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MATHEMATICAL MODELING, ANALYSIS AND OPTIMAL CONTROL OF AN ALCOHOL DRINKING MODEL WITH LIVER COMPLICATION

BOUCHAIB KHAJJI[1,*], ABDELFATAH KOUIDERE[1], OMAR BALATIF[2], MOSTAFA RACHIK[1]

[1]Laboratory of Analysis, Modeling, and Simulation (LAMS), Department of Mathematics and Computer Science,Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca. BP 7955, Sidi Otheman, Casablanca, Morocco

[2]Laboratory of Dynamical Systems,Mathematical Engineering Team (INMA), Department of Mathematics, Faculty of Sciences El Jadida, Chouaib Doukkali University, El Jadida, Morocco

Abstract. We want to develop our model [2]. So, this study discusses the influence of awareness programs and treatment on drinking behavior of the drinker's classes through mathematical models. There are five categories of population in this model, namely: potential drinkers, moderate drinkers, heavy drinkers, heavy drinkers with liver complications, recovered and quitters of drinking. The model is analyzed using stability theory of nonlinear differential equations. Based on analysis result, the model has two equilibrium points: drinking-free equilibrium point and drinking present equilibrium point. These equilibrium points are locally and globally asymptotically stable under certain conditions. We also study the sensitivity analysis of the model parameters to know the parameters that have a high impact on the reproduction number R_0. Moreover, the controls used are awareness programs and treatment. The purpose theses optimal controls as to minimize the heavy drinkers with and without complications as well as the control costs. Pontryagin's principle is then implemented to solve optimal control problems. Finally, numerical simulations are carried out to determine the effectiveness of the controls used.

Keywords: alcohol drinking model; liver complication; optimal control.

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*Corresponding author

E-mail address: khajjibouchaib@gmail.com

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1. INTRODUCTION

Phenomenon of addiction to drinking alcohol is a problem that has received the attention of several researchers and scholars in many fields including psychology, sociology, psychiatry, mathematics etc, in an attempt to highlight the reasons behind this phenomenon and identify effective methods of prevention and treatment to this problem. Alcoholism is the misuse and excessive use of alcohol, which may cause physical, social, and moral damage to all strata of society (poor, rich, undemanding, young men, women....). According to the World Health Organization's 2016 report, there are 3 million deaths a year, which accounts for 6% of all deaths due to drinking alcohol. Long-term alcohol consumption can lead to a number of physical symptoms including cirrhosis of the liver, pancreatitis, alcoholic liver disease, and many cancers. Also, can impact other areas of our life such as relationship problems with family or friends, legal trouble, financial issues and poor performance at work or in school [20].

Drink more alcohol intake may lead to fatty liver problems and then to hepatic failure, type 2 diabetes and cirrhosis. Alcohol is involved in about half of all deaths due to liver disease in the United States of America each year. Alcoholic liver cirrhosis passes from fatty liver stage to alcoholic hepatitis and then to alcoholic cirrhosis. According to the American Liver Foundation, between 10 and 20 percent of people who drink alcohol will have cirrhosis [21]. The largest increases were related to alcoholic cirrhosis among people aged 25 to 34 years old [18].

Table (1) shown deaths caused by liver cirrhosis disease, age-standardized death rates (15+), per 100,000 population in 2016 [21].

Table(1): Liver cirrhosis, age-standardized death rates (15+) per 100,000 population in 2016

Country	**Male**	**Female**
Afghanistan	28.2	19.6
Albania	15.8	6.2
Algeria	19	6.3
Brazil	26.7	6.4
Egypt	200.4	6.6
Cameroon	76.4	6.7
Germany	18.9	6.8
Russian Federation	40.3	6.9
Azerbaijan	53.8	6.10
Morocco	16.2	6.11
United States of America	19.7	6.13
United Arab Emirates	13.6	6.14
Turkey	14.2	6.15

Some of the measures adopted to reduce the harmful use of alcohol worldwide are inclusion of alcohol-related targets in major global policy and strategic frameworks such as the 2030 Agenda for Sustainable Development, increased health consciousness in populations, decreased youth alcohol consumption as observed in a wide range of countries, recognition of the role of alcohol control policies in reducing health and gender inequalities, and accumulating evidence of effectiveness and cost effectiveness of a number of alcohol control measures[20].

Several mathematicians did a lot of work in order to understand the dynamics and analysis of drinking and reduce its harm on the drinker and society as well as minimizing the number of addicted drinkers. For example, S. H. Ma et al [15] modeled alcoholism as a contagious disease and used an optimal control to study their mathematical model with awareness programs and time delay. S. Sharma et al [17] developed a mathematical model of alcohol abuse and discussed the existence and stability of drinking-free, endemic equilibria and sensitivity analysis of R_0. They demonstrated that backward bifurcation can occur when $R_0 = 1$. X. Y. Wang et al [19] proposed and analyzed a non-linear alcoholism model and used optimal control for the purpose of hindering interaction between susceptible individuals and infected individuals. B. Benedict [3] used a SIR-type model with a contact rate between susceptibles and alcoholism, he getted alcoholism reproductive number and discussed the existence and stability of two equilibria. H. F. Huo et al [10] proposed a new social epidemic model to depict alcoholism with media coverage which was proven to be an effective way in pushing people to quit drinking. I. k. Adu et al [1] used a non-linear $SHTR$ mathematical model to study the dynamics of drinking epidemic. They divided their population into four classes: non-drinkers (S), heavy drinkers (H), drinkers receiving treatment (T) and recovered drinkers (R). They discussed the existence and stability of drinking-free and endemic equilibrium. Other mathematical models have also been widely used to study this phenomenon (For example, [5,11,12...]). Besides these works, we want to develop our model [2]talking about "A Discrete Mathematical Modeling of the Influence of Alcohol Treatment Centers on the Drinking Dynamics Using Optimal Control" by change some compartments by to new compartments as C represents liver complications.

So, we will study the dynamics and analysis of a mathematical alcohol model $PMHCQ$ which contains the following additions:

• Compartment C represents the number of the heavy drinkers with liver complications associated with prolonged and excessive alcohol consumption (alcoholic hepatitis, fibrosis and cirrhosis).

•The death rate induced by the heavy drinkers δ_1.

•The death rate induced by the heavy drinkers with liver complications δ_2. The drinker's classes of this model are divided into five compartments: Potential drinkers (P), Moderate drinkers (M), Heavy drinkers (H), Heavy drinkers with liver complications (C) and the recovered and quitters of drinking(Q). We propose a mathematical model that describes the dynamics of the drinker's classes. By using Routh- Hurwitz criteria and constructing Lyapunov functions, the local and the global stability of drinking-free equilibrium and drinking present equilibrium are obtained. We also study the sensitivity analysis of the model parameters to know the parameters that have a high impact on the reproduction number R_0. Also, we seek to find the optimal strategies to minimize the number of drinkers with and without complications and maximize the number of the recovered and quitters of drinking (Q). In order to achieve this purpose, we use optimal control strategies associated with three types of controls: the first represents awareness programs for potential drinkers, the second is the effort of treatment for heavy drinkers and the third represents treatment for the heavy drinkers with liver complications.

The paper is organized as follows: In Section 2, we present our *PMHCQ* mathematical model that describes the dynamics of the drinker's classes. In Section 3, we discuss basic properties and positivity of solutions. In Section 4 and 5, we analyse the local and global stability and the problem of parameters sensitivity. Some numerical simulations are discussed in section 6. In section 7, we present the optimal control problem for the proposed model where we give some results concerning the existence of the optimal controls and we characterize these optimal controls using Pontryagin's maximum principle. Also, numerical simulations are given in section 8. Finally, we conclude the paper in Section 9.

2. A Mathematical Model

We propose a continuous-time model *PMHCQ* to describe the population dynamics and analyze the interactions between the drinker's classes. The population is divided into five compartments: potential drinkers $P(t)$, moderate drinkers $M(t)$, heavy drinkers $H(t)$, heavy drinkers with liver complications $C(t)$ and the recovered and quitters of drinking $Q(t)$.

The graphical representation of the proposed model is shown in FIGURE 1.

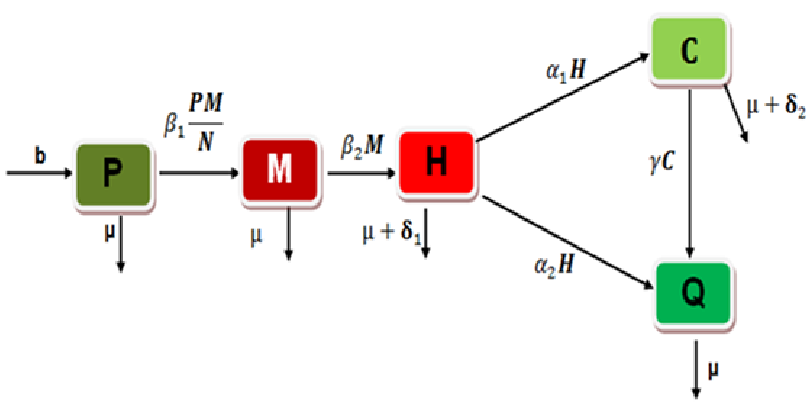


FIGURE 1. Schematic diagram of the five drinking classes in the model

We consider the following system of five non-linear differential equations:

$$
\begin{cases}
\frac{dP(t)}{dt} = b - \beta_1 \frac{P(t)M(t)}{N} - \mu P(t) \\
\frac{dM(t)}{dt} = \beta_1 \frac{P(t)M(t)}{N} - (\beta_2 + \mu) M(t) \\
\frac{dH(t)}{dt} = \beta_2 M(t) - (\mu + \alpha_1 + \alpha_2 + \delta_1) H(t) \\
\frac{dC(t)}{dt} = \alpha_1 H(t) - (\mu + \gamma + \delta_2) C(t) \\
\frac{dQ(t)}{dt} = \alpha_2 H(t) + \gamma C(t) - \mu Q(t)
\end{cases}
\tag{1}
$$

The potential drinkers $P(t)$ represents individuals whose age is over adolescence and adulthood and are susceptible of drinking alcohol. The number of individuals of this compartment is increased by the recruitment rate denoted by b and decreased by an effective contact with the moderate drinkers at β_1 rate and natural death μ. Due to effective contact with moderate drinkers in some social occasions like weddings, celebrating graduation ceremonies, week-end parties and end of the year celebration, potential drinkers can acquire drinking behavior and can become moderate drinkers. In other words, it is assumed that the acquisition of a drinking behavior is analogous to acquiring disease infection.

Moderate drinkers M:

$$
\frac{dM(t)}{dt} = \beta_1 \frac{P(t)M(t)}{N} - (\mu + \beta_2) M(t) \tag{2}
$$

The compartment M is composed of moderate drinkers who are able to control their intake of alcohol during some events and occasions or they drink in a way that is unapparent to their social environment. This category of drinkers do not face any problems or negative consequences. Friends or family do not complain about their consumption of alcohol. A moderate drinker does not think about drinking very often or often feel a need to drink. Alcohol does not dominate their thoughts and they do not need to set limits when they drink. They are not prone to extreme mood swings, fighting or being violent. This compartment is increased by potential drinkers who turn to be moderate drinkers at rate β_1. It is decreased when moderate drinkers become heavy drinkers at a rate β_2 and also by natural death at rate μ.

Heavy drinkers H:

$$\frac{dH(t)}{dt} = \beta_2 M(t) - (\mu + \delta_1 + \alpha_1 + \alpha_2)H(t) \tag{3}$$

The compartment H contains heavy drinkers who are addicted to alcohol. An alcoholic person faces a great difficulty to control or set limits for their consumption. The majority of alcoholics begin as potential drinkers and then turn to moderate drinkers. Alcohol seems to exert a control on the alcoholic's life. Their job, their family, social circle and health are all endangered. Despite these negative consequences, the alcoholic is unable to quit drinking. The alcoholics may begin to disclaim that they have a problem; this disclaim can make it even more difficult for the person to get help. Alcohol addiction is considered to be a disease; it changes chemicals in the addict's brain and has made alcohol the most important thing in their life. At the time a person is an alcoholic, they will usually need to get help at a rehab to overcome their addiction. This compartment becomes larger as the number of heavy drinkers increases by the rate β_2 and decreases by the rates α_1(α_1 is a rate the heavy drinkers individuals becomes heavy drinkers with liver complications) and the rate α_2 (α_2 is a rate the heavy drinkers individuals they became recovered and quitters of drinking) and δ_1(δ_1 is the death rate induced by H) and also by natural death at rate μ.

Heavy drinkers with liver complications C:

$$\frac{dC(t)}{dt} = \alpha_1 H(t) - (\mu + \gamma + \delta_2)C(t) \tag{4}$$

This compartment represents the heavy drinkers with liver complications associated with prolonged and excessive alcohol consumption (alcoholic hepatitis, fibrosis and cirrhosis). It is increased by the rate α_1 and decreased by the rates γ , δ_2 and μ. Where δ_2 is the death rate induced by the liver complications of heavy drinking and γ is the number of individuals who stopped drinking and were cured from these complications.

Recovered and quitters of drinking Q:

$$\frac{dQ(t)}{dt} = \gamma C(t) + \alpha_2 H(t) - \mu Q(t) \tag{5}$$

$Q(\mathbf{t})$ refers to the individuals who recovered and quitters of drinking. It is increased by the rates α_2 and γ and decreased by the rate μ.

The total population size at time t is denoted by $N(t)$ with $N(t)$=$P(t)+M(t)+H(t)+C(t)+Q(t)$.

3. Basic Properties

3.1. Invariant Region.

It is necessary to prove that all solutions of system (1) with positive initial data will remain positive for all times $t > 0$. This will be established by the following lemma.

Lemma 1. *All feasible solution $P(t)$,$M(t)$,$H(t)$,$C(t)$ and $Q(t)$ of system equation (1) are bounded by the region*

$$\Omega = \left\{ (P,M,H,C,Q) \in IR^5_+ : P+M+H+C+Q \leq \frac{b}{\mu} \right\}. \tag{6}$$

Proof. From the system equation(1)

$$\frac{dN(t)}{dt} = \frac{dP(t)}{dt} + \frac{dM(t)}{dt} + \frac{dH(t)}{dt} + \frac{dC(t)}{dt} + \frac{dQ(t)}{dt} \tag{7}$$

$$\frac{dN(t)}{dt} = b - \mu N(t) - \delta_1 H - \delta_2 C$$

implie that

$$\frac{dN(t)}{dt} \leq b - \mu N(t).$$

it follows that

$$N(t) \leq \frac{b}{\mu} + N(0)e^{-\mu t} \tag{8}$$

Where $N(0)$ is the initial value of total number of people, thus, $\lim\limits_{t\to+\infty} \sup N(t) \leq \frac{b}{\mu}$

then $$P(t)+M(t)+H(t)+C(t)+Q(t) \leq \frac{b}{\mu}$$

Hence, for the analysis of model (1), we get the region which is given by the set:

$$\Omega = \left\{ (P,M,H,C,Q) \in IR_{+}^{5} : P+M+H+C+Q \leq \frac{b}{\mu} \right\}.$$

wich is a positively invariant set for (1), so we only need to consider dynamics of system on the set Ω non-negative of solutions. □

3.2. Positivity of the solutions of the model.

Theorem 2. *If* $P(0) \geq 0, M(0) \geq 0, H(0) \geq 0, C(0) \geq 0$ *and* $Q(0) \geq 0$, *then the solution of system equations* (1) $P(t), M(t), H(t), C(t)$ *and* $Q(t)$ *are positive for all* $t > 0$.

Proof. From the first equation of the system (1) we have:

$$\frac{dP(t)}{dt} = b - \left[\beta_1 \frac{M(t)}{N} + \mu \right] P(t), \tag{9}$$

We consider

$$A(t) = \beta_1 \frac{M(t)}{N} + \mu \tag{10}$$

It follows from the equation (9) that

$$\frac{dP(t)}{dt} + A(t)P(t) \geqslant 0 \tag{11}$$

We multiply inequality (11) by

$$\exp\left(\int_0^t (A(s))\, ds\right). \tag{12}$$

we find

$$\frac{dP(t)}{dt} * \exp\left(\int_0^t (A(s))\, ds\right) + A(t)P(t) * \exp\left(\int_0^t (A(s))\, ds\right) \geqslant 0, \tag{13}$$

Implies

$$\frac{d}{dt}\left(P(t) \exp\left(\int_0^t (A(s))\, ds\right)\right) \geqslant 0, \tag{14}$$

integrating (14) between 0 and t gives

$$P(t) \geqslant P(0)\exp(\int_0^t (-A(s))\,ds, \tag{15}$$

So, the solution P(t) is positive. Similarly, From the second equation of system (1), we have:

$$M(t) \geqslant M(0)\exp(\int_0^t (-B(s))\,ds, \tag{16}$$

where

$$B(t) = \beta_1 \frac{P(t)}{N} - (\mu + \beta_2) \tag{17}$$

Similarly, From the other equations of system (1), we have

$$H(t) \geqslant H(0)\exp(-(\mu + \delta_1 + \alpha_1 + \alpha_2)t) \geqslant 0, \tag{18}$$

$$C(t) \geqslant C(0)\exp(-(\mu + \delta_2 + \gamma)t) \geqslant 0, \tag{19}$$

and

$$Q(t) \geqslant Q(0)\exp(-\mu t) \geqslant 0, \tag{20}$$

Therfore, we can see that $P(t) \geqslant 0$, $M(t) \geqslant 0$, $H(t) \geqslant 0$, $C(t) \geqslant 0$ and $Q(t \geqslant 0$ $\forall t \geq 0$, this completes the proof.

The first three equations in system (1) are independent of the variables C and Q. Hence, the dynamics of equation system (1) is equivalent to the dynamics of equation system :

$$\begin{cases} \frac{dP(t)}{dt} = b - \beta_1 \frac{PM}{N} - \mu P, \\ \frac{dM(t)}{dt} = \beta_1 \frac{PM}{N} - (\beta_2 + \mu)M, \\ \frac{dH(t)}{dt} = \beta_2 M - (\mu + \alpha_1 + \alpha_2 + \delta_1)H, \end{cases} \tag{21}$$

4. Equilibria and Their Stability Analysis

4.1. Equilibrium Point: The standard method is used to analyzed the model (21). In this model, there are two equilibrium points, drinking-free equilibrium point and drinking present equilibrium point. The equilibrium point are found by setting the right hand side of equations (1) – (3) egual to zero.

The drinking-free equilibrium $E^0\left(\frac{b}{\mu},0,0\right)$ is achieved in the absence of drinking ($M = H = 0$).

The drinking present equilibrium $E^*\left(P^*,M^*,H^*\right)$ is achieved when drinkers exist ($M \neq 0$ and $H \neq 0$). Where:

$$\begin{cases} P^*=\frac{b}{\mu R_0}, \\ M^*=\frac{b(R_0-1)}{\beta_1}, \\ H^*=\frac{b\beta_2(R_0-1)}{\beta_1(\mu+\alpha_1+\alpha_2+\delta_1)}, \\ R_0 = \frac{\beta_1}{\mu+\beta_2}, \end{cases} \tag{22}$$

R_0 is the basic reproduction number that measures the average number of new drinkers generated by single drinker in a population of potential drinkers. The value of R_0 will indicates whether the epidemic could occur or not. The reproduction basic number can be determined by using the next generation matrix method formulated in (Driessche et al (2002)).

4.2. Local stability analysis. Now we proceed to study the stability behavior of equilibria E^0 and E^* .

4.2.1. *The drinking-free equilibrium.* In this section, we analyze the local stability of the drinking-free equilibrium.

Theorem 3. *The drinking-free equilibrium* $E^0\left(\frac{b}{\mu},0,0\right)$ *of the system* (21) *is asymptotically stable if* $R_0 \leq 1$ *and unstable if* $R_0 > 1$.

Proof. The jacobian matrix at E is given by

$$J(E)=\begin{pmatrix} -\beta_1\frac{M}{N}-\mu & -\beta_1\frac{P}{N} & 0 \\ \beta_1\frac{M}{N} & \beta_1\frac{P}{N}-\beta_2-\mu & 0 \\ 0 & \beta_2 & -\mu-\alpha_1-\alpha_2-\delta_1 \end{pmatrix} \tag{23}$$

The jacobian matrix for the drinking-free equilibrium is given by

$$J(E^0)=\begin{pmatrix} -\mu & -\beta_1 & 0 \\ 0 & \beta_1-\beta_2-\mu & 0 \\ 0 & \beta_2 & -\mu-\alpha_1-\alpha_2-\delta_1 \end{pmatrix} \tag{24}$$

where $P_0=\frac{b}{\mu}=N$.

The characteristic equation of this matrix is given by $\det(J(E^0)-\lambda I_3)=0$ where I_3 is a square identity matrix of order 3. Therefore, eigenvalues of the characteristic equation of $J(E^0)$ are

$$\begin{cases} \lambda_1=-\mu \\ \lambda_2=-(\beta_2+\mu-\beta_1)=-(\mu+\beta_2)\left(1-\frac{\beta_1}{\mu+\beta_2}\right) \\ \lambda_3=-(\mu+\alpha_1+\alpha_2+\delta_1) \end{cases} \tag{25}$$

$$R_0=\frac{\beta_1}{\mu+\beta_2}, \tag{26}$$

Therefore, all the eigenvalues of the characteristic equation are clearly real and negatives if $R_0\leq 1$. We conclude the drinking-free equilibrium is locally asymptotically stable if $R_0\leq 1$ and unstable if $R_0>1$.

4.2.2. *Drinking present equilibrium.* In this section, we analyze the local stability of the drinking present equilibrium.

Theorem 4. *The drinking present equilibrium E^* is locally asymptotically stable if $R_0>1$, and unstable otherwise.*

Proof. We present $E^*(P^*, M^*, H^*)$ as drinking present equilibrium of system (21) and $P^* \neq 0, M^* \neq 0$, $H^* \neq 0$ The Jacobian matrix is

$$J(E^*) = \begin{pmatrix} -\beta_1 \frac{M^*}{N} - \mu & -\beta_1 \frac{P^*}{N} & 0 \\ \beta_1 \frac{M^*}{N} & \beta_1 \frac{P^*}{N} - \beta_2 - \mu & 0 \\ 0 & \beta_2 & -\mu - \alpha_1 - \alpha_2 - \delta_1 \end{pmatrix}. \tag{27}$$

where

$$\begin{cases} P^* = \frac{b}{\mu R_0}, \\ M^* = \frac{b(R_0 - 1)}{\beta_1}, \\ H^* = \frac{b\beta_2(R_0 - 1)}{\beta_1(\mu + \alpha_1 + \alpha_2 + \delta_1)}, \end{cases} \tag{28}$$

We see that the characteristic equation $P(\lambda)$ of $J(E^*)$ has an eigenvalue $\lambda_1 = -(\mu + \alpha_1 + \alpha_2 + \delta_1)$ whose real part is negative. So, in order to determine the stability of the drinking present equilibrium of model (21), we discuss the roots of the following equation $P(\varphi)$:

$$P(\varphi) = \varphi^2 + a_1 \varphi + a_2 \tag{29}$$

where

$$\begin{cases} a_1 = \beta_1 \frac{M^*}{N} + \mu > 0, \\ a_2 = \beta_1^2 \frac{P^*}{N} \frac{M^*}{N} > 0, \end{cases} \tag{30}$$

By routh- Hurwitz Criterrion, the system(21) is locally asymptotically stable if $a_1 > 0$ and $a_2 > 0$.

Thus, the drinking present equilibrium E^* of system(21) is locally asymptotically stable.

4.3. Global Stability.

4.3.1. *Global stabilty of the drinking-free equilibruim.* To show that the system (21) is globally asymptotically stable, we use the Lyapunov function theory for both the drinking-free equilibrium and the drinking present equilibrium. First, we present the global stability of the drinking-free equilibrium E^0 when $R_0 \leq 1$

Theorem 5. *The drinking-free equilibruim $E^0$is globally asymptotically stable if $R_0 \leq 1$, and unstable otherwise.*

Proof. Consider the following Lyapunov function

$$V(P,M,H,C,Q) = M, \tag{31}$$

The derivative of $V(P,M,H,C,Q)$ with respect to t gives

$$\begin{aligned} \tfrac{dV}{dt} &= \tfrac{dM}{dt} \\ &= \left[\tfrac{\beta_1 P}{N} - (\mu+\beta_2)\right] M \\ &= (\mu+\beta_2)\left[\tfrac{\beta_1 P}{(\mu+\beta_2)N} - 1\right] M \\ &\leq (R_0 - 1)M. \end{aligned} \tag{32}$$

where $R_0 = \frac{\beta_1}{\mu+\beta_2}$,

So, $\frac{dV}{dt} \leq 0$ if $R_0 \leq 1$.

Furthermore $\frac{dV}{dt} = 0$ if and only if $M = 0$, Hence, by Lasalle's invariance principle [14], E^0 is globally asymptotically stable.

4.3.2. *Global stabilty of the drinking present equilibrium.* The final result of the global stability of E^* in this section is as follows:

Theorem 6. *The drinking present equilibrium point E^* is globally asymptotically stable if $R_0 > 1$.*

Proof. Consider the Lyapunov function V:

$$\begin{aligned} V \quad &: \quad \Gamma \to IR \\ V(P,M) \quad &= \quad c_1\left[P - P^*\ln\left(\frac{P}{P^*}\right)\right] + c_2\left[M - M^*\ln\left(\frac{M}{M^*}\right)\right]. \end{aligned} \tag{33}$$

Where c_1 and c_2 are positive constant to be chosen latter and $\Gamma = \{(P,M) \in \Gamma / P > 0, M > 0\}$

Then, the time derivative of the Lyapunov function is given by

$$\frac{dV(P,M)}{dt} = -bc_1\frac{[P-P^*]^2}{PP^*} + \frac{\beta_1}{N}(c_2 - c_1)[P-P^*][M-M^*]. \tag{34}$$

For $c_1 = c_2 = 1$, we have

$$\frac{dV\left(P,M\right)}{dt} = -b\frac{\left[P-P^*\right]^2}{PP^*} \leq 0, \tag{35}$$

Also, we obtain

$$\frac{dV\left(P,M\right)}{dt} = 0 \Leftrightarrow P = P^* \tag{36}$$

Hence, by LaSalle's invariance principle (LaSalle et al (1976)) the drinking present equilibrium point E^* is globally asymptotically stable on Γ.

5. Sensitivity Analysis of $\Re_0$

Sensitivity analysis is commonly used to determine the model robustness to parameter values, that is, to help us know the parameters that have a high impact on the reproduction number $\Re_0$. Using the approach in Chitnis et al (Chitnis et al (2008)) we calculate the normalized forward sensitivity indices of $\Re_0$. Let

$$\Upsilon_m^{\Re_0} = \frac{m}{\Re_0} * \frac{\partial \Re_0}{\partial m}. \tag{37}$$

denote the sensitivity index of $\Re_0$ with respect to the parameter m. We get

$$\begin{cases} \Re_0 = \frac{\beta_1}{\mu+\beta_2}, \\ \Upsilon_{\beta_1}^{\Re_0} = 1, \\ \Upsilon_{\beta_2}^{\Re_0} = -\frac{\beta_2}{\mu+\beta_2}, \\ \Upsilon_{\mu}^{\Re_0} = -\frac{\mu}{\mu+\beta_2}, \end{cases} \tag{38}$$

From the above discussion we observe that the basic reproduction number $\Re_0$ is most sensitive to changes in β_1. If β_1 will increase $\Re_0$ will also increase with same proportion and if β_1 will decrease in same proportion, μ and β_2 have an inversely proportional relationship with $\Re_0$. So, an increase in any of them will bring about a decrease in $\Re_0$, however, the size of the decrease will be proportionally smaller. Recall that μ is the natural death rate of the population. It is clear that increase in either of these rates is neither ethical nor practical. Given $\Re_0$'s sensitivity to β_1, it seems sensible to focus efforts on the reduction of β_1. 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 drinkers than efforts to increase the numbers of individuals accessing treatment.

In table(2), we present the sensitivity indices of all model parameters $\Re_0$. The parameters are arranged from the most sensitive to the least sensitive.

Table(2)

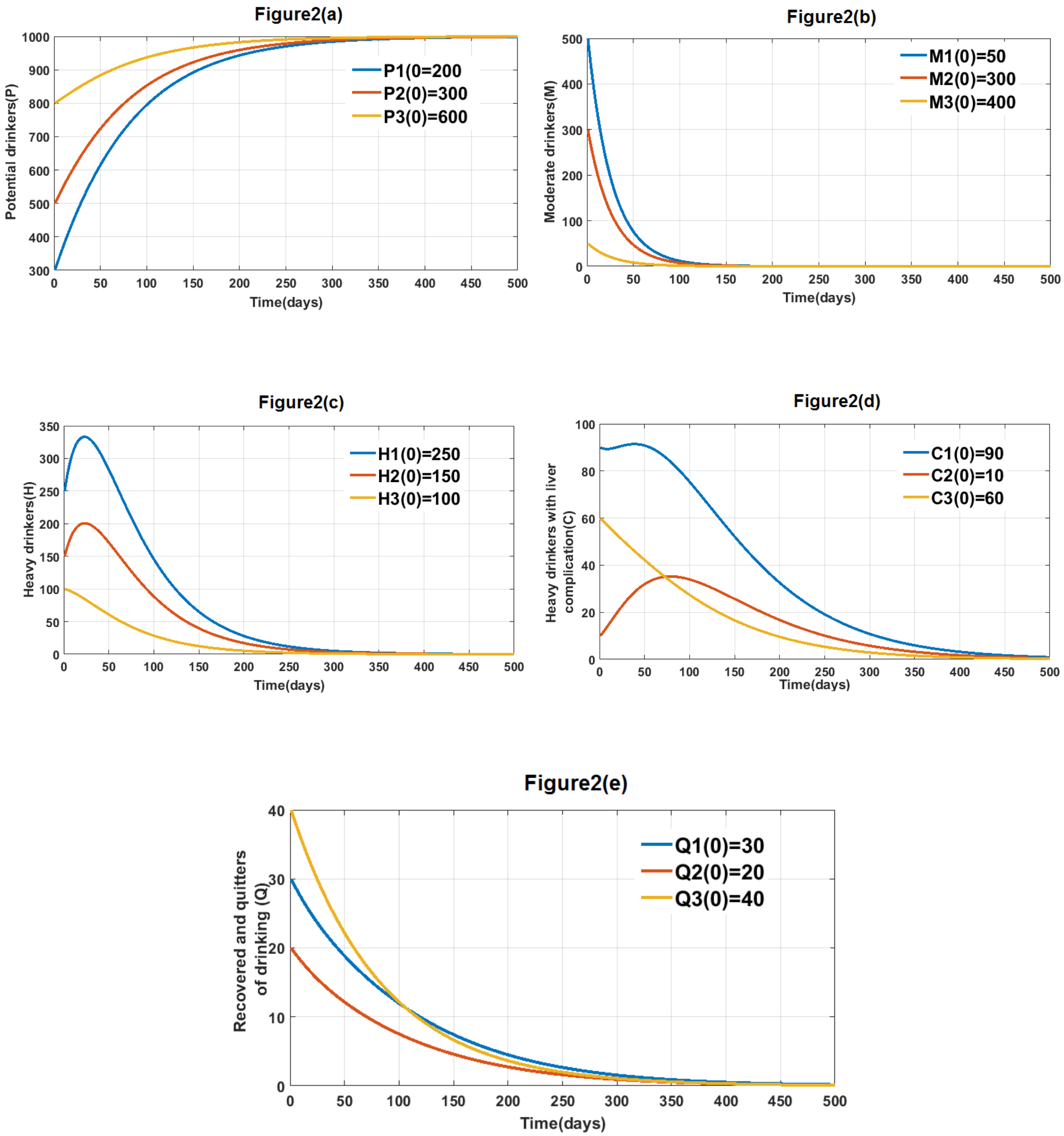
Parameter	Description	Sensitivity index
β_1	The effective contact rate	$+\mathbf{1}$
μ	The natural death rate	$-\mathbf{0,32}$
β_2	coefficient of transmission the M at H	$-\mathbf{0,68}$

)

Hence, with sensitivity analysis, one can get insight on the appropriate intervention strategies to prevent and control the spread of drinking behavior of the population on drinkers classes that described by model (1).

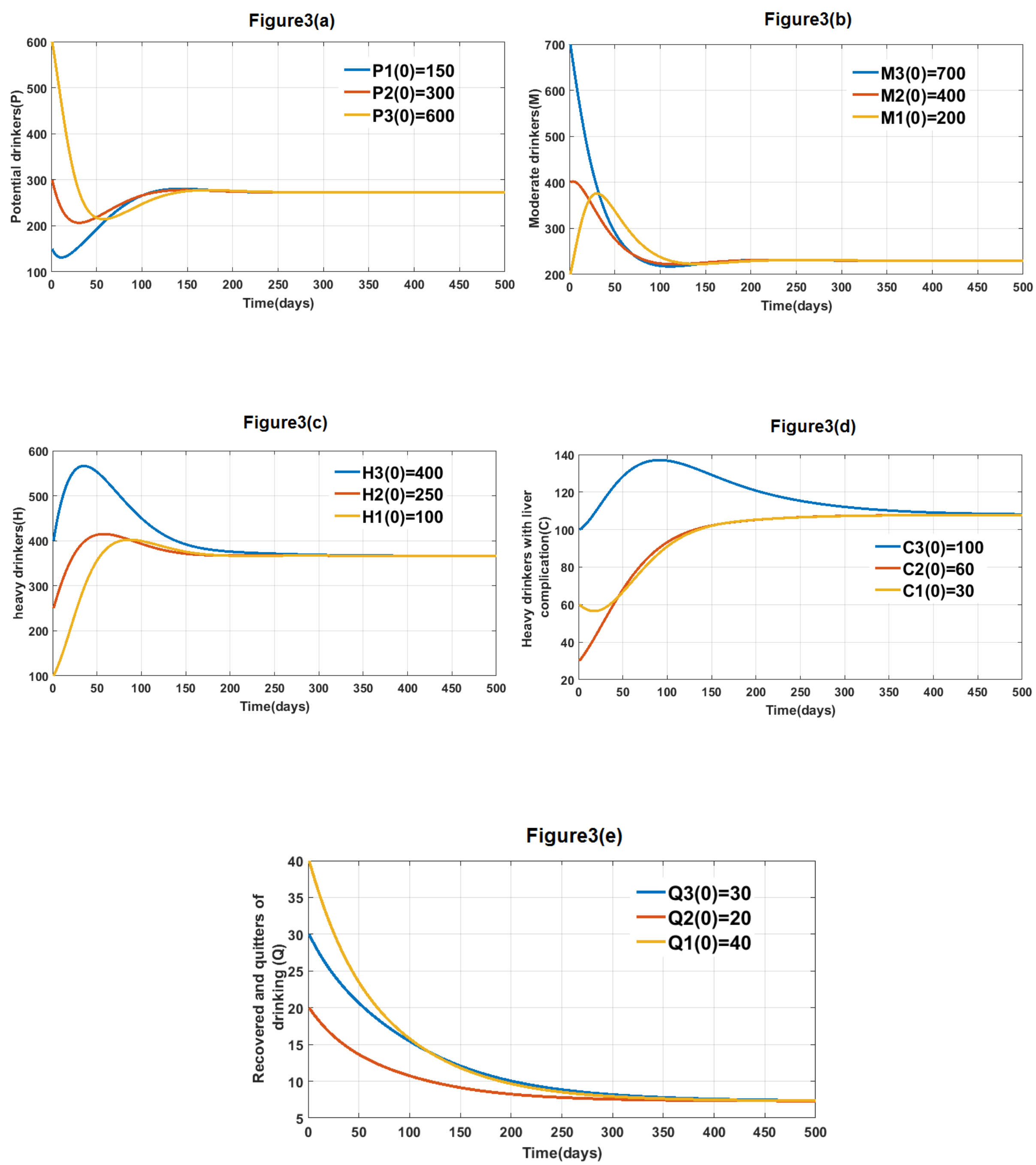
6. Numerical Simulations

In this section, we illustrate some numerical solutions of model (1) for different values of the parameters. The resolution of the system (1) was created using the Gauss-Seidel-like implicit finite-difference method developed by Gumel (Gumel et al (2001)), presented in (Karrakchou et al (2006)) and denoted GSS1 method. We use the following different initial values such that $P+M+H+C+Q=1000$. We present some numerical simulations in order to illustrate our theoretical results, we consider system (1) with the following parameter values $b=65$**,** $N=1000$ **,** $\delta_1=0.002$, $\mu=0.065$, $\beta_1=0.02$, $\beta_2=0.14$, $\alpha_1=0.02$, $\alpha_2=0.001$, $\delta_2=0.002$, $\gamma=0.001$, $h=0.2$**,** $t_f=500$. We begin by a graphic representation of the drinking-free equilibrium $E^0$and we use the same parameters and different initial values, $\Re_0=0.097$ and $\Re_0<1$. We have the drinking-free equilibrium $E^0=(1000;0;0;0;0)$. In this case, according to theorem (5), the drinking-free equilibrium E^0 of the system (1) is globally asymptotically stable on Γ: (See Figure2).



We present some numerical simulations in order to illustrate our theoretical results, we consider system (1) with the following parameter values $b = 65$**,** $N = 1000$ **,** $\delta_1 = 0.002$, $\mu = 0.065$, $\beta_1 = 0.75$, $\beta_2 = 0.14$, $\alpha_1 = 0.02$, $\alpha_2 = 0.001$, $\delta_2 = 0.002$, $\gamma = 0.001$, $h = 0.2$**,** $t_f = 500$.

Thorfore, we begin by a graphic representation of the drinking present equilibrium $E^*$and we use the same parameters and different initial values, $\Re_0 = 5.32$. We have the drinking present equilibrium $E^* = (273.3; 230.4; 230.4; 366; 7.34)$. In this case, according to theorem (6), the drinking present equilibrium E^* of the system (1) is globally asymptotically stable on Γ: (See Figure3).



7. The Optimal Control Problem

Most countries of the world suffer from the phenomenon of alcohol addiction, which leads to health and economic damage and as consequence it impacts negatively the classification of these countries by some international organizations. For these reasons, we suggest some strategies that will contribute to minimize the number of heavy drinkers $H(t)$ and the heavy drinkers with liver complications $C(t)$, maximize the number of the recovered and quitters of drinking $Q(t)$ during the time interval $[t_0;t_f]$ and also minimize the cost spent in an awareness program and treatment. In the model (1), we include three controls $u_1(t), u_2(t)$ and $u_3(t)$ for $t \in [t_0;t_f]$. The controls u_1 represents the awareness programs effort (education, media programs...) applied on the potential drinkers to protect them from drinking. The second control u_2 measures the effort of treatment applied on the heavy drinkers. We note that the control function εu_2 represents the fraction of the heavy drinkers who will be treated and return to be moderate drinkers and the fraction $(1-\varepsilon)u_2$ represents the heavy drinkers who will be treated and quit drinking. Finally, u_3 measures the effort of treatment given to the heavy drinkers with liver complications. So, the controlled mathematical system is given by the following system of differential equations.

$$
(39) \qquad \begin{cases}
\frac{dP(t)}{dt} = b - \beta_1 \frac{P(t)M(t)}{N} - \mu P(t) - u_1(t)P(t) \\
\frac{dM(t)}{dt} = \beta_1 \frac{P(t)M(t)}{N} - \beta_2 M(t) - \mu M(t) + \varepsilon u_2(t)H(t) \\
\frac{dH(t)}{dt} = \beta_2 M(t) - (\mu + \delta_1 + \alpha_1 + \alpha_2)H(t) - u_2(t)H(t) \\
\frac{dC(t)}{dt} = \alpha_1 H(t) - (\delta_2 + \mu + \gamma)C(t) - u_3(t)C(t) \\
\frac{dQ(t)}{dt} = \alpha_2 H(t) + \gamma C(t) - \mu Q(t) + u_1(t)P(t) + (1-\varepsilon)u_2(t)H(t) + u_3(t)C(t)
\end{cases}
$$

where $P(0) \geq 0$, $M(0) \geq 0$, $H(0) \geq 0$, $C(0) \geq 0$ and $Q(0) \geq 0$ are the given initial states.

Then, the problem is to minimize the objective functional

$$
(40) \qquad \begin{aligned}
J(u_1,u_2,u_3) = H_{t_f} + C_{t_f} - Q_{t_f} \\
+ \int_{t_0}^{t_f} \left(H(t) + C(t) - Q(t) + \frac{A_1}{2}u_1^2(t) + \frac{A_2}{2}u_2^2(t) + \frac{A_3}{2}u_3^2(t) \right) dt.
\end{aligned}
$$

Where the parameters A_1, A_2 and A_3 are the strictly positive cost coefficients. They are selected to weigh the relative importance of u_1, u_2 and u_3 at time t and t_f is the final time. In other words, we seek the optimal controls u_1, u_2 and u_3 such that

$$J(u_1^*, u_2^*, u_3^*) = \min_{(u_1,u_2,u_3)\in U_{ad}^3} J(u_1, u_2, u_3).$$

Where U_{ad} is the set of admissible controls defined by

$$U_{ad} = \left\{ u_i(t) : 0 \leq u_i(t) \leq 1, \text{ for } i = 1,2,3 \text{ and } t \in [t_0, t_f] \right\} \tag{41}$$

7.1. Existence of optimal controls. The existence of the optimal controls can be obtained using a result by Fleming and Rishel (Fleming et al (1975)),.

Theorem 7. *Consider the control problem with system (40). There exists the optimal control (u_1^*, u_2^*, u_3^*) such that*

$$J(u_1^*, u_2^*, u_3^*) = \min_{(u_1,u_2,u_3)\in U_{ad}^3} J(u_1, u_2, u_3) \tag{42}$$

If the following conditions are met:

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

(2) The control set is convex and closed.

(3) The right-hand side of the state system is bounded by a linear function in the state and control variables.

(4)The integrand of the objective functional is convex.

(5) The integrand of the objective functional is bounded below by $c_1(\frac{A_1u_1^2}{2} + \frac{A_1u_2^2}{2} + \frac{A_1u_3^2}{2})^{\frac{\varphi}{2}} - c_2$, where $c_1 > 1$, $c_2 > 1$ and $\varphi > 1$.

Proof. Proof To prove the existence of the optimal control, we use the result in ((Boyce et al (2009)), Balatif et al (2020))).

7.2. Characterization of optimal controls. We apply the Pontryagin's Maximum Principle (Pontryagin et al (1962)). The key idea is introducing the adjoint function to attach the system of differential equations to the objective functional resulting in the formation of a function called the Hamiltonian. This principle converts the problem of finding the control to optimize the objective functional subject to the state differential equations with initial condition to find the control to optimize Hamiltonian pointwise (with respect to the control).

Now we have the Hamiltonian $\hat{H}$ in time t, defined by

$$\hat{H}(t) = H(t) + C(t) - Q(t) + \frac{A_1}{2}u_1^2(t) + \frac{A_2}{2}u_2^2(t) + \frac{A_3}{2}u_3^2(t) + \sum_{k=1}^{5}\lambda_k f_k. \tag{43}$$

where f_k is the right side of the system of differencial equations (40) of the k^{th} state variable.

Theorem 8. *Given an optimal control* $(u_1^*, u_2^*, u_3^*) \in U_{ad}^3$ *, and solutions* P^**,* M^* *,* H^**,* C^* *and* Q^**of corresponding state system* (37)*, there exists adjoint functions,* λ_1*,* λ_2 *,* λ_3*,* λ_4 *and* λ_5 *satisfying*

$$\begin{cases} \dot{\lambda}_1 = -\frac{\partial \hat{H}}{\partial P} = (\lambda_1 - \lambda_2)\beta_1 \frac{M(t)}{N} + (\lambda_1 - \lambda_5)u_1(t) + \mu\lambda_1. \\ \dot{\lambda}_2 = -\frac{\partial \hat{H}}{\partial M} = (\lambda_1 - \lambda_2)\beta_1 \frac{P(t)}{N} + \beta_2(\lambda_2 - \lambda_3) + \mu\lambda_2. \\ \dot{\lambda}_3 = -\frac{\partial \hat{H}}{\partial H} = -1 + \{\lambda_3 - (1-\varepsilon)\lambda_5 - \varepsilon\lambda_2\}u_2(t) - \alpha_1\lambda_4 - \alpha_2\lambda_5 + (\mu + \beta_2)\lambda_3. \\ \dot{\lambda}_4 = -\frac{\partial \hat{H}}{\partial C} = -1 + \lambda_4(\mu + \gamma + \delta_2) + (\lambda_3 - \lambda_5)u_3(t). \\ \dot{\lambda}_5 = -\frac{\partial \hat{H}}{\partial Q} = 1 + \mu\lambda_5. \end{cases} \tag{44}$$

with the transversality conditions at time t_f

$$\lambda_1(t_f) = \lambda_2(t_f) = 0,\ \lambda_3(t_f) = 1,\ \lambda_4(t_f) = 1 \text{ and } \lambda_5(t_f) = -1. \tag{45}$$

Futhermore, for $t \in [t_0; t_f]$*the optimal controls* $u_1^*(t)$ *,*$u_2^*(t)$*and* $u_3^*(t)$ *are given by:*

$$u_1^*(t) = \min\left(1, \max\left(0, \frac{1}{A_1}(\lambda_1 - \lambda_5)P(t)\right)\right). \tag{46}$$

$$u_2^*(t) = \min\left(1, \max\left(0, \frac{1}{A_2}\{\lambda_3 - \varepsilon\lambda_2 - (1-\varepsilon)\lambda_5\}H(t)\right)\right). \tag{47}$$

$$u_3^*(t) = \min\left(1, \max\left(0, \frac{1}{A_3}(\lambda_4 - \lambda_5)C(t)\right)\right). \tag{48}$$

Proof. Proof The Hamiltonian $\hat{H}$ at time t is given by

$$\begin{aligned}
\hat{H}(t) &= H(t)+C(t)-Q(t)+\frac{A_1}{2}u_1^2(t)+\frac{A_2}{2}u_2^2(t)+\frac{A_3}{2}u_3^2(t)\\
&+\lambda_1\left\{b-\beta_1\frac{P(t)M(t)}{N}-\mu P(t)-u_1(t)P(t)\right\}\\
&+\lambda_2\left\{\beta_1\frac{P(t)M(t)}{N}-\beta_2 M(t)-\mu M(t)+\varepsilon u_2(t)H(t)\right\}\\
&+\lambda_3\left\{\beta_2 M(t)-(\mu+\delta_1+\alpha_1+\alpha_2)H(t)-u_2(t)H(t)\right\}\\
&+\lambda_4\left\{\alpha_1 H(t)-(\delta_2+\mu+\gamma)C(t)-u_3(t)C(t)\right\}\\
&+\lambda_5\left\{\alpha_2 H(t)+\gamma C(t)-\mu Q(t)+u_1(t)P(t)+(1-\varepsilon)u_2(t)H(t)+u_3(t)C(t)\right\}.
\end{aligned}$$

For $t\in[t_0;t_f]$, the adjoint equations and transversality conditions can be obtained by using Pontryagin's Maximum Principle given in [16] such that

$$\left\{\begin{array}{l}
\dot{\lambda}_1=-\frac{\partial\hat{H}}{\partial P},\ \lambda_1(t_f)=0,\\
\dot{\lambda}_2=-\frac{\partial\hat{H}}{\partial M},\ \lambda_2(t_f)=0,\\
\dot{\lambda}_3=-\frac{\partial\hat{H}}{\partial H},\ \lambda_2(t_f)=1,\\
\dot{\lambda}_4=-\frac{\partial\hat{H}}{\partial C},\ \lambda_4(t_f)=1,\\
\dot{\lambda}_5=-\frac{\partial\hat{H}}{\partial Q},\ \lambda_5(t_f)=-1,
\end{array}\right. \tag{49}$$

For $t\in[t_0;t_f]$, the optimal controls $u_1^*(t)$,$u_2^*(t)$ and $u_3^*(t)$ can be solved from the optimality condition,

$$\frac{\partial\hat{H}}{\partial u_1}=0,\ \frac{\partial\hat{H}}{\partial u_2}=0 \text{ and } \frac{\partial\hat{H}}{\partial u_3}=0. \tag{50}$$

that is

$$\begin{aligned}
\frac{\partial\hat{H}}{\partial u_1} &= A_1u_1(t)+(\lambda_5-\lambda_1)P(t)=0,\\
\frac{\partial\hat{H}}{\partial u_2} &= A_2u_2(t)+\{-\lambda_3+\varepsilon\lambda_2+(1-\varepsilon)\lambda_5\}H(t)=0,\\
\frac{\partial\hat{H}}{\partial u_3} &= A_3u_3(t)+(\lambda_5-\lambda_4)C(t)=0,
\end{aligned}$$

So, we have

$$u_1(t) = \frac{P(t)}{A_1}(\lambda_1 - \lambda_5), \tag{51}$$

$$u_2(t) = \frac{H(t)}{A_2}\{\lambda_3 - \varepsilon\lambda_2 - (1-\varepsilon)\lambda_5\}, \tag{52}$$

$$u_3(t) = \frac{C(t)}{A_3}(\lambda_4 - \lambda_5), \tag{53}$$

By the bounds in U_{ad} of the controls, it is easy to obtain $u_1^*(t), u_2^*(t)$ and $u_3^*(t)$ in the form of $(46-47-48)$.

8. Numerical Simulation

In this section, we shall solve numerically the optimal control problem for our *PMHCQ* model. Here, we obtain the optimality system from the state and adjoint equations. The proposed optimal control strategy is obtained by solving the optimal system which consists of five differencial equations and boundary conditions. The optimality system can be solved by using an iterative method. Using an initial guess for the control variables, $u_1(t)$,$u_2(t)$ and $u_3(t)$, the state variables P, M, H, C and Q are solved forward and the adjoint variables λ_i for $i = 1,2,3,4,5$ are solved backwards at times step $k = t_0$ and $k = t_f$. If the new values of the state and adjoint variables differ from the previous values, the new values are used to update u_{1k}, u_{2k} and u_{3k}, and the process is repeated until the system converges.

We present some numerical simulations in order to illustrate our theoretical results, we consider system (1) with the following parameter values $b = 65$, $N = 1000$, $\delta = 0.002$, $\theta = 0.02$, $\mu = 0.065$, $\beta_1 = 0.75$, $\beta_2 = 0.14$, $\alpha_1 = 0.001$, $\alpha_2 = 0.001$, $\alpha_3 = 0.001$, $\gamma_1 = 0.001$, $\gamma_2 = 0.002$ and the initial values $P_0 = 600$, $M_0 = 200$, $H_O = 100$, $C_0 = 60$ and $Q_O = 40$. The proposed control strategies in this work help to achieve several objectives:

First Strategy: Considering preventing the potential drinkers through awareness and educational programs.

To realize this strategy, we apply only the control u_1 i.e. the implementation of awareness, and educational programs on potential drinkers to make them know the risks of this phenomenon on health and society.

Figure $4(a)$ shows that the number of moderate drinkers decreased from 407.3 (without control)$to127.8(withcontrol)$ at the end of the proposed control.l. It indicates the effectiveness of optimal control in controlling the growth of moderate drinker's population.

Figure $4(b)$ shows that optimal control affects the number of the heavy drinker's population. Before the control is executed, the number of heavy drinkers increases gradually until 580.7 at the end of the proposed control. However, when the control is applied, the number of the heavy drinkers population increases gradually until 266.76 at the end of the proposed control. These changes indicates the effectiveness of optimal control in controlling the growth of heavy drinker's population.

Figure $4(c)$ shows that optimal control affects the number of heavy drinker's population with liver complications. Before being controlled, the number of heavy drinkers with liver complications continuously increases until 113.46 at the end of the proposed control. Whereas, when the control is applied, the number of population of heavy drinkers with liver complications increases and it is will at maximum value 72.38 at the end of the proposed control. It indicates the effectiveness of optimal control in controlling the growth of population of heavy drinkers with liver complications population.

Figure4(a)

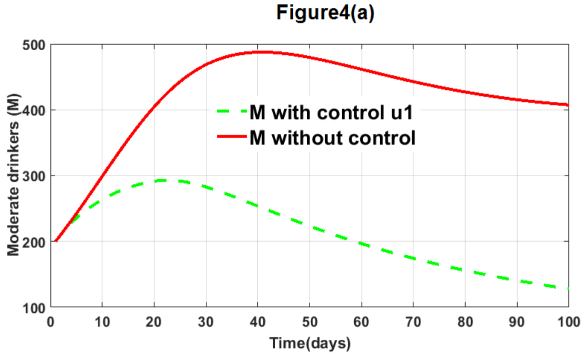
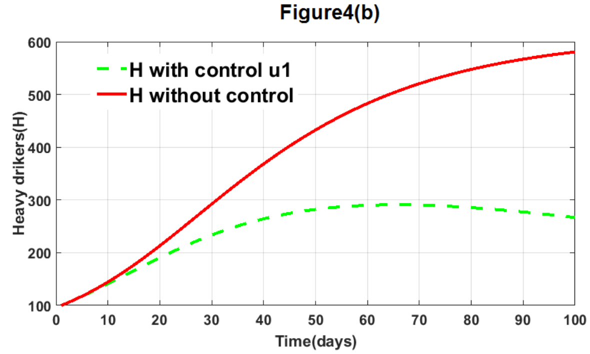
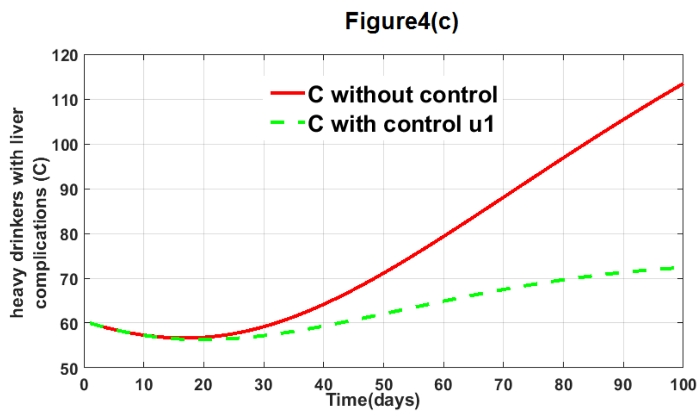


Figure4(b)

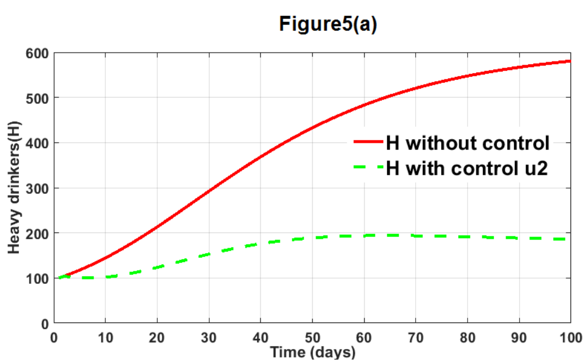


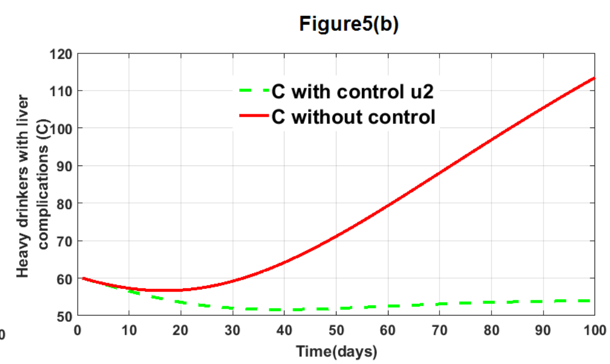
Second Strategy: Considering treatment of heavy drinkers H.

To achieve this strategy, we only use the control u_2 i.e. treatment of heavy drinkers. In Figure $5(a)$, it is observed that there is a significant decrease in the number of the heavy drinkers with control compared to a situation when there is no control where the decrease is from 580.69 to 185.76 at the end of the proposed control strategy. Figure $5(b)$ shows that the number of heavy drinkers with liver complications decreased from 113.46 (without control)$to53.96(withcontrol)$



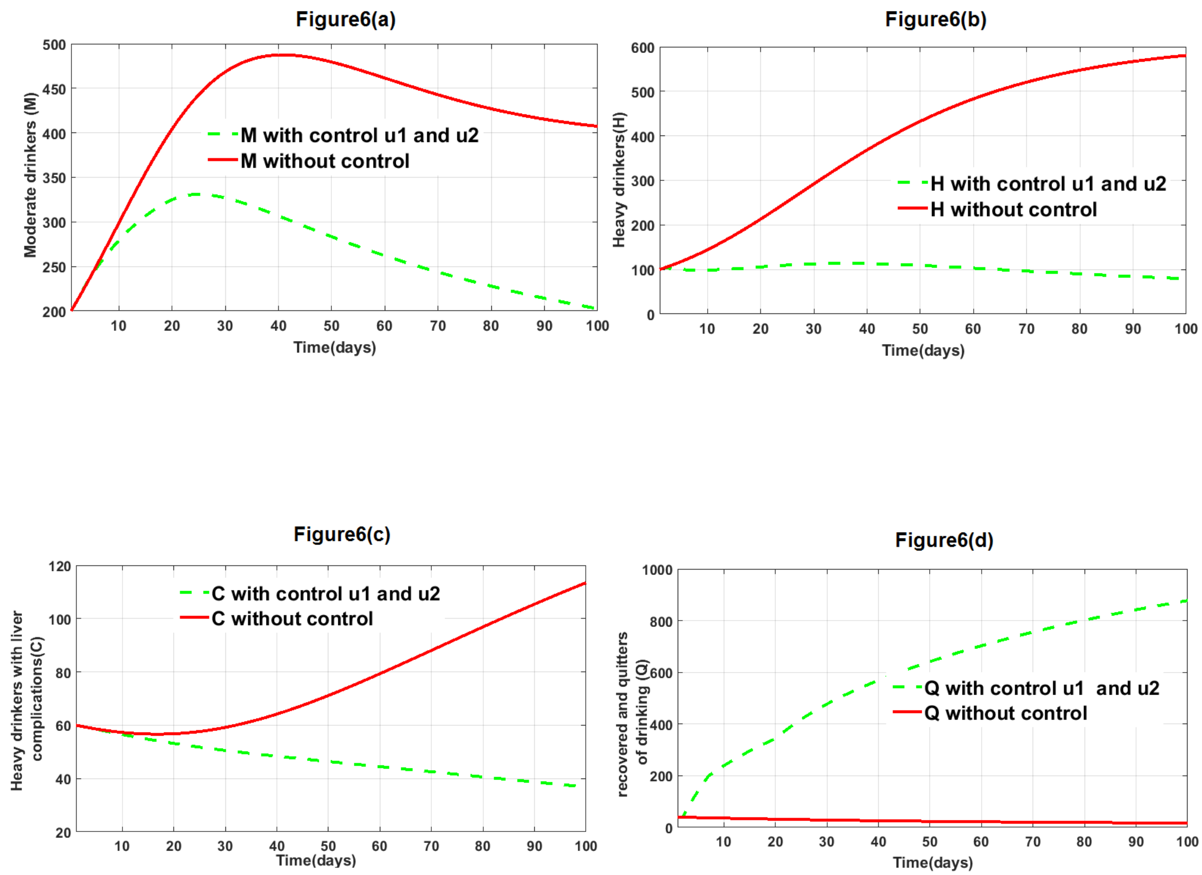
at the end of the proposed control. To improve this result, we applied three controls.





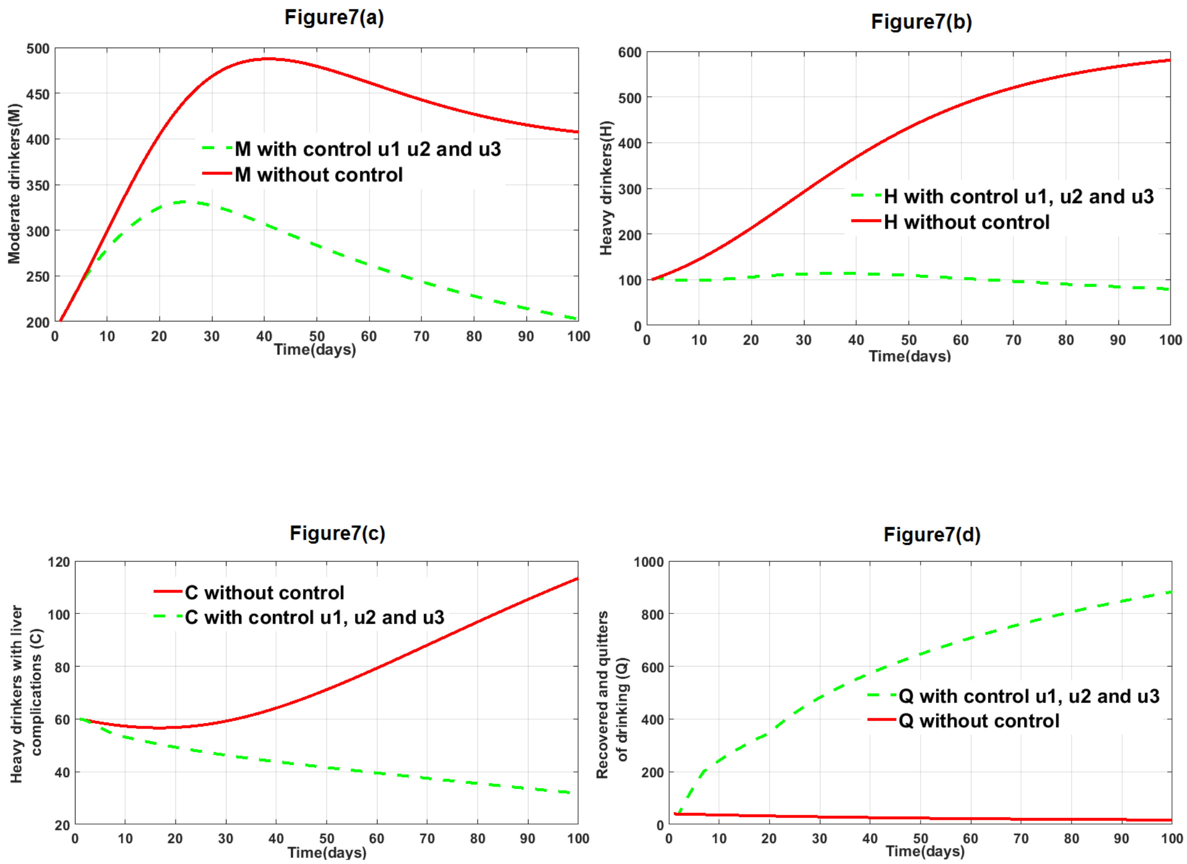
Third strategy: which considers Prevention and treatment of drinkers individuals.

To meet this strategy, we use the controls u_1 and u_2 i.e. awareness programs for the potential drinkers and treatment for heavy drinkers. Figure $6(a)$ shows that the number of the moderate drinkers decreases from the value 407.33 (without controls) to 202.56 (with controls) at the end of the proposed control. Figure $6(b)$ shows that the number of the heavy drinkers decreases from 580.69 (without controls) to 79.25 (with controls) at the end of the proposed control. Also, figure $6(c)$ shows that the number of the heavy drinkers with liver complications decreases from 113.46 (without controls) to 36.83 (with controls) at the end of the proposed control. Also, Figure $6(d)$ depicts clearly an increase in the number of the recovered and quitters of drinking from 17.04 (without controls) to 877.61 (with controls). As a result, the strategy set before has been achieved.



Forth strategy: Considering prevention and treatment of heavy drinkers with and without liver complications using medicaments.

To meet this strategy, we use the controls u_1, u_2 and u_3 i.e. awareness programs for the potential drinkers, treatment for heavy drinkers and treatment for heavy drinkers with liver complication. Figure $7(a)$ shows that the number of the moderate drinkers decreases from 407.33 (without controls) to 202.56 (with controls) at the end of the proposed control. Figure $7(b)$ shows that the number of the heavy drinkers decreases from 580.69 (without controls) to 79.25 (with controls) at the end of the proposed control. Also, figure $7(c)$ shows that the number of the heavy drinkers with liver complication decreases from 113.46 (without controls) to 31.80 (with controls) at the end of the proposed control. Also, Figure $7(d)$ depicts clearly an increase in the number of the recovered and quitters of drinking from 17.04 (without controls) to 882.74 (with controls). As a result, the strategy set before has been achieved.



9. Conclusion

In this work, we formulated a mathematical model that describes the dynamics of drinking. By using Routh-Hurwitz criteria and constructing Lyapunov functions, the local and the global stability of drinking-free equilibrium and drinking present equilibrium are obtained. We also studied the sensitivity analysis of model parameters to know the parameters that have a high impact on the reproduction number R_0. In addition, we proposed an optimal strategy for an awareness program and treatment that help potential drinkers to know the risks of this phenomenon and its consequences on health and society. Pontryagin's maximum principle is used to characterize the optimal controls and the optimality system is solved by an iterative method. The numerical simulation was carried out using Matlab. We proposed an algorithm based on the forward and backward difference approximation and we show that the optimal strategy becomes more effective when we combined three optimal controls.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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