

# On stability analysis study and strategies for optimal control of a mathematical model of hepatitis HCV with the latent state

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In this work, we analyze a viral hepatitis C model. This epidemic remains a major problem for global public health, in all communities, despite the efforts made. The model is analyzed using the stability theory of systems of nonlinear differential equations. Based on the results of the analysis, the proposed model has two equilibrium points: a disease-free equilibrium point  $E_0$  and an endemic equilibrium point  $E^*$ . We investigate the existence of equilibrium point of the model. Furthermore, based on the indirect Lyapunov method, we study the local stability of each equilibrium point of the model. Moreover, by constructing the appropriate Lyapunov function and by using LaSalle invariance principle, we get some information on the global stability of equilibrium points under certain conditions. The basic reproduction number  $R_0$  is calculated using the Next Generation method. The positivity of the solutions and their bornitude have been proven, the existence of the solutions has also been proven. Optimal control of the system was studied by proposing three types of intervention: awareness program, early detection, isolation and treatment. The maximum principle of Pontryagin was used to characterize the optimal controls found. Numerical simulations were carried out with a finite numerical difference diagram and using MATLAB to confirm acquired results.

**Keywords:** *optimal control; equilibrium point; Lagrange function; objective function; Pontryagin maximum principle; HCV.*

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## 1. Introduction

The field of mathematical modeling provides additional and substantial information on the mechanisms of transmission and spread of epidemics in general, exploitable in preventive studies especially with the appearance of new strains of old viruses that are still alive with the human species. A mathematical model is a description of how the real world works using symbols, equations and mathematical formulas [1–13]. In epidemiology, this allows us to study how diseases spread, predict the future trajectory of an outbreak, estimate the risks associated with infection, and help guide public health planning and infectious disease control. The World Health Organization report confirms that viral hepatitis is an international public health problem comparable to other major communicable diseases such as

HIV, tuberculosis and malaria. Despite the heavy burden it places on people in all parts of the world, hepatitis was not really considered a health and development priority until recently. It will no longer be neglected with the adoption of the resolution on the program for sustainable development to 2030. This strategy addresses five hepatitis viruses (hepatitis A, B, C, D and E), with a special focus on hepatitis B and C because of the relative high public health burden. In particular, the third goal specifically calls for action to combat viral hepatitis [14–16]. This field provides further information concerning the mechanisms of epidemic transmission and spread.

There are several major hepatitis virus types, according to research and investigations conducted by the World Health Organization, namely hepatitis A, hepatitis B, hepatitis D, hepatitis E and hepatitis C. Our motivation behind the study of hepatitis C (HCV) is mainly the lack of vaccine for this viral variant, the incubation period associated with this virus which is long and due to the heavy relative burden it represents for public health [14, 15].

Hepatitis C is an inflammation of the liver caused by the hepatitis C virus. HCV is an RNA virus with a variety of rather important genomes. There are six main genotypes, rated from 1 to 6, and many subtypes. The virus can cause both acute and chronic hepatitis, ranging in severity from a mild illness to a serious, lifelong illness including liver cirrhosis and cancer. The hepatitis C virus is a blood-born virus and most infection occur through exposure to blood from unsafe injection practices, unsafe health care, unscreened blood transfusions, injection drug use and sexual practices that lead to exposure to blood. Globally, an estimated 58 million people have chronic hepatitis C virus infection, with about 1.5 million new infections occurring per year. WHO estimated that in 2019, approximately 290000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer). Antiviral medicines can cure more than 95% of persons with hepatitis C infection, but access to diagnosis and treatment is low. There is currently no effective vaccine against hepatitis C [16, 17]. The period of the 90s was that of the first treatments and therapeutic trials, the development of screening tests, the first recommendations of screening and management and the structuring of the supply of care. In terms of screening, ELISA tests for the detection of very sensitive and specific 3rd generation anti-HCV antibodies (Ac) were developed as early as 1993. Effective tests for the detection of HCV RNA in serum by PCR (polymerase chain reaction) have been developed and used in clinical practice. The pharmaceutical industry and the research of Moroccan laboratories have contributed to the fight against this human virus. Hepatitis C patients in Morocco now have relatively effective treatments, thanks to the production of generic drugs principles in the country. On the other hand, access to screening and biological examinations remains largely insufficient and the capacity to access care against HCV [17]. Currently, there is no effective hepatitis C vaccine, so this was also one of the goals that prompted us to start this study [15–17].

## 2. Formulation of the mathematical model

We introduce in this work a mathematical model  $S_n S_a EICQR$  with seven compartments. People in the  $S_a$  compartment are less likely to contract the HCV virus than those in the  $S_n$  compartment because of their knowledge due to several factors such as: education, prevention and assistance in awareness sessions. In general the infection of these two classes occurs through contact with an infected individual of high viral load prevent from one of the compartments  $I$  or  $C$ . The infection by individuals under incident treatment of the  $Q$  compartment is extremely negligible. The chronic phase is more infectious than the acute phase.

### 2.1. Description of the model

- **The compartment  $S_n$ :** represents the unawareness susceptible, how are individuals at risk of infection who do not have information about hepatitis C and its severity. They have never been to prevention sessions. It also contains the category of illiterates and newborns. In general, individuals in the  $S_n$  compartment are more likely to be infected with the virus than those in the

$S_a$  compartment. Contamination in individuals from compartment  $S_n$  is by contact with a sick individual from one of the compartments  $I, C$ .

- **The compartment  $S_a$ :** refers to the compartment of potentially infected individuals who already have information about viral hepatitis C or who have attended awareness and prevention sessions on this subject. Contamination in individuals from compartment  $S_a$  is by contact with a sick individual from one of the compartments  $I, C$ .

Note that: two groups  $S_n$  and  $S_a$  include, mainly, people who change blood especially during transfusion, people with chronic diseases other than hepatitis C [16, 17].

- **The compartment  $E$ :** this compartment represents exposed individuals who are in the incubation period of the epidemic, subjects during this phase are asymptomatic, and they are generally infected but not infectious. The incubation period for hepatitis C ranges from 2 weeks to 6 months [11, 16].
- **The compartment  $I$ :** this compartment includes individuals who have acute viral hepatitis C infections. This phase of the infection has a short duration, after this period the patient passes to the chronic phase at a rate of 75% [14] otherwise the patient heals spontaneously [6].
- **The compartment  $C$ :** this compartment groups together individuals who have chronic viral hepatitis C infections, during this phase the virus can take a lifelong hold. The  $\delta_1$  coefficient represents the mortality rate of chronic individuals due to hepatitis C after having reached cirrhosis during the terminal stage of this viral disease.
- **The compartment  $Q$ :** this compartment represents the individuals hospitalized due to the deterioration of their health or the individuals of the same situation who are isolated at home while following the protocol of treatment discussed by their doctors. The coefficient  $\delta_2$  represents the mortality rate of some patients under treatment due to the deterioration of their health.
- **The compartment  $R$ :** represents individuals cured and established with a cure rate  $\gamma$  after treatment either in hospitals or at home.

The following diagram will demonstrate the flow directions of individuals among the compartments. These directions will be represented by directed arrows, see the following diagram (see Fig. 1).

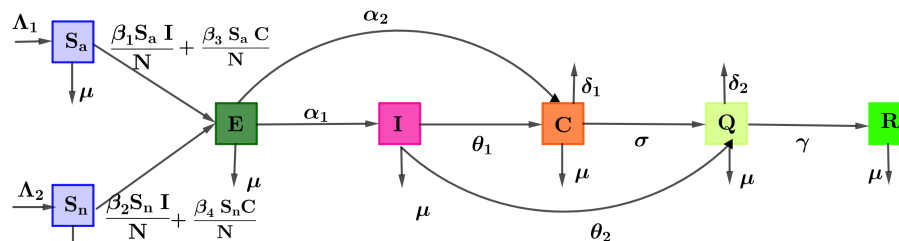


Fig. 1.

## 2.2. Model equations

We consider a system of differential equations

$$\begin{cases} \frac{dS_a(t)}{dt} = \Lambda_1 - \frac{\beta_1 S_a(t)I(t)}{N} - \frac{\beta_3 S_a(t)C(t)}{N} - \mu S_a(t), \\ \frac{dS_n(t)}{dt} = \Lambda_2 - \frac{\beta_2 S_n(t)I(t)}{N} - \frac{\beta_4 S_n(t)C(t)}{N} - \mu S_n(t), \\ \frac{dE(t)}{dt} = \frac{\beta_1 S_a(t)I(t)}{N} + \frac{\beta_3 S_a(t)C(t)}{N} + \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} - (\alpha_1 + \alpha_2 + \mu)E(t), \\ \frac{dI(t)}{dt} = \alpha_1 E(t) - (\mu + \theta_1 + \theta_2)I(t), \\ \frac{dC(t)}{dt} = \alpha_2 E(t) + \theta_1 I(t) - (\mu + \sigma + \delta_1)C(t), \\ \frac{dQ(t)}{dt} = \theta_2 I(t) + \sigma C(t) - (\gamma + \mu + \delta_2)Q(t), \\ \frac{dR(t)}{dt} = \gamma Q(t) - \mu R(t) \end{cases} \quad (1)$$

subject to the following initial conditions:

$$S_a(0) \geq 0, \quad S_n(0) \geq 0, \quad E(0) \geq 0, \quad I(0) \geq 0, \quad C(0) \geq 0, \quad Q(0) \geq 0, \quad R(0) \geq 0,$$

where:

- $\Lambda_1$  is the incidence rate of individuals in the compartment  $S_a$ ;
- $\Lambda_2$  is the incidence rate of individuals in the compartment  $S_n$ ;
- $\mu$  is natural mortality;
- $\beta_1$  is infection rate of an individual in the compartment  $S_a$  due to contact with acute individual infection;
- $\beta_2$  is infection rate of an individual in the compartment  $S_n$  due to contact with acute individual infection;
- $\beta_3$  is infection rate of an individual in the compartment  $S_a$  due to contact with chronic individual infection;
- $\beta_4$  is infection rate of an individual in the compartment  $S_n$  due to contact with chronic individual infection;
- $\alpha_1$  is the rate of people infected with the HCV virus who are symptomless;
- $\alpha_2$  is rate of people who have developed HCV virus rapidly, with a very short incubation time, and dangerously due to immune failure, other chronic diseases, immunodeficiency, old age or very fragile living conditions;
- $\theta_1$  is the rate of acute infections that resulted in chronic infection;
- $\theta_2$  is the rate of people with serious complications who have been quarantined;
- $\gamma$  is the cure rate;
- $\sigma$  is the percentage of chronically infected who will be treated by the therapeutic protocol in the hospitals or in their homes, following the deterioration of their health;
- $\delta_1$  is the rate of deaths due to complications of hepatitis HCV;
- $\delta_2$  is the rate of people who died under quarantine in hospitals.

### 2.3. Model basic properties

#### 2.3.1. Positivity of solutions

**Theorem 1.** If  $S_a(0) \geq 0$ ,  $S_n(0) \geq 0$ ,  $E(0) \geq 0$ ,  $I(0) \geq 0$ ,  $C(0) \geq 0$ ,  $Q(0) \geq 0$  and  $R(0) \geq 0$ , the solutions  $S(t)$ ,  $S_a(t)$ ,  $E(t)$ ,  $I(t)$ ,  $C(t)$ ,  $Q(t)$  and  $R(t)$  of system (1) are positive for all  $t \geq 0$ .

**Proof.** It follows from the first equation of system (1) that

$$\begin{aligned} \frac{dS_a(t)}{dt} &= \Lambda_1 - \frac{\beta_1 S_a(t) I(t)}{N} - \frac{\beta_3 S_a(t) C(t)}{N} - \mu S_a(t) \\ &\geq -\frac{\beta_1 S_a(t) I(t)}{N} - \frac{\beta_3 S_a(t) C(t)}{N} - \mu S_a(t), \end{aligned}$$

$\frac{dS_a(t)}{dt} + \left( \mu + \beta_1 \frac{I(t)}{N} + \beta_3 \frac{C(t)}{N} \right) S_a(t) \geq 0$ , where  $F(t) = \mu + \beta_1 \frac{I(t)}{N} + \beta_3 \frac{C(t)}{N}$ . The both sides in last inequality are multiplied by  $\exp \left( \int_0^t F(s) ds \right)$ . We obtain

$$\exp \left( \int_0^t F(s) ds \right) \cdot \frac{dS_a(t)}{dt} + F(t) \exp \left( \int_0^t F(s) ds \right) \cdot S_a(t) \geq 0,$$

then  $\frac{d}{dt} (S_a(t) \exp (\int_0^t F(s) ds)) \geq 0$ . Integrating this inequality from 0 to  $t$  gives

$$\int_0^t \frac{d}{ds} \left( S_a(s) \exp \left( \int_0^s \left( \mu + \beta_1 \frac{I(s)}{N} + \beta_3 \frac{C(s)}{N} \right) ds \right) \right) ds \geq 0,$$

then

$$S_a(t) \geq S_a(0) \exp \left( - \int_0^t \left( \mu + \beta_1 \frac{I(s)}{N} + \beta_3 \frac{C(s)}{N} \right) ds \right) \implies S(t) \geq 0.$$

Similarly, we prove that  $S_n(0) \geq 0$ ,  $E(0) \geq 0$ ,  $I(0) \geq 0$ ,  $C(0) \geq 0$ ,  $Q(0) \geq 0$  and  $R(0) \geq 0$ . ■

#### 2.3.2. Boundedness of the solutions

**Theorem 2.** The set  $\Omega = \left\{ (S_a, S_n, E, I, C, Q, R) \in \mathbb{R}_+^6 / 0 \leq S_a + S_n + E + I + C + Q + R \leq \frac{\Lambda}{\mu} \right\}$  positively invariant under system (1) with initial conditions  $S_a(0) \geq 0$ ,  $S_n(0) \geq 0$ ,  $E(0) \geq 0$ ,  $I(0) \geq 0$ ,  $C(0) \geq 0$ ,  $Q(0) \geq 0$  and  $R(0) \geq 0$ .

**Proof.** Also, one assumes that  $\frac{dN}{dt} = \Lambda_1 + \Lambda_2 - \mu N - \delta_1 C \leq \Lambda_1 + \Lambda_2 - \mu N \implies N(t) \leq \frac{\Lambda_1 + \Lambda_2}{\mu} + N(0)e^{-\mu t}$ . If we take limit  $t \rightarrow \infty$  we have  $0 \leq N(t) \leq \frac{\Lambda_1 + \Lambda_2}{\mu}$ . It implies that the region  $\Omega$  is a positively invariant set for the system (1). ■

### 3. Existence of solutions

**Theorem 3.** The system (1) that satisfies a given initial condition  $(S_a(0), S_n(0), E(0), I(0), C(0), Q(0), R(0))$  has a unique solution.

**Proof.** Let  $X = (S_a(t), S_n(t), E(t), I(t), C(t), Q(t), R(t))^T$ , and  $\varphi(X) = \left( \frac{dS_a(t)}{dt}, \frac{dS_n(t)}{dt}, \frac{dE(t)}{dt}, \frac{dI(t)}{dt}, \frac{dC(t)}{dt}, \frac{dQ(t)}{dt}, \frac{dR(t)}{dt} \right)^T$ , so the system (1) can be rewritten in the following form:  $\varphi(X) = AX + B(X)$ , where

$$A = \begin{pmatrix} -\mu & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -(\mu + \alpha_1 + \alpha_2) & 0 & 0 & 0 & 0 \\ 0 & 0 & \alpha_1 & -(\alpha_2 + \theta_1 + \mu) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & \theta_1 & -(\sigma + \mu + \delta_1) & 0 & 0 \\ 0 & 0 & 0 & \theta_2 & \sigma & -(\mu + \sigma + \delta_2) & 0 \\ 0 & 0 & 0 & 0 & \gamma & -\mu & 0 \end{pmatrix},$$

and

$$B(X) = \begin{pmatrix} \Lambda_1 - \beta_1 \frac{S_a(t)I(t)}{N} - \beta_3 \frac{S_a(t)C(t)}{N} \\ \Lambda_2 - \beta_2 \frac{S_n(t)I(t)}{N} - \beta_4 \frac{S_n(t)C(t)}{N} \\ \beta_1 \frac{S_a(t)I(t)}{N} + \beta_2 \frac{S_n(t)I(t)}{N} + \beta_3 \frac{S_a(t)C(t)}{N} + \beta_4 \frac{S_n(t)C(t)}{N} \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}.$$

The second term on the right-hand side of (1) satisfies

$$\begin{aligned} |B(X_1) - B(X_2)| &= 2 \left| \begin{array}{l} \beta_1 \frac{S_{a,1}(t)I_1(t)}{N} + \beta_2 \frac{S_{n,1}(t)I_1(t)}{N} + \beta_3 \frac{S_{a,1}(t)C_1(t)}{N} + \beta_4 \frac{S_{n,1}(t)C_1(t)}{N} \\ - \beta_1 \frac{S_{a,2}(t)I_2(t)}{N} - \beta_2 \frac{S_{n,2}(t)I_2(t)}{N} - \beta_3 \frac{S_{a,2}(t)C_2(t)}{N} - \beta_4 \frac{S_{n,2}(t)C_2(t)}{N} \end{array} \right| \\ &= 2 \left| \begin{array}{l} \beta_1 \frac{S_{a,1}(t)I_1(t)}{N} + \beta_1 \frac{S_{a,1}(t)I_2(t)}{N} - \beta_2 \frac{S_{n,1}(t)I_2(t)}{N} - \beta_2 \frac{S_{n,1}(t)I_1(t)}{N} \\ + \beta_3 \frac{S_{a,1}(t)C_1(t)}{N} + \beta_3 \frac{S_{a,1}(t)C_2(t)}{N} - \beta_4 \frac{S_{n,1}(t)C_2(t)}{N} - \beta_4 \frac{S_{n,1}(t)C_1(t)}{N} \\ + \beta_2 \frac{S_{n,1}(t)I_2(t)}{N} - \beta_2 \frac{S_{n,1}(t)I_1(t)}{N} - \beta_1 \frac{S_{a,2}(t)I_2(t)}{N} + \beta_2 \frac{S_{n,2}(t)I_2(t)}{N} \\ + \beta_4 \frac{S_{n,1}(t)C_2(t)}{N} - \beta_4 \frac{S_{n,1}(t)C_1(t)}{N} - \beta_3 \frac{S_{a,2}(t)C_2(t)}{N} + \beta_4 \frac{S_{n,2}(t)C_2(t)}{N} \end{array} \right| \\ &\leq 2 \left( \left| \frac{\beta_1 S_{a,1}(t)}{N} \right| |I_1(t) - I_2(t)| + \left| \frac{\beta_1 I_2(t)}{N} \right| |S_{a,1}(t) - S_{a,2}(t)| \right. \\ &\quad + \left| \frac{\beta_2 S_{n,1}(t)}{N} \right| |I_1(t) - I_2(t)| + \left| \frac{\beta_2 I_2(t)}{N} \right| |S_{n,1}(t) - S_{n,2}(t)| \\ &\quad + \left| \frac{\beta_3 S_{a,1}(t)}{N} \right| |C_1(t) - C_2(t)| + \left| \frac{\beta_3 C_2(t)}{N} \right| |S_{a,1}(t) - S_{a,2}(t)| \\ &\quad \left. + \left| \frac{\beta_4 S_{a,1}(t)}{N} \right| |C_1(t) - C_2(t)| + \left| \frac{\beta_4 C_2(t)}{N} \right| |S_{a,1}(t) - S_{a,2}(t)| \right) \\ &\leq 2 \frac{Z}{\mu} \left( \left| \frac{\beta_1}{N} \right| |I_1(t) - I_2(t)| + \left| \frac{\beta_1}{N} \right| |S_{a,1}(t) - S_{a,2}(t)| \right. \\ &\quad + \left| \frac{\beta_2}{N} \right| |I_1(t) - I_2(t)| + \left| \frac{\beta_2}{N} \right| |S_{n,1}(t) - S_{n,2}(t)| \Big) \\ &\quad + 2 \frac{Z}{\mu} \left( \left| \frac{\beta_3}{N} \right| |C_1(t) - C_2(t)| + \left| \frac{\beta_3}{N} \right| |S_{a,1}(t) - S_{a,2}(t)| \right. \\ &\quad + \left| \frac{\beta_4}{N} \right| |C_1(t) - C_2(t)| + \left| \frac{\beta_4}{N} \right| |S_{n,1}(t) - S_{n,2}(t)| \Big) \\ &\leq M (|X_1(t) - X_2(t)|), \end{aligned}$$

where  $M = 2 \frac{Z}{\mu} \left( \left| \frac{\beta_1}{N} \right| + \left| \frac{\beta_2}{N} \right|; \left| \frac{\beta_1}{N} \right| + \left| \frac{\beta_2}{N} \right|; \left| \frac{\beta_3}{N} \right| + \left| \frac{\beta_4}{N} \right|; \left| \frac{\beta_3}{N} \right| + \left| \frac{\beta_4}{N} \right| \right)$ ,  $Z$  is a strictly positive number.

Then  $\|\varphi(X_1) - \varphi(X_2)\| \leq V \cdot \|X_1 - X_2\|$ , where  $V = \max(M, \|A\|) < \infty$ .

Thus, it follows that the function  $\varphi$  is uniformly Lipschitz continuous, and the restriction on  $S_a(t) \geq 0$ ,  $S_n(t) \geq 0$ ,  $E(t) \geq 0$ ,  $I(t) \geq 0$ ,  $C(t) \geq 0$ ,  $Q(t) \geq 0$  and  $R(t) \geq 0$ . We see that a solution of the system exists [18]. ■

## 4. Stability analysis of equilibrium point

### 4.1. The disease free equilibrium

To find the disease free equilibrium point, we equated the right hand side of model (1) to zero, evaluating it at  $E = I = 0$  and solving for the noninfected and noncarrier state variables. Therefore, the disease free equilibrium point  $E^0 = \left(\frac{\Lambda_1}{\mu}, \frac{\Lambda_2}{\mu}, 0, 0\right)$ .

### 4.2. The endemic equilibrium

The endemic equilibrium point  $E^* = (S_a^*, S_n^*, E^*, I^*)$  it occurs when the disease persists in the community. To obtain it, we equate all the model Eq. (1) to zero. Then we obtain

$$S_a^* = \frac{\Lambda_1}{\mu R_0}, \quad S_n^* = \frac{\Lambda_2}{\mu R_0}, \quad E^* = \frac{(\Lambda_1 + \Lambda_2)(R_0 - 1)}{(\mu + \alpha_1 + \alpha_2)R_0}, \quad I^* = \frac{\alpha_1(\Lambda_1 + \Lambda_2)(R_0 - 1)}{(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)R_0}.$$

Where  $R_0$  is the basic reproduction number given by  $R_0 = \frac{(\beta_1\Lambda_1 + \beta_2\Lambda_2)\alpha_1 + (\beta_3\Lambda_1 + \beta_4\Lambda_2)(\alpha_2(\theta_1 + \theta_2 + \mu) + \theta_1\alpha_1)}{N\mu(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)(\mu + \sigma + \delta_1)}$ .

**Proof of the basic reproductive number  $R_0$ .** The basic reproduction number denoted by  $R_0$  is the expected value of infection rate per time unit. The infection occurs in a susceptible population, caused by an infected individual. Based on the system (1), the article generates an equation that involves the classes of exposed and infected population. The disease reproduction number  $R_0$  of the proposed model (1) is defined in the infected classes. In all cases,  $R_0 < 1$  implies that disease will decline, whereas  $R_0 > 1$  implies that disease will persist within a community and  $R_0 = 1$  requires further investigation.  $R_0$  is obtained using the next generation matrix approach [9, 19] where several authors have used it.

We implore the use of a next-generation matrix to find the basic reproduction number for the model (1). Without loss of generality, it is clear from the model (1), the article generates an equation that involves the classes of the exposed population, infected population without symptom, and infected population with symptom as follows:

$$\begin{cases} \frac{dE(t)}{dt} = \frac{\beta_1 S_a(t)I(t)}{N} + \frac{\beta_3 S_a(t)C(t)}{N} + \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} - (\alpha_1 + \alpha_2 + \mu)E(t), \\ \frac{dI(t)}{dt} = \alpha_1 E(t) - (\mu + \theta_1 + \theta_2)I(t), \\ \frac{dC(t)}{dt} = \alpha_2 E(t) + \theta_1 I(t) - (\mu + \sigma + \delta_1)C(t), \\ \frac{dQ(t)}{dt} = \theta_2 I(t) + \sigma C(t) - (\gamma + \mu + \delta_2)Q(t). \end{cases} \quad (2)$$

Referring to [9, 19], from the equations (2), the study generates matrix  $\mathcal{F}$  and  $\mathcal{V}$ , i.e.

$$\mathcal{F} = \begin{pmatrix} \frac{\beta_1 S_a(t)I(t)}{N} + \frac{\beta_3 S_a(t)C(t)}{N} + \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

$$\mathcal{V} = \begin{pmatrix} (\mu + \alpha_1 + \alpha_2)E \\ (\theta_1 + \theta_2 + \mu)I(t) - \alpha_1 E(t) \\ -\alpha_2 E(t) - \theta_1 I(t) + (\mu + \sigma + \delta_1)C(t) \\ -\theta_2 I(t) - \sigma C(t) + (\gamma + \mu + \delta_2)Q(t) \end{pmatrix},$$

where

$$F = \begin{pmatrix} 0 & \frac{\beta_1 \Lambda_1 + \beta_2 \Lambda_2}{N\mu} & \frac{\beta_3 \Lambda_1 + \beta_4 \Lambda_2}{N\mu} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} (\mu + \alpha_1 + \alpha_2) & 0 & 0 & 0 \\ -\alpha_1 & (\theta_1 + \theta_2 + \mu) & 0 & 0 \\ -\alpha_2 & -\theta_1 & (\mu + \sigma + \delta_1) & 0 \\ 0 & -\theta_2 & -\sigma & (\gamma + \mu + \delta_2) \end{pmatrix}.$$

Therefore,  $FV^{-1}$  is the next generation matrix of the model structure (2). So, as described in [9, 19]  $R_0 = \rho(FV^{-1})$  where  $\rho$  stands for spectral radius of the next-generation matrix  $FV^{-1}$ . Thus,

$$FV^{-1} = \begin{pmatrix} FV_1 & FV_2 & \frac{(\beta_3 \Lambda_1 + \beta_4 \Lambda_2)}{N\mu(\mu + \sigma + \delta_1)} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

with

$$FV_1 = \frac{(\beta_1 \Lambda_1 + \beta_2 \Lambda_2)\alpha_1 + (\beta_3 \Lambda_1 + \beta_4 \Lambda_2)(\alpha_2(\theta_1 + \theta_2 + \mu) + \theta_1 \alpha_1)}{N\mu(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)(\mu + \sigma + \delta_1)},$$

$$FV_2 = \frac{(\beta_1 \Lambda_1 + \beta_2 \Lambda_2)}{(\theta_1 + \theta_2 + \mu)} + \frac{(\beta_3 \Lambda_1 + \beta_4 \Lambda_2)\theta_1}{N\mu(\mu + \alpha_1 + \alpha_2)(\mu + \sigma + \delta_1)}.$$

Finally, we have

$$R_0 = \rho(FV^{-1})$$

$$= \frac{(\beta_1 \Lambda_1 + \beta_2 \Lambda_2)\alpha_1 + (\beta_3 \Lambda_1 + \beta_4 \Lambda_2)(\alpha_2(\theta_1 + \theta_2 + \mu) + \theta_1 \alpha_1)}{N\mu(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)(\mu + \sigma + \delta_1)}.$$

## 5. Local stability of disease free equilibrium

**Theorem 4.** The disease free equilibrium point  $E^0$  is locally asymptotically stable if  $R_0 < 1$  and unstable if  $R_0 > 1$ .

**Proof.** The Jacobian matrix with respect to the system (1) is given by

$$J = \begin{pmatrix} A_1 & 0 & 0 & \frac{\beta_1 S_a(t)}{N} & \frac{\beta_3 S_a(t)}{N} & 0 & 0 \\ 0 & \frac{\beta_2 I(t) + \beta_4 C(t)}{N} - \mu & 0 & \frac{\beta_2 S_n(t)}{N} & \frac{\beta_4 S_n(t)}{N} & 0 & 0 \\ A_2 & \frac{\beta_2 I(t) + \beta_4 C(t)}{N} & -(\alpha_1 + \alpha_2 + \mu) & \frac{\beta_1 S_a(t) + \beta_2 S_n(t)}{N} & \frac{\beta_3 S_a(t) + \beta_4 S_n(t)}{N} & 0 & 0 \\ 0 & 0 & \alpha_1 & -(\mu + \theta_1 + \theta_2) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & \theta_1 & -(\mu + \sigma + \delta_1) & 0 & 0 \\ 0 & 0 & 0 & \theta_2 & \sigma & -(\gamma + \mu + \delta_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -\mu \end{pmatrix}.$$

Where  $A_1 = \frac{\beta_1 I(t) + \beta_3 C(t)}{N} - \mu$  and  $A_2 = \frac{\beta_1 I(t) + \beta_3 C(t)}{N}$ .

The Jacobian at the disease free equilibrium point  $E^0$  as follows:

$$J = \begin{pmatrix} -\mu & 0 & 0 & \frac{\beta_1 \Lambda_1}{N\mu} & \frac{\beta_3 \Lambda_1}{N\mu} & 0 & 0 \\ 0 & -\mu & 0 & \frac{\beta_2 \Lambda_2}{N} & \frac{\beta_4 \Lambda_2}{N} & 0 & 0 \\ 0 & 0 & -(\alpha_1 + \alpha_2 + \mu) & \frac{\beta_1 \Lambda_1 + \beta_2 \Lambda_2}{N\mu} & \frac{\beta_3 \Lambda_1 + \beta_4 \Lambda_2}{N\mu} & 0 & 0 \\ 0 & 0 & \alpha_1 & -(\mu + \theta_1 + \theta_2) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & \theta_1 & -(\mu + \sigma + \delta_1) & 0 & 0 \\ 0 & 0 & 0 & \theta_2 & \sigma & -(\gamma + \mu + \delta_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -\mu \end{pmatrix}. \quad (3)$$

The characteristic polynomial of the Jacobian matrix at DFE is given by  $\det(J_{E(0)} - \lambda I) = 0$ , where  $\lambda$  is the eigenvalue and  $I$  is  $7 \times 7$  identity matrix. Thus, the determinant of  $(J_{E(0)} - \lambda I)$  is

$$\det(J_{E(0)} - \lambda I) = \begin{vmatrix} -\mu - \lambda & 0 & 0 & \frac{\beta_1 \Lambda_1}{N\mu} & \frac{\beta_3 \Lambda_1}{N\mu} & 0 & 0 \\ 0 & -\mu - \lambda & 0 & \frac{\beta_2 \Lambda_2}{N} & \frac{\beta_4 \Lambda_2}{N} & 0 & 0 \\ 0 & 0 & -(\alpha_1 + \alpha_2 + \mu) - \lambda & \frac{\beta_1 \Lambda_1 + \beta_2 \Lambda_2}{N\mu} & \frac{\beta_3 \Lambda_1 + \beta_4 \Lambda_2}{N\mu} & 0 & 0 \\ 0 & 0 & \alpha_1 & -(\mu + \theta_1 + \theta_2) - \lambda & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & \theta_1 & -(\mu + \sigma + \delta_1) - \lambda & 0 & 0 \\ 0 & 0 & 0 & \theta_2 & \sigma & -(\gamma + \mu + \delta_2) - \lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -\mu - \lambda \end{vmatrix}.$$

Simplifying and solving for  $\lambda$ , gives

$$\lambda_1 = -\mu < 0, \quad \lambda_2 = -\mu < 0, \quad \lambda_7 = -\mu < 0, \quad \lambda_5 = -(\mu + \sigma + \delta_1) < 0, \quad \lambda_6 = -(\mu + \gamma + \delta_2) < 0, \\ \lambda_3 = -(\mu + \alpha_1 + \alpha_2) < 0, \quad \lambda_4 = (\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)(R_0 - 1) < 0,$$

provided that  $R_0 < 1$ . This completes the proof.  $\blacksquare$

## 6. Local stability analysis of the endemic equilibrium $E^*$

**Theorem 5.** *The endemic equilibrium  $E^*$  is locally asymptotically stable if  $R_0 > 1$ .*

**Proof.** The Jacobian matrix with respect to the system (1) is given by

$$J = \begin{pmatrix} \frac{\beta_1 I(t) + \beta_3 C(t)}{N} - \mu & 0 & 0 & \frac{\beta_1 S_a(t)}{N} & \frac{\beta_3 S_a(t)}{N} & 0 & 0 \\ 0 & \frac{\beta_2 I(t) + \beta_4 C(t)}{N} - \mu & 0 & \frac{\beta_2 S_n(t)}{N} & \frac{\beta_4 S_n(t)}{N} & 0 & 0 \\ \frac{\beta_1 I(t) + \beta_3 C(t)}{N} & \frac{\beta_2 I(t) + \beta_4 C(t)}{N} & -(\alpha_1 + \alpha_2 + \mu) & \frac{\beta_1 S_a(t) + \beta_2 S_n(t)}{N} & \frac{\beta_3 S_a(t) + \beta_4 S_n(t)}{N} & 0 & 0 \\ 0 & 0 & \alpha_1 & -(\mu + \theta_1 + \theta_2) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & \theta_1 & -(\mu + \sigma + \delta_1) & 0 & 0 \\ 0 & 0 & 0 & \theta_2 & \sigma & -(\gamma + \mu + \delta_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -\mu \end{pmatrix},$$

which implies,

$$J(E^*) = \begin{pmatrix} J_{11} & 0 & 0 & J_{14} & J_{15} & 0 & 0 \\ 0 & J_{22} & 0 & J_{24} & J_{25} & 0 & 0 \\ J_{31} & J_{32} & (\alpha_1 + \alpha_2 + \mu) & J_{34} & J_{35} & 0 & 0 \\ 0 & 0 & \alpha_1 & -(\mu + \theta_1 + \theta_2) & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & \theta_1 & -(\mu + \sigma + \delta_1) & 0 & 0 \\ 0 & 0 & 0 & \theta_2 & \sigma & -(\gamma + \mu + \delta_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -\mu \end{pmatrix},$$

with

$$J_{11} = \frac{\beta_1}{N} \frac{\alpha_1(\Lambda_1 + \Lambda_2)(R_0 - 1)}{(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)R_0} - \mu, \quad J_{14} = \frac{\beta_1}{N} \frac{\Lambda_1}{\mu R_0}, \quad J_{22} = \frac{\beta_2}{N} \frac{\alpha_1(\Lambda_1 + \Lambda_2)(R_0 - 1)}{(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)R_0} - \mu, \quad J_{24} = \frac{\beta_2}{N} \frac{\Lambda_2}{\mu R_0}, \\ J_{31} = \frac{\beta_1}{N} \frac{\alpha_1(\Lambda_1 + \Lambda_2)(R_0 - 1)}{(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)R_0}, \quad J_{32} = \frac{\beta_2}{N} \frac{\alpha_1(\Lambda_1 + \Lambda_2)(R_0 - 1)}{(\theta_1 + \theta_2 + \mu)(\mu + \alpha_1 + \alpha_2)R_0}, \quad J_{33} = \frac{\beta_1}{N} \frac{\Lambda_1}{\mu R_0} + \frac{\beta_2}{N} \frac{\Lambda_2}{\mu R_0}.$$



The characteristic polynomial of the Jacobian matrix at  $E^*$  is given by  $\det(J_{E^*} - \lambda I) = 0$ , where  $\lambda$  is the eigenvalue and  $I$  is  $7 \times 7$  identity matrix. Thus,

$$\det(J(E^*) - \lambda I) = \begin{vmatrix} J_{11} - \lambda_1 & 0 & 0 & J_{14} & J_{15} & 0 & 0 \\ 0 & J_{22} - \lambda_2 & 0 & J_{24} & 0 & 0 & 0 \\ J_{31} & J_{32} & (\alpha_1 + \alpha_2 + \mu) - \lambda_3 & J_{34} & J_{35} & 0 & 0 \\ 0 & 0 & \alpha_1 & -(\mu + \theta_1 + \theta_2) - \lambda_4 & 0 & 0 & 0 \\ 0 & 0 & \alpha_2 & \theta_1 & -(\mu + \sigma + \delta_1) - \lambda_5 & 0 & 0 \\ 0 & 0 & 0 & \theta_2 & \sigma & -(\gamma + \mu + \delta_2) - \lambda_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & \gamma & -\mu - \lambda_7 \end{vmatrix},$$

$$\det(J(E^*) - \lambda I) = (J_{11} - \lambda_1)(J_{22} - \lambda_2)[(-\mu - \lambda_7)(-\gamma + \mu + \delta_2) - \lambda_6](-(\mu + \sigma + \delta_1) - \lambda_5) \\ \times [(\alpha_1 + \alpha_2 + \mu)(-(\mu + \theta_1 + \theta_2) - \lambda_4) - \alpha_1 J_{33} - \lambda_3] - J_{14}.$$

Simplifying the characteristic polynomial, we get

$$\begin{aligned} \lambda_1 &= -\mu < 0, & \lambda_2 &= -\mu < 0, & \lambda_7 &= -\mu < 0, \\ \lambda_5 &= -(\mu + \sigma + \delta_1) < 0, & \lambda_6 &= -(\mu + \gamma + \delta_2) < 0, \\ \lambda_3 &= -(\mu + \alpha_1 + \alpha_2) < 0, & \lambda_4 &= -(\theta_1 + \theta_2 + \mu) < 0. \end{aligned}$$

The other polynomial coefficients has all terms positive and thus, its roots must all be negative. This completes the proof. ■

## 7. Global stability of free equilibrium point

**Theorem 6.** If  $\mathcal{R}_0 < 1$  then free equilibrium point of the system is globally asymptotically stable.

**Proof.** To prove the global stability of free equilibrium point, we consider Lyapunov function  $V: \Omega \rightarrow \mathbb{R}$  given by  $V(S_a; S_n, E, A) = \frac{1}{2} ((S_a + S_n) - (S_a + S_n)^0)^2 + 2 \frac{(\Lambda_1 + \Lambda_2)}{\mu} (E + A)$ . Using system (1) and the coordinates of the free equilibrium point we have  $D_t V(S_a, S_n, E, A) \leq -\mu((S_a + S_n) - (S_a + S_n)^0)^2 - (\mu + \gamma)E^2 - (\mu + \alpha_2)A^2 - \frac{(\Lambda_1 + \Lambda_2)}{\mu}(\gamma E + \alpha_2 A) - (2\mu + \alpha_2 + \gamma)AE - (1 - \mathcal{R}_0)(S_a + S_n)(E + A)$ . Thus,  $D_t V(S_a, S_n, E, A) \leq 0$  for  $\mathcal{R}_0 \leq 1$ . Also we obtain  $D_t V(S_a, S_n, E, A) = 0 \Leftrightarrow S_a = S_a^0; S_n = S_n^0$  and  $A = E = 0$ .

Hence, by La Salle's invariance principle [10], free equilibrium point is globally asymptotically stable on  $\Omega$ . ■

## 8. Global stability of the endemic equilibrium point

**Theorem 7.** If  $\mathcal{R}_0 > 1$  then the endemic equilibrium point of the system is globally asymptotically stable.

**Proof.** Consider Lyapunov function  $V: \Omega \rightarrow \mathbb{R}$  given by

$$V(S_a, S_n, E) = \left( (S_a + S_n) - (S_a + S_n)^* - (S_a + S_n)^* \ln \frac{(S_a + S_n)}{(S_a + S_n)^*} \right) + \left( E - E^* - E^* \ln \frac{E}{E^*} \right).$$

Then by using the property of fractional derivatives, we have

$$D_t V(S_a, S_n, E) \leq \left( 1 - \frac{(S_a + S_n)^*}{P} \right) D_t (S_a + S_n) + \left( 1 - \frac{E^*}{E} \right) D_t E.$$

Using system (1) and the coordinates of the endemic equilibrium point

$$D_t V(S_a, S_n, E) \leq -\frac{(\Lambda_1 + \Lambda_2)((S_a + S_n) - (S_a + S_n)^*)^2}{(S_a + S_n)(S_a + S_n^*)} \leq 0.$$

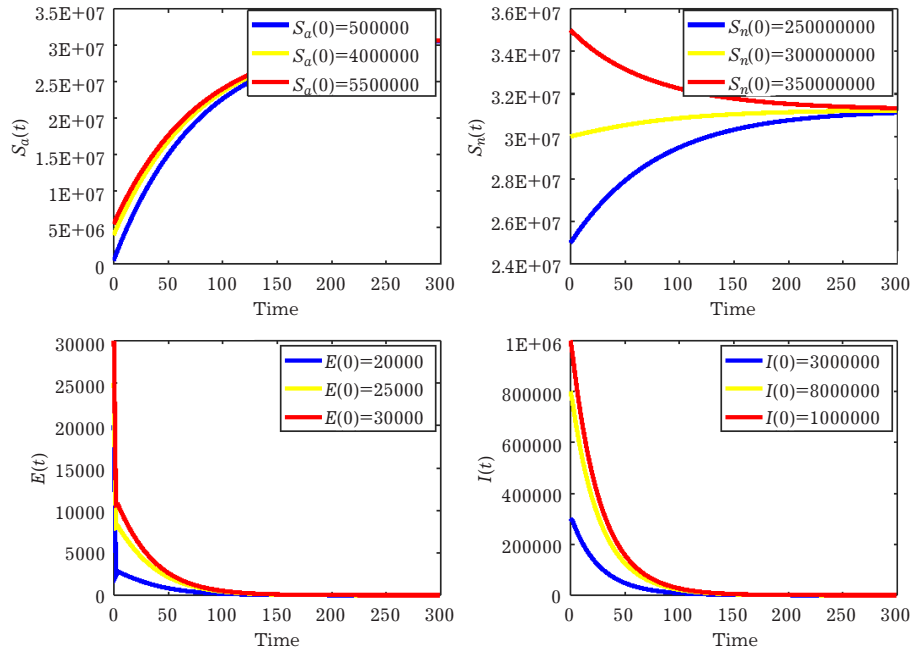
Also we obtain  $D_t V(S_a, S_n, E) = 0 \Leftrightarrow S_a = S_a^*; S_n = S_n^*$ .

Hence by La Salle's invariance principle [10], the endemic equilibrium point is globally asymptotically stable on  $\Omega$ . ■

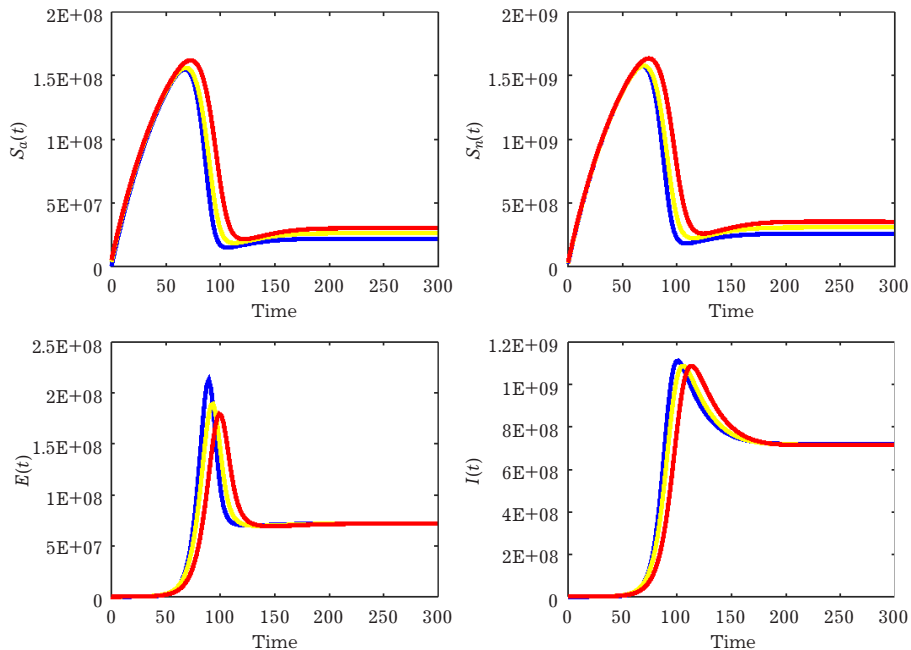
## 9. Numerical simulation

In this section, we present some numerical solutions of system (1) for different values of the parameters. The resolution of system (1) was created using the finite-difference method. We use the different initial

values for each variable of state, and we use the following parameters:  $\Lambda_1 = 7.5 \cdot 10^5$ ,  $\Lambda_2 = 7.5 \cdot 10^5$ ,  $\mu = 0.024$ ,  $\alpha_1 = 0.8$ ,  $\alpha_2 = 0.2$ ,  $\alpha_3 = 0.03$ ,  $\beta_1 = 0.12$ ,  $\beta_2 = 0.1$ ,  $\theta_1 = 0.03$ ,  $\theta_2 = 0.05$ ,  $\sigma = 5.7341 \cdot 10^{-5}$  we have the Disease free Equilibrium point  $E^0 = (3.124 \cdot 10^7, 3.026 \cdot 10^7, 0, 0, 0, 0)$  and  $\mathcal{R}_0 = 0.243238520541080 < 1$ . In this case, over time, we notice that the number of susceptible people is close to  $E^0$ , in other words, all the state variables converge towards the equilibrium point and this for three different initial values in each of the state variables considered. We also note that the number of the exposed people and the number of the infected people with symptoms, are close to zero (see Fig. 2).



**Fig. 2.** Model with a disease-free equilibrium.



**Fig. 3.** Model with an epidemic equilibrium.

Also, for the different initial values for each variable of state, and the following parameters:  $\Lambda_1 = 7.5 \cdot 10^6$ ,  $\Lambda_2 = 7.5 \cdot 10^7$ ,  $\mu = 0.03$ ,  $\alpha_1 = 0.8$ ,  $\alpha_2 = 0.2$ ,  $\alpha_3 = 0.03$ ,  $\beta_1 = 0.12$ ,  $\beta_2 = 0.1$ ,  $\theta_1 = 0.03$ ,

$\theta_2 = 0.05$ ,  $\sigma = 5.7341 \cdot 10^{-5}$  we have the endemic equilibrium point  $E^*$  and  $R_0 = 9.8487 > 1$  and state variables converge to the equilibrium point  $E^*$ . In this case, over time, we notice that the number of  $S_a$  and  $S_n$  people are convergent to same value for each of them. We also note that the number of the people infected and people exposed are convergent to same value (see Fig. 3).

## 10. The optimal control problem

To control the spread of hepatitis HCV we will introduce three types of controls  $u_1$ ,  $u_2$  and  $u_3$ , respectively representing awareness, early detection and treatment. Thus our model with optimal control is defined as follows:

$$\begin{cases} \frac{dS_a(t)}{dt} = \Lambda_1 - \frac{\beta_1 S_a(t)I(t)}{N} - \frac{\beta_3 S_a(t)C(t)}{N} - \mu S_a(t) + \frac{u_1(t)\beta_2 S_n(t)I(t)}{N} + \frac{u_1(t)\beta_4 S_n(t)C(t)}{N}, \\ \frac{dS_n(t)}{dt} = \Lambda_2 - \frac{\beta_2 S_n(t)I(t)}{N} - \frac{\beta_4 S_n(t)C(t)}{N} - \mu S_n(t) - \frac{u_1(t)\beta_2 S_n(t)I(t)}{N} - \frac{u_1(t)\beta_4 S_n(t)C(t)}{N}, \\ \frac{dE(t)}{dt} = \frac{\beta_1 S_a(t)I(t)}{N} + \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_3 S_a(t)C(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} - (\alpha_1 + \alpha_2 + \mu)E(t) - u_2(t)E(t), \\ \frac{dI(t)}{dt} = \alpha_1 E(t) - (\mu + \theta_1 + \theta_2)I(t), \\ \frac{dC(t)}{dt} = \alpha_2 E(t) + \theta_1 I(t) - (\mu + \sigma + \delta_1)C(t), \\ \frac{dQ(t)}{dt} = \theta_2 I(t) + \sigma C(t) - (\gamma + \mu + \delta_2)Q(t) + u_2(t)E(t) - u_3(t)Q(t), \\ \frac{dR(t)}{dt} = \gamma Q(t) - \mu R(t) + u_3(t)Q(t). \end{cases} \quad (4)$$

### 10.1. The optimal control: existence and characterization

The problem is to minimize the objective functional

$$J(u_1, u_2, u_3) = E(T) + I(T) + C(T) + Q(T) + \int_0^T [E(t) + I(t) + C(t) + Q(t) + \frac{A}{2}u_1^2(t) + \frac{B}{2}u_2^2(t) + \frac{D}{2}u_3^2(t)] dt,$$

where  $A$ ,  $B$  and  $D$  are the cost coefficients. They are selected to weigh the relative importance of  $u_1(t)$ ,  $u_2(t)$  and  $u_3(t)$  at time  $t$ ,  $T$  is the final time. In other words, we seek the optimal controls  $u_1^*$ ,  $u_2^*$  and  $u_3^*$  such that

$$J(u_1^*, u_2^*, u_3^*) = \min_{(u_1, u_2, u_3) \in U} J(u_1, u_2, u_3),$$

where  $U$  is the set of admissible controls defined by

$$U = \left\{ (u_1, u_2, u_3) : \begin{aligned} 0 \leq u_{1,\min} \leq u_1(t) \leq u_{1,\max} \leq 1, \\ 0 \leq u_{2,\min} \leq u_2(t) \leq u_{2,\max} \leq 1, \\ 0 \leq u_{3,\min} \leq u_3(t) \leq u_{3,\max} \leq 1, \quad t \in [0, T]. \end{aligned} \right.$$

### 10.2. Existence of an optimal control

In this section we introduce a result concerning the existence of optimal control.

**Theorem 8.** Consider the control problem with system (4). There exists an optimal control  $(u_1^*, u_2^*, u_3^*) \in U$  such that

$$J(u_1^*, u_2^*, u_3^*) = \min_{(u_1, u_2, u_3) \in U} J(u_1, u_2, u_3). \quad (5)$$

**Proof.** The existence of the optimal control can be obtained using a result by Fleming and Rishel [20], checking the following steps.

- The set of controls and corresponding state variables is non-empty. To prove this condition we use a simplified version of an existence result of Boyce and DiPrima ([21], Theorem 7.1.1).
- $J$  is convex in  $U$ .

- The control set  $U$  is convex and closed by definition. Take any controls  $u_1, u_2 \in U$  and  $\lambda \in [0, 1]$ . Then  $0 \leq \lambda u + (1 - \lambda)v$ . Additionally, we observe that  $\lambda u_1 \leq \lambda$  and  $(1 - \lambda)u_2 \leq (1 - \lambda)$  then  $\lambda u_1 + (1 - \lambda)u_2 \leq \lambda + (1 - \lambda) = 1$ . Hence,  $0 \leq \lambda u_1 + (1 - \lambda)u_2 \leq 1$ , for all  $u_1, u_2 \in U$  and  $\lambda \in [0, 1]$ .
- The right hand sides of equations of system (4) are continuous, bounded above by linear function in the state and controls variable.

The integrand  $L(E, \dots, Q, u_1, u_2, u_3)$  of the objective functional is clearly convex on  $U$ . There exists constants  $\zeta_1$ ,  $\zeta_2$ , and  $\beta > 1$  such that the integrand in the objective functional satisfies

$$L(E, \dots, Q, u_1, u_2, u_3) \geq \zeta_1 + \zeta_2 (|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\beta}{2}}.$$

Indeed

$$E(t) + I(t) + C(t) + Q(t) + \frac{A}{2}u_1^2(t) + \frac{B}{2}u_2^2(t) + \frac{D}{2}u_3^2(t) \geq \zeta_1 + \zeta_2 (|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\beta}{2}}.$$

The state variables being bounded, let

$$\zeta_1 = 4 \inf_{t \in [0, T]} (E(t) + I(t) + C(t) + Q(t)), \quad \zeta_2 = \inf \left( \frac{A}{2}, \frac{B}{2}, \frac{D}{2} \right), \quad \text{and} \quad \beta = 2.$$

Therefore, from Fleming and Rishel [9], we conclude that there exists an optimal control. ■

### 10.3. Characterization of the optimal control

In order to derive the necessary conditions for the optimal control, we apply Pontryagin's maximum principle [12, 22] we have the Hamiltonian  $H$  at time  $t$  defined by

$$H(t) = E(t) + I(t) + C(t) + Q(t) + \frac{A}{2}u_1^2(t) + \frac{B}{2}u_2^2(t) + \frac{D}{2}u_3^2(t) + \sum_{i=1}^7 \lambda_i(t) f_i(S_a, S_n, E, I, C, Q, R).$$

Where  $f_i$  is the right side of the difference equation of the  $i$ -th state variable.

**Theorem 9.** *Given the optimal controls  $(u_1^*, u_2^*, u_3^*)$  and the solutions  $S_a^*, S_n^*, E^*, I^*, C^*, T^*$  and  $R^*$  of the corresponding state system (1), there exists adjoint variables  $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6$  and  $\lambda_7$  satisfying:*

$$\begin{aligned} \lambda'_1 &= \frac{\partial H}{\partial S_a} = \lambda_1 \left( -\frac{\beta_1 I(t) + \beta_3 C(t)}{N} - \mu \right) + \lambda_3 \frac{\beta_1 I(t) + \beta_3 C(t)}{N}, \\ \lambda'_2 &= \frac{\partial H}{\partial S_n} = \lambda_1 u_1(t) \frac{\beta_2 I(t) + \beta_4 C(t)}{N} + \lambda_2 \left( -\frac{\beta_2 I(t) + \beta_4 C(t)}{N} - u_1(t) \frac{\beta_2 I(t) + \beta_4 C(t)}{N} - \mu \right) + \lambda_3 \frac{\beta_2 I(t) + \beta_4 C(t)}{N}, \\ \lambda'_3 &= \frac{\partial H}{\partial E} = 1 + \lambda_3 (-(\alpha_1 + \alpha_2 + \mu) - u_2(t)) + \lambda_4 \alpha_1 + \lambda_5 \alpha_2 + \lambda_6 u_2(t), \\ \lambda'_4 &= \frac{\partial H}{\partial I} = 1 + \lambda_1 \left( -\frac{\beta_1 S_a(t)}{N} + u_1(t) \frac{\beta_2 S_n(t)}{N} \right) + \lambda_2 \left( -\frac{\beta_2 S_n(t)}{N} - u_1(t) \frac{\beta_2 S_n(t)}{N} \right) \\ &\quad + \lambda_3 \left( \frac{\beta_1 S_a(t)}{N} + \frac{\beta_2 S_n(t)}{N} \right) - \lambda_4 (\mu + \theta_1 + \theta_2) + \lambda_5 \theta_1 + \lambda_6 \theta_2, \\ \lambda'_5 &= \frac{\partial H}{\partial C} = 1 + \lambda_1 \left( -\frac{\beta_3 S_a(t)}{N} + u_1(t) \frac{\beta_4 S_n(t)}{N} \right) + \lambda_2 \left( -\frac{\beta_4 S_n(t)}{N} - u_1(t) \frac{\beta_4 S_n(t)}{N} \right) + \lambda_3 \left( \frac{\beta_3 S_a(t)}{N} + \frac{\beta_4 S_n(t)}{N} \right) \\ &\quad - \lambda_5 (\mu + \sigma + \delta_1) + \lambda_6 \sigma, \\ \lambda'_6 &= \frac{\partial H}{\partial Q} = 1 - \lambda_6 (\gamma + \mu + \delta_2 + u_3(t)) + \lambda_7 (\gamma + u_3(t)), \\ \lambda'_7 &= \frac{\partial H}{\partial R} = -\lambda_7 \mu. \end{aligned}$$

With the transversality conditions at time  $T_f$ :  $\lambda_1(T_f) = 0$ ,  $\lambda_2(T_f) = 0$ ,  $\lambda_3(T_f) = 1$ ,  $\lambda_4(T_f) = 1$ ,  $\lambda_5(T_f) = 1$ ,  $\lambda_6(T_f) = 1$  and  $\lambda_7(T_f) = 0$ . Furthermore, for  $t \in [0, T]$ , the optimal controls  $u_1^*$ ,  $u_2^*$  and  $u_3^*$  are given by

$$\begin{aligned} u_1^* &= \min \left[ 1, \max \left[ 0, \frac{1}{A} \left( \lambda_1 \left( \frac{\beta_2 S_n(t) I(t)}{N} + \frac{\beta_4 S_n(t) C(t)}{N} \right) - \lambda_2 \left( \frac{\beta_2 S_n(t) I(t)}{N} + \frac{\beta_4 S_n(t) C(t)}{N} \right) \right) \right] \right], \\ u_2^* &= \min \left[ 1, \max \left[ 0, \frac{\lambda_3 E(t) - \lambda_6 E(t)}{B} \right] \right], \\ u_3^* &= \min \left[ 1, \max \left[ 0, \frac{\lambda_6 Q(t) - \lambda_7 Q(t)}{D} \right] \right]. \end{aligned}$$

**Proof.** The Hamiltonian  $H$  is defined as follows:

$$H(t) = E(t) + I(t) + C(t) + Q(t) + \frac{A}{2}u_1^2(t) + \frac{B}{2}u_2^2(t) + \frac{D}{2}u_3^2(t) + \sum_{i=1}^7 \lambda_i(t)f_i(S_a, S_n, E, I, C, Q, R).$$

$$\begin{cases} f_1 = \Lambda_1 - \frac{\beta_1 S_a(t)I(t)}{N} - \frac{\beta_3 S_a(t)C(t)}{N} - \mu S_a(t) + \frac{u_1(t)\beta_2 S_n(t)I(t)}{N} + \frac{u_1(t)\beta_4 S_n(t)C(t)}{N}, \\ f_2 = \Lambda_2 - \frac{\beta_2 S_n(t)I(t)}{N} - \frac{\beta_4 S_n(t)C(t)}{N} - \mu S_n(t) - \frac{u_1(t)\beta_2 S_n(t)I(t)}{N} - \frac{u_1(t)\beta_4 S_n(t)C(t)}{N}, \\ f_3 = \frac{\beta_1 S_a(t)I(t)}{N} + \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_3 S_a(t)C(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} - (\alpha_1 + \alpha_2 + \mu)E(t) - u_2(t)E(t), \\ f_4 = \alpha_1 E(t) - (\mu + \theta_1 + \theta_2)I(t), \\ f_5 = \alpha_2 E(t) + \theta_1 I(t) - (\mu + \sigma + \delta_1)C(t), \\ f_6 = \theta_2 I(t) + \sigma C(t) - (\gamma + \mu + \delta_2)Q(t) + u_2(t)E(t) - u_3(t)Q(t), \\ f_7 = \gamma Q(t) - \mu R(t) + u_3(t)Q(t). \end{cases}$$

For  $t \in [0, T]$ , the adjoint equations and transversality conditions can be obtained by using Pontryagin's maximum principle [1, 23] such that

$$\begin{aligned} \lambda'_1 &= \frac{\partial H}{\partial S_a} = \lambda_1 \left( -\frac{\beta_1 I(t) + \beta_3 C(t)}{N} - \mu \right) + \lambda_3 \frac{\beta_1 I(t) + \beta_3 C(t)}{N}, \\ \lambda'_2 &= \frac{\partial H}{\partial S_n} = \lambda_1 u_1(t) \frac{\beta_2 I(t) + \beta_4 C(t)}{N} + \lambda_2 \left( -\frac{\beta_2 I(t) + \beta_4 C(t)}{N} - u_1(t) \frac{\beta_2 I(t) + \beta_4 C(t)}{N} - \mu \right) + \lambda_3 \frac{\beta_2 I(t) + \beta_4 C(t)}{N}, \\ \lambda'_3 &= \frac{\partial H}{\partial E} = 1 + \lambda_3 (-(\alpha_1 + \alpha_2 + \mu) - u_2(t)) + \lambda_4 \alpha_1 + \lambda_5 \alpha_2 + \lambda_6 u_2(t), \\ \lambda'_4 &= \frac{\partial H}{\partial I} = 1 + \lambda_1 \left( -\frac{\beta_1 S_a(t)}{N} + u_1(t) \frac{\beta_2 S_n(t)}{N} \right) + \lambda_2 \left( -\frac{\beta_2 S_n(t)}{N} - u_1(t) \frac{\beta_2 S_n(t)}{N} \right) \\ &\quad + \lambda_3 \left( \frac{\beta_1 S_a(t)}{N} + \frac{\beta_2 S_n(t)}{N} \right) - \lambda_4 (\mu + \theta_1 + \theta_2) + \lambda_5 \theta_1 + \lambda_6 \theta_2, \\ \lambda'_5 &= \frac{\partial H}{\partial C} = 1 + \lambda_1 \left( -\frac{\beta_3 S_a(t)}{N} + u_1(t) \frac{\beta_4 S_n(t)}{N} \right) + \lambda_2 \left( -\frac{\beta_4 S_n(t)}{N} - u_1(t) \frac{\beta_4 S_n(t)}{N} \right) + \lambda_3 \left( \frac{\beta_3 S_a(t)}{N} + \frac{\beta_4 S_n(t)}{N} \right) \\ &\quad - \lambda_5 (\mu + \sigma + \delta_1) + \lambda_6 \sigma, \\ \lambda'_6 &= \frac{\partial H}{\partial Q} = 1 - \lambda_6 (\gamma + \mu + \delta_2 + u_3(t)) + \lambda_7 (\gamma + u_3(t)), \\ \lambda'_7 &= \frac{\partial H}{\partial R} = -\lambda_7 \mu. \end{aligned}$$

For  $t \in [0, T]$ , the optimal controls  $u_1^*$ ,  $u_2^*$ ,  $u_3^*$  and  $u_4^*$  can be solved from the optimality condition,

$$\frac{\partial H(t)}{\partial u_1(t)} = 0, \quad \frac{\partial H(t)}{\partial u_2(t)} = 0, \quad \frac{\partial H(t)}{\partial u_3(t)} = 0.$$

That are

$$\begin{aligned} Au_1(t) + \lambda_1 \left( \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} \right) - \lambda_2 \left( \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} \right) &= 0, \\ Bu_2(t) - \lambda_3 E(t) + \lambda_6 E(t) &= 0, \\ Du_3(t) - \lambda_6 Q(t) + \lambda_7 Q(t) &= 0. \end{aligned}$$

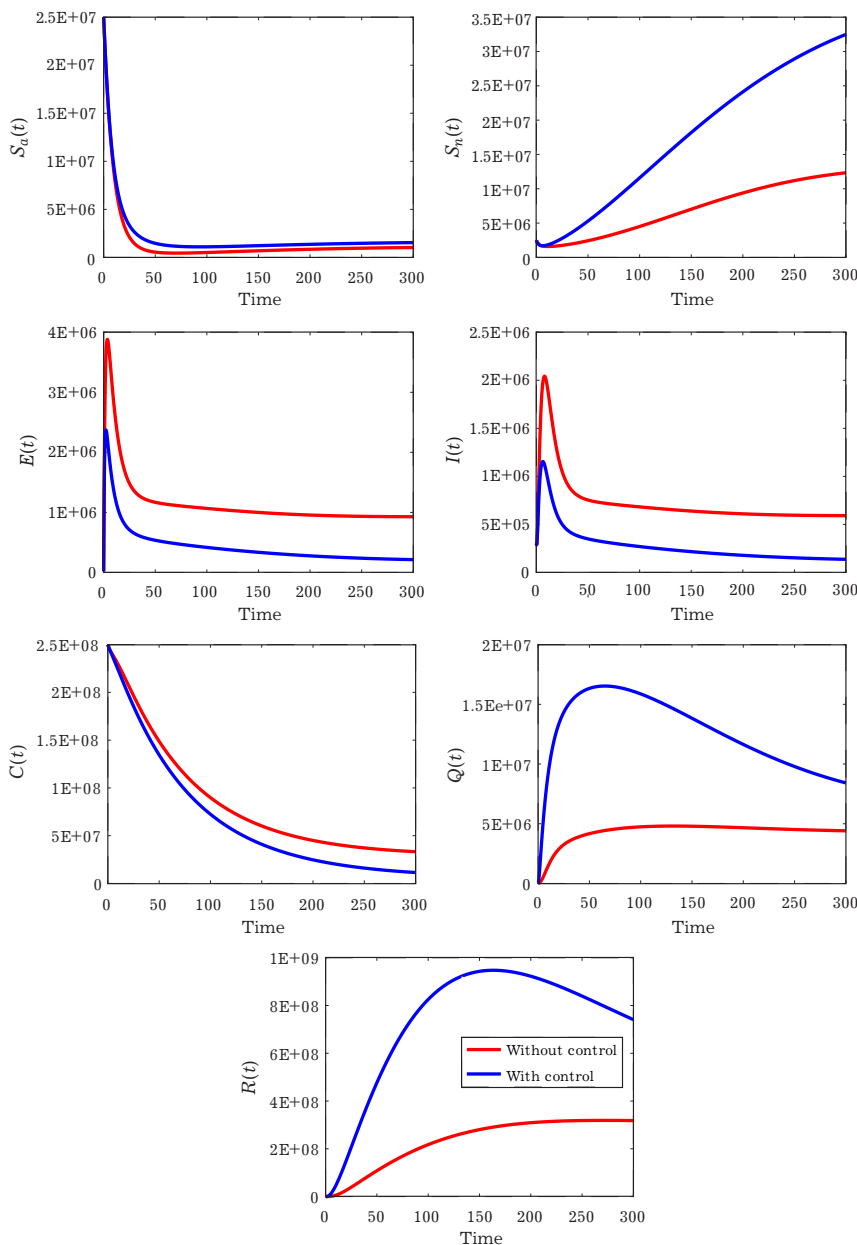
We obtain

$$\begin{aligned} u_1(t) &= \frac{1}{A} \left( \lambda_1 \left( \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} \right) - \lambda_2 \left( \frac{\beta_2 S_n(t)I(t)}{N} + \frac{\beta_4 S_n(t)C(t)}{N} \right) \right), \\ u_2(t) &= \frac{\lambda_3 E(t) - \lambda_6 E(t)}{B}, \\ u_3(t) &= \frac{\lambda_6 Q(t) - \lambda_7 Q(t)}{D}. \end{aligned}$$

■

## 11. Numerical simulation

In this section, we present the results obtained by numerically solving the optimality system. In our control problem, we have initial conditions for the state variables and terminal conditions for the adjoints. We solve the optimality system by an iterative method with forward solving of the state system followed by backward solving of the adjoint system. We start with an initial guess for the controls at the first iteration and then before the next iteration, we update the controls by using the characterization. We continue until convergence of successive iterates is achieved. A code is written and compiled in MatLab using the following data.



**Fig. 4.** Simulations of the model showing the effects of the optimal in case  $u_1 = 0$ ,  $u_2 \neq 0$ ,  $u_3 \neq 0$ .

in the number of individuals exposed  $E$  from the beginning of the second week, and the same behaviour for individuals in compartment  $I$ . For chronic infections  $C$  there is a sharp decrease from the first week. On the other hand, there is an increase in the number of people hospitalized  $Q$ , including those who have isolated themselves in their homes. For people who are cured  $R$ , there is also an

Different simulations can be carried out using various values of parameters.

### 11.1. Strategy A

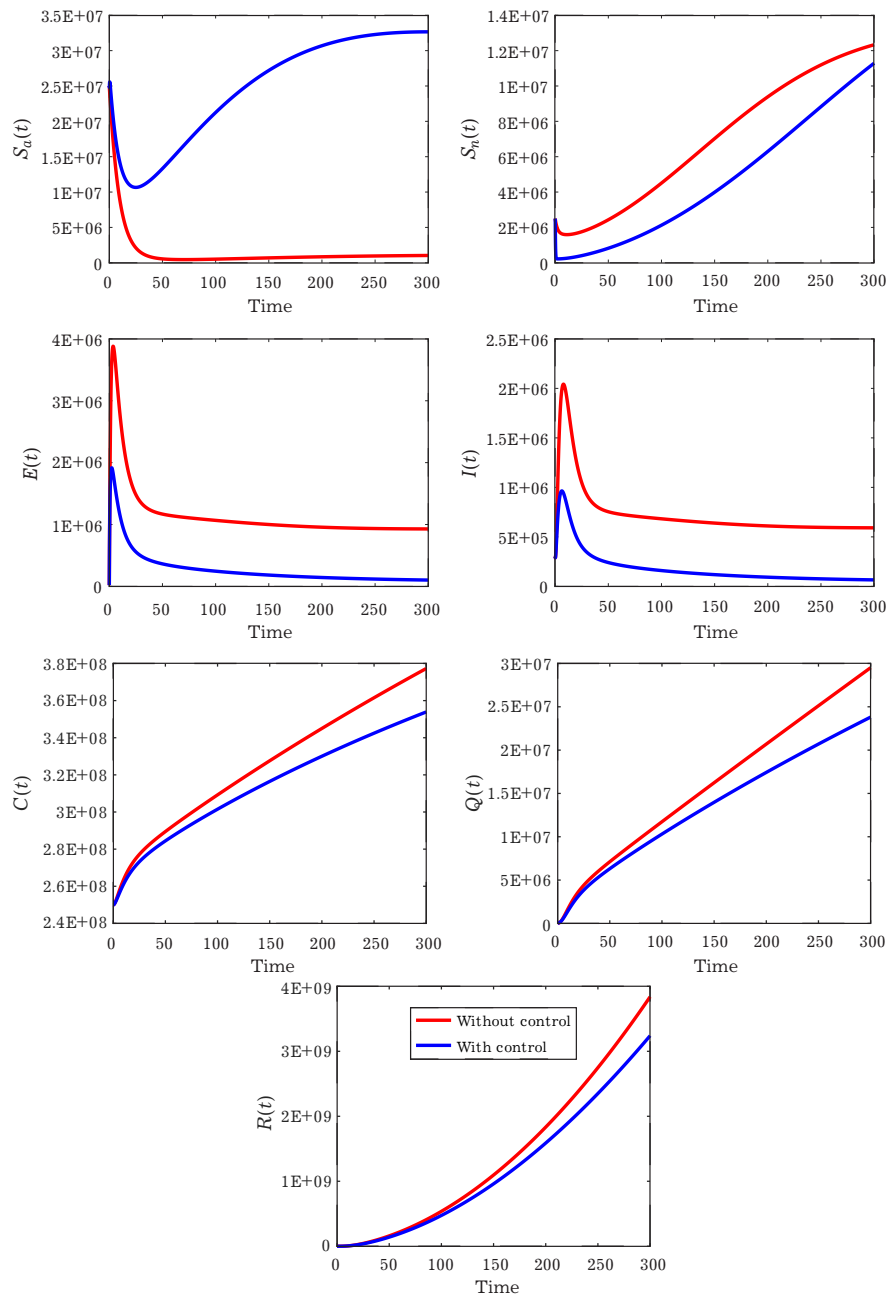
In this strategy, we considered two controls  $u_2$  and  $u_3$  representing access to early detection and treatment respectively. There is a significant decrease in the number of individuals exposed  $E$  from the beginning of the second week, and the same behaviour for individuals in compartment  $I$ . For chronic infections  $C$ , there is a sharp decrease from the first week. On the other hand, there is an increase in the number of people hospitalized  $Q$ , including those who have isolated themselves in their homes. For people who are cured  $R$ , there is also an increase in the first week, which confirms the effectiveness of early treatment with the therapeutic protocol (see Fig 4).

### 11.2. Strategy B

In this strategy, two  $u_1$  and  $u_2$  controls representing advertising and awareness and access to early detection were combined.

There is a significant decrease

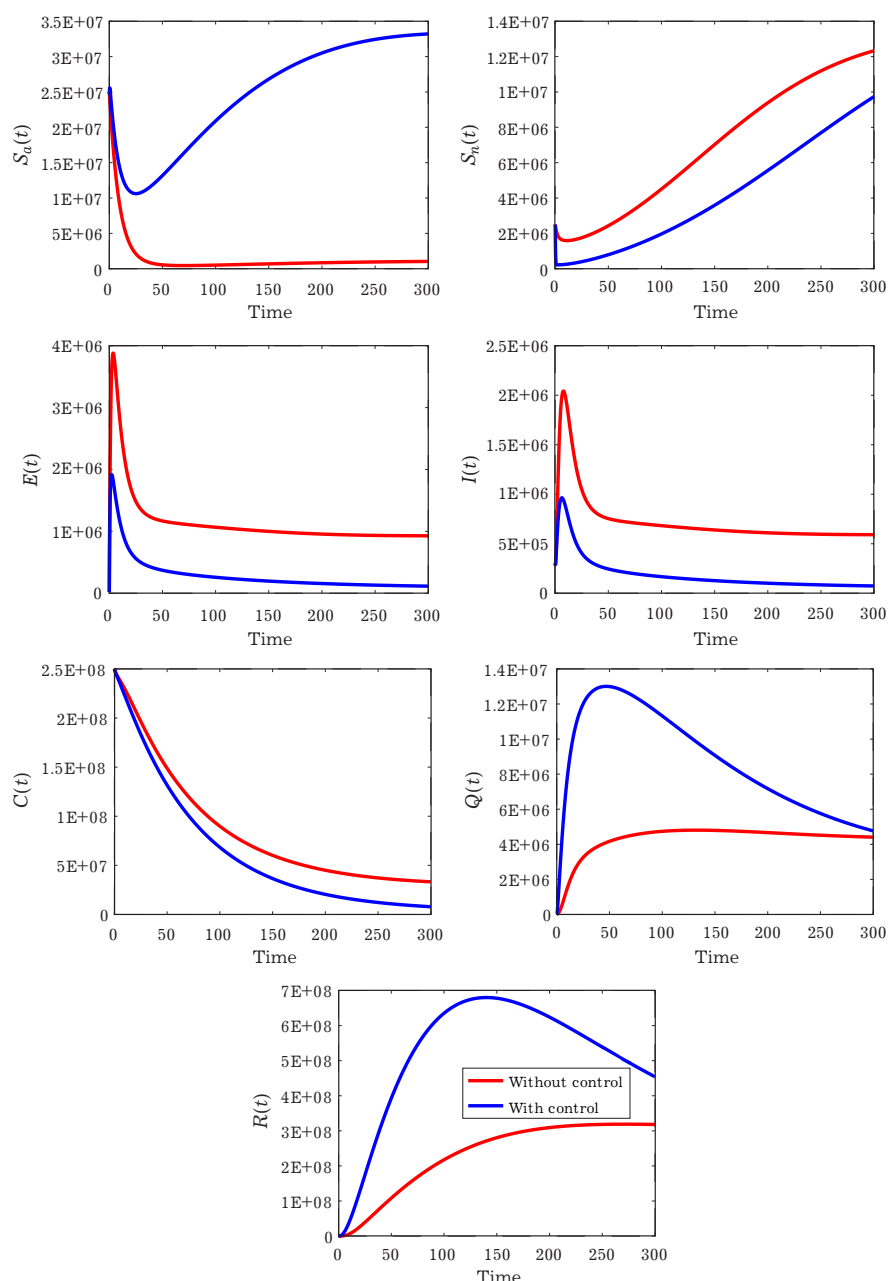
increase in the first week. There is a very significant increase in individuals of  $S_a$  through prevention and awareness which means the positive results of this strategy also (see Fig. 5).



**Fig. 5.** Simulations of the model showing the effects of the optimal in case  $u_1 \neq 0$ ,  $u_2 \neq 0$ ,  $u_3 = 0$ .

### 11.3. Strategy C

In this strategy we have combined three controls  $u_1$ ,  $u_2$  and  $u_3$ . There is a significant decrease in the number of individuals exposed  $E$  from the beginning of the second week, and the same behaviour for individuals in compartment  $I$ . For chronic infections  $C$  there is a sharp decrease from the first week. On the other hand, there is an increase in the number of people hospitalized  $Q$ . For people who are cured  $R$ , there is also an increase very important from the first week, which highlights the effectiveness of the combination of the three controls, relative to other strategies (see Fig. 6).



**Fig. 6.** Simulations of the model showing the effects of the optimal in case  $u_1 \neq 0$ ,  $u_2 \neq 0$ ,  $u_3 \neq 0$ .

## 12. Conclusion

In this article we have introduced a nonlinear system of viral hepatitis HCV that can be applied in other types of pathologies. Currently, there is no effective hepatitis C vaccine, so this was also one of the goals that prompted us to start this study. Stability analysis and optimal control were studied. Numerical simulation of the results, using MATLAB software, demonstrated the effectiveness of the strategies used and the convergence of state variables to equilibrium points under certain conditions. We plan to study other viruses and infectious diseases, generally, with or without delay in the continuous or discrete case by also introducing the spatial variable and considering several study approaches (age, sex, living environment, etc.).



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## Про дослідження аналізу стійкості та стратегії оптимального керування в математичній моделі гепатиту С з латентним станом

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У цій роботі аналізуємо модель вірусного гепатиту С. Ця епідемія, незважаючи на докладені зусилля, залишається серйозною проблемою для глобальної системи громадської охорони здоров'я в усіх спільнотах. Модель аналізується за допомогою теорії стійкості систем нелінійних диференціальних рівнянь. За результатами аналізу запропонована модель має дві точки рівноваги: точку рівноваги  $E_0$  без захворювання та точку рівноваги  $E^*$  ендемічного захворювання. Досліджено існування точки рівноваги моделі. Крім того, на основі непрямого методу Ляпунова досліджено локальна стійкість кожної точки рівноваги моделі. Крім того, побудувавши відповідну функцію Ляпунова та використовуючи принцип інваріантності Ла Салле, отримуємо деяку інформацію про глобальну стійкість точок рівноваги за певних умов. Базове число відтворення  $R_0$  обчислюється за допомогою методу Next Generation. Доведено додатність розв'язків, а також їх існування. Досліджено оптимальне керування системи, пропонуючи три типи втручання: програма інформування, раннє виявлення, ізоляція та лікування. Для характеристики знайдених оптимальних керувань використано принцип максимуму Понтрягіна. Чисельне моделювання було проведено з скінченною чисельною різницевою діаграмою та використанням MATLAB для підтвердження отриманих результатів.

**Ключові слова:** оптимальне керування; точка рівноваги; функція Лагранжа; цільова функція; принцип максимуму Понтрягіна; вірус гепатиту С.