varepsilon_1 P(t) + \varepsilon_2 A(t))$$

$$\leqslant K - dN(t) - \left(\varepsilon_1 \epsilon_1 + \frac{\beta \varepsilon_2 \epsilon_1}{\gamma + d + \varepsilon_2}\right)$$

Consider the comparison equation for $t > k_5 T$,

$$n'(t) = K - dn(t) - \left(\varepsilon_1 + \frac{\beta \varepsilon_2}{\gamma + d + \varepsilon_2}\right) \epsilon_1.$$

We can see that $\lim_{t\to\infty} n(t) = \frac{K}{d}$. By the comparison theorem, for $k_5 > k_4$ we have

$$\lim_{t \to \infty} N(t) = \frac{K}{d}.$$
(4.29)

Let $V(t) = |S(t) - \tilde{S}(t)|$. Then, from (4.12),(4.24),(4.27) and the first equation of model (4.1), there exists an integer $k_6 > k_5$ such that between two consecutive pulses

$$D^{+}V(t) \leq \left| \eta e^{-(d+\varepsilon_{3})\tau} \left(N(t-T) - \frac{K}{d} \right) \right| + \alpha \frac{S(t)P(t)}{N(t)} + \eta e^{-(d+\varepsilon_{3})\tau} (P(t-T) + A(t-T)) - dV(t)\eta e^{-(d+\varepsilon_{3})\tau}V(t-T)$$

$$\leq H\epsilon_{1} - dV(t) + \eta e^{-(d+\varepsilon_{3})\tau}V(t-T)$$

$$(4.30)$$

for $t > k_6 T$, where $H = \alpha + \eta e^{-(d+\varepsilon_3)\tau} \left(1 + \frac{\beta}{\gamma+d+\varepsilon_2}\right)$. When t = kT, $V^+(t) = (1-\theta)V(t)$.

Consider the following delayed differential equations for $t > k_6 T$,

$$v(t) = H\epsilon_1 - dv(t) + \eta e^{-(d+\varepsilon_3)\tau} v(t-T).$$
(4.31)

By Lemma 4.2, we get

$$\lim_{t \to \infty} v(t) = \frac{H\epsilon_1}{d - \eta e^{-(d + \varepsilon_3)\tau}},$$

which is one of the fixed solutions v(t) of equation (4.31) with initial condition $v(t) = \left| S(t) - \tilde{S}(t) \right|$ for $t \in (k_6T, (k_6+1)T)$. Thus there exists an integer $k_7 > k_6$ such that

$$0 \le V(t) \le \frac{H\epsilon_1}{d - \eta e^{-(d + \varepsilon_3)\tau}} \tag{4.32}$$

for all $t > k_7 T$. Because ϵ_1 can be arbitrarily small, we have

$$\lim_{t \to \infty} S(t) = \tilde{S}(t). \tag{4.33}$$

Finally, it follows from (4.23), (4.28), (4.29) and (4.33) that the drinking-free periodic solution $\left(\widetilde{S}(t), 0, \frac{K}{d} - \widetilde{S}(t), \frac{K}{d}\right)$ of system (4.1) is globally attractive. The proof of Theorem 4.3 is completed.

Corollary 4.5. The drinking free periodic solution $\left(\widetilde{S}_e(t), 0, \frac{K}{d} - \widetilde{S}_e(t), \frac{K}{d}\right)$ of the system (4.9) is globally attractive provided that $\theta > \theta^*$ or $\omega > \omega^*$ or $\tau > \tau^*$ where

$$\theta^* = 1 - e^{dT} + \frac{\alpha(d + \eta e^{-(d+\varepsilon_3)\tau})(e^{dT} - 1)}{d(d + \varepsilon_1 + \beta e^{-(d+\varepsilon_1)\omega})},$$
(4.34)

$$\omega^* = -\frac{1}{d+\varepsilon_1} \ln\left[\frac{\alpha(d+\eta e^{-(d+\varepsilon_3)\tau})(1-e^{-dT})}{\beta d\left(1-(1-\theta)e^{-dT}\right)} - \frac{(d+\varepsilon_1)}{\beta}\right]$$
(4.35)

$$\tau^* = -\frac{1}{d+\varepsilon_3} \ln \left[\frac{d(d+\varepsilon_1 + \beta e^{-(d+\varepsilon_1)\omega})(1-(1-\theta)e^{-dT})}{\alpha\eta(1-e^{-dT})} - \frac{d}{\eta} \right]$$
(4.36)

4.4 Permanence of drinking

In this section, we consider the permanence of drinking in the pulse vaccination *SPARS* model with two time-delays, on which the drinking becomes endemic if the drinking population always persists above a certain positive level.

Definition 4.6. In system (4.9), the drinking is said to be permanent if there is a positive constant Υ such that $\lim_{t\to\infty} \inf P(t) > \Upsilon$ for any positive solution (S(t), P(t), A(t), R(t)) of the system (4.9).

Denote

$$R_* = \frac{\alpha(1-\theta)(1-e^{-dT})}{d(d+\varepsilon_1+\beta e^{-(d+\varepsilon_1)\omega})(1-(1-\theta)e^{-dT})}$$
(4.37)

$$P^* = \frac{(1-\theta)(1-e^{-dT})}{(d+\varepsilon_1+\beta e^{-(d+\varepsilon_1)\omega})(1-(1-\theta)e^{-dT})} - \frac{d}{\alpha}$$
(4.38)

It is easily to see that

$$P^* = \frac{d}{\alpha}(R_* - 1). \tag{4.39}$$

Theorem 4.7. If $R_* > 1$, the drinking is permanent in the model (4.9).

Proof. Note that the second equation of (4.9) can be written as

$$P'(t) = \alpha \frac{S(t)P(t)}{N(t)} - \beta P(t-\omega)e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1)P(t)$$

= $\alpha \frac{S(t)P(t)}{N(t)} - \beta P(t)e^{-(d+\varepsilon_1)\omega} + \beta e^{-(d+\varepsilon_1)\omega} (P(t) - P(t-\omega)) - (d+\varepsilon_1)P(t)$
= $P(t) \left(\alpha \frac{S(t)}{N(t)} - \beta e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1) \right) + \beta e^{-(d+\varepsilon_1)\omega} \frac{d}{dt} \int_{t-\omega}^t P(\sigma)d\sigma$
(4.40)

For a positive solution (S(t), P(t), A(t), R(t)) of the system (4.9), we define

$$V(t) = P(t) - \beta e^{-(d+\varepsilon_1)\omega} \int_{t-\omega}^{t} P(\sigma) d\sigma$$
(4.41)

Using (4.40), we have from (4.9) that

$$V'(t) = P(t) \left(\alpha \frac{S(t)}{N(t)} - \beta e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1) \right).$$
(4.42)

Since $R_* > 1$, it is easy to see that $P_* > 0$, and thus there exists sufficiently small $\epsilon > 0$ such that

$$\frac{\alpha}{\beta e^{-(d+\varepsilon_1)\omega} + d + \varepsilon_1}\delta > 1 \tag{4.43}$$

where

$$\delta = \frac{K(1-\theta) \left(1 - e^{-(d+\alpha P^*)T}\right)}{(d+\alpha P^*) \left(1 - (1-\theta)e^{-(d+\alpha P^*)T}\right)} - \epsilon.$$

We claim that it is possible that $P(t) \leq P^*$ for all $t \geq t_0$ where t_0 is a certain nonnegative constant. Suppose the contrary, then as $t \geq t_0$

$$S'(t) = K - \alpha \frac{S(t)P(t)}{N(t)} - dS(t) + \eta R(t-\tau)e^{(d+\varepsilon_3)\tau}$$

$$\geq K - (d+\alpha P^*)\frac{S(t)}{N(t)}$$
(4.44)

Consider the following comparison system :

$$v'(t) = K - (d + \alpha P^*)v(t) , kT < t \le (k+1)T, k \in \mathbb{N}$$

$$v(t^+) = (1 - \theta)v(t) , t = kT$$

$$(4.45)$$

By Lemma 4.2, we obtain

$$\widetilde{v_e}(t) = \frac{K}{d + \alpha P^*} + \left(v^* - \frac{K}{d + \alpha P^*}\right) e^{-(d + \alpha P^*)(t - kT)}, kT < t \le (k + 1)T, \quad (4.46)$$

which is the unique globally asymptotically stable periodic solution of system (4.45), where $v^* = \frac{K(1-\theta)(1-e^{-(d+\alpha P^*)T})}{(d+\alpha P^*)(1-(1-\theta)e^{-(d+\alpha P^*)T})}$.

Thus, there exists a $T^* > 0$ satisfying

$$S(t) > \widetilde{v_e}(t) - \epsilon \ge v^* - \epsilon = \delta \tag{4.47}$$

for all $t \ge t_0 + T^* \triangleq t_1$. By (4.42) and (4.47), we have

$$V'(t) \ge P(t) \left(\alpha \frac{S(t)}{N(t)} - (d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega}) \right)$$

$$= \frac{P(t)}{d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega}} \left(\frac{\alpha \delta}{d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega}} - 1 \right) \quad , t \ne kT$$

$$(4.48)$$

for all $t \ge t_1$. Set

$$P_l = \min_{t \in [t_1, t_1 + \omega]} P(t) > 0.$$
(4.49)

We will now show that $P(t) \ge P_l$ for all $t \ge t_1$. Suppose the contrary. Then there exists a $T_0 \ge 0$ such that $P(t) \ge P_l$ for all $t_1 \le t \le t_1 + \omega + T_0$, and $P'(t_1 + \omega + T_0) \le 0$.

Then, the second equation of system (4.9) can be written as

$$P'(t) = \alpha \frac{S(t)P(t)}{N(t)} - \beta P(t-\omega)e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1)P(t)$$

$$\geq \alpha \delta P(t) - \beta P(t-\omega)e^{-(d+\varepsilon_1)\omega} - (d+\varepsilon_1)P(t).$$
(4.50)

Thus,

$$P'(t_{1} + \omega + T_{0}) \geq \alpha \delta P(t_{1} + \omega + T_{0}) - \beta P(t_{1} + \omega + T_{0})e^{-(d + \varepsilon_{1})\omega}$$

-(d + \varepsilon_{1})P(t_{1} + \omega + T_{0})
\geq P_{l} (\alpha \delta - (\beta e^{-(d + \varepsilon_{1})\omega} + d + \varepsilon_{1}))
> 0 \qquad (4.51)

This is the contradiction. Therefore, $P(t) \ge P_l$ for all $t \ge t_1$. Consequently, for all $t \ge t_1$, we have that

$$V'(t) \ge \frac{P_l}{d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega}} \left(\frac{\alpha\delta}{d + \varepsilon_1 + \beta e^{-(d + \varepsilon_1)\omega}} - 1\right) \quad , t \ge t_1, \qquad (4.52)$$

which implies that as $t \to \infty$, $V(t) \to \infty$.

This contradicts $V(t) \leq \frac{K}{d} \left(1 - \beta e^{-(d+\varepsilon_1)\omega}\right)$. Therefore, the claim is proved. \Box

Corollary 4.8. The drinking is uniformly persistent provided that $\theta < \theta_*$ or $\omega < \omega_*$.

$$\theta_* = 1 - \frac{d\left(d + \varepsilon_1 + \beta e^{(d + \varepsilon_1)\omega}\right)}{\alpha(1 - e^{-dT}) + de^{-dT}\left(d + \varepsilon_1 + \beta e^{(d + \varepsilon_1)\omega}\right)}$$
(4.53)

$$\omega_* = -\frac{1}{d+\varepsilon_1} \ln\left[\frac{\alpha(1-\theta)(1-e^{-dT})}{\beta d\left(1-(1-\theta)e^{-dT}\right)} - \frac{d+\varepsilon_1}{\beta}\right]$$
(4.54)

4.5 Numerical Simulations

In this section, various numerical investigations are carried out to illustrate the theoretical results in sections 4.3 and 4.4. The parameter values used in the numerical simulations are : $\mu = 0.0085$, $\alpha = 0.02$, $\beta = 0.01$, $\gamma = 0.001$, d = 0.0075, $\eta = 0.001$, $\epsilon_1 = 0.001$, $\epsilon_2 = 0.01$ and $\epsilon_3 = 0.002$. The percentages of initial individuals in susceptible, periodic, alcoholics and recovered classes are 50, 30, 15 and 5, respectively. The evolution of each class of population without vaccination , i.e. $\theta = 0$, is shown in Figures 4.1 and 4.2. The numerical results from pulse vaccination with rate $\theta = 0.1$, $\theta = 0.3$, $\theta = 0.6$ and $\theta = 0.9$ are shown in Figures 4.3 - 4.10.

In Figure 4.1, we can see that the number of occasional drinkers dramatically increases in the first month of no vaccination. Conversely, the number of susceptible drinkers decreases rapidly. The amounts of alcoholics and recovered drinkers slightly decrease first, then the number of alcoholics gradually increases until reaching a stable state. Overall, in the non-vaccination community, alcohol drinkers are more than the number of people who do not drink and recovered from drinking.

Figures 4.2 - 4.10, illustrated the effect of pulse vaccination for controlling drinking epidemics with rate 0.1, 0.3, 0.6 and 0.9, respectively. The fluctuation of recovered drinkers is always greater than that for periodic drinkers and alcoholics, that is, the drinking epidemic cannot be permanent.



Figure 4.1: The evolutions of the four classes of populations without vaccination.



Figure 4.2: Three dimensional trajectory in periodic drinker-alcoholics-recovered drinker (P, A, R)-Space without vaccination.



Figure 4.3: The evolutions of the four classes of populations with pulse vaccination rate $\theta=0.1.$



Figure 4.4: Three dimensional trajectory in periodic drinker-alcoholics-recovered drinker (P, A, R)-Space with pulse vaccination rate $\theta = 0.1$.



Figure 4.5: The evolutions of the four classes of populations with pulse vaccination rate $\theta=0.3.$



Figure 4.6: Three dimensional trajectory in periodic drinker-alcoholics-recovered drinker (P, A, R)-Space with pulse vaccination rate $\theta = 0.3$.



Figure 4.7: The evolutions of the four classes of populations with pulse vaccination rate $\theta=0.6.$



Figure 4.8: Three dimensional trajectory in periodic drinker-alcoholics-recovered drinker (P, A, R)-Space with pulse vaccination rate $\theta = 0.6$.



Figure 4.9: The evolutions of the four classes of populations with pulse vaccination rate $\theta=0.9.$



Figure 4.10: Three dimensional trajectory in periodic drinker-alcoholics-recovered drinker (P, A, R)-Space with pulse vaccination rate $\theta = 0.9$.

4.6 Concluding Remarks

In this chapter, we have studied the dynamical behavior of a drinking epidemic model with two time-delays and impulsive vaccination. Two thresholds R_* and R^* are derived and it is shown that if $R_* < 1$ then the drinking will disappear, while if $R^* > 1$ then the drinking will be permanent which means that after some period of time the drinking will become hazardous. Analytical expression of three critical values θ^* , ω^* and τ^* have been established and it is shown that $\theta > \theta^*$ or $\omega > \omega^*$ or $\tau > \tau^*$ implies that the drinking will eradicate, while $\theta < \theta_*$ or $\omega < \omega_*$ implies that the drinking will be uniformly persistent. The research indicates that the long latent period of drinking or a long recovered period or a large pulse vaccination rate will lead to eradication of drinking.

CHAPTER 5

Summary and Further Research

5.1 Summary

In this thesis, we have investigated a mathematical model describing the dynamics of drinking. This model consists of four differential equations describing the rate of change for four subpopulation S, P, A and R. We investigated the stability of the model and have demonstrated that the model is asymptotically stable. Furthermore, we studied two strategies to eradicate the drinking epidemic and investigate the optimal control of treatment and impulsive vaccination. Based on previous work in the field, some new analytical and numerical results have been derived. The main results are summarized as follows:

(1) Results for the stability analysis of the SPARS drinking epidemic model

(i) The threshold quantity that determines the average number of secondary drinkers produced when one drinker individual is introduced into a group of susceptible individuals, the basic reproduction number, is $R_0 = \frac{\alpha \mu}{d(d+\beta+\varepsilon_1)}$ where α is the contact rate, μ is the rate of the general population entering the susceptible population, d is the natural death rate , β is the proportion becoming alcoholic and ε_1 is the death rate of occasional drinkers.

(ii) From the investigation, it can be concluded that the drinking free equilibrium is stable if $R_0 < 1$, or otherwise unstable. Moreover, persistent drinking is always stable. The model was shown to be stable, which is an important feature of a good model.

(iii) Numerical simulation has been carried out and the results have confirmed the verification of analytical results. (2) Results for the optimal control strategy

(i) An optimal control strategy has been established to minimize the number of drinkers, including occasional drinkers and alcoholics, and to maximize the number of recovered individuals.

(ii) Numerical simulations show that, under the optimal control strategy, the numbers of periodic drinkers and the alcoholic individuals decrease while the numbers of recovered group and total population increase in the optimality system.

(3) Results for the impulsive vaccination.

(i) Based on the mathematical model constructed, we investigated the drinking epidemic model with two time-delays and impulsive vaccination. The pulse term is $(1 - \theta)S(t)$, which means that the vaccination is applied every T time interval and $\theta \in (0, 1)$ denotes the proportion of successful vaccination.

(ii) By analysing the *SPARS* model, two thresholds have been established, one for global interactivity of the drinking-free solution and another for the permanence of drinking solution.

(iii) As summarized in Corollaries 4.5 and 4.8, drinking disappears when $\theta > \theta^*$ whereas drinking persists when $\theta < \theta_*$ where θ^* and θ_* are shown in Corollaries 4.5 and 4.8, respectively.

(iv) Our results indicate that a long latent period of the disease or a large pulse vaccination rate will lead to eradication of drinking.

5.2 Further Research

In this project, we minimize the number of drinkers by finding the optimal control for the drinking epidemic model with numerical verification of the results with the corresponding parameters to the thresholds. Using real data to demonstrate how the optimal control theory can be applied in real situation will be continued in future research. One possible extension is to consider the optimal control strategy of the *SPARS* drinking epidemic model with time delay. Moreover, the two epidemic control strategies, namely the optimal control and impulsive vaccination, may be extended to study other epidemics.

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