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Optimal Control Strategies Applied to a Mathematical Model of Meningitis

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Abstract. In this paper, we deal with the problem of optimal control for the transmission dynamics of the meningococcal meningitis. The problem is a mathematical model described by a system of nonlinear differential equations. Based on this, two controls are formulated and the resulting system is solved as an optimal control problem. Aiming to minimize the number of illnesses or deaths in the population, we use a control representing a vaccination and another one representing a treatment strategy. We prove that these controls are capable of reducing the number of carriers and infectious individuals. Numerical simulations are carried out to show how to perform the two strategies.

2020 Mathematics Subject Classifications: 49J15, 49K15, 34A12, 34A45

Key Words and Phrases: Mathematical Biology, Meningitis, Optimal Control, Vaccination, Treatment

1. Introduction

Meningitis is an inflammation of a membrane, called the meninges, that covers the brain and spinal cord. Meningitis is a severe acute infectious disease caused by several microorganisms, including viruses, bacteria, parasites, and fungi. Fatality rates associated with this disease can be as low as 2% in infants and children, and as high as 20–30% in

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neonates and adults [1]. Damage to the meninges produces a variety of problems, ranging from a high fever with headaches to unconsciousness and death [2].

As mentioned in [3], meningococcal meningitis affects sub-Saharan Africa in a unique and distinctive way. In a region known as the meningitis belt, which spans the continent from Senegal to Ethiopia there is an increase in incidence of meningococcal meningitis every dry season, which dies out when the first rains arrive. At intervals ranging from 6 to 14 years, major epidemics occur, the largest of which killed more than 25 000 people in 10 countries in 1996 –1997. In some areas, this epidemic lasts for more than 1 year, dying out in the rainy season, only to return afterwards. In a single community, however, an epidemic may last only a few weeks.

It is well known that mathematical models play a significant role in understanding the dynamics of biological systems. In most cases, these models are described by autonomous systems of nonlinear ordinary/or partial differential equations. Mathematical models for meningitis are explored by many researchers. Below, we mention a few of them.

Martínez *et al.* [4] introduced a novel mathematical model to study the spreading of meningococcal meningitis. The model is a discrete mathematical model based on cellular automata where the population is divided in five classes: susceptible, asymptomatic infected, infected with symptoms, carriers, recovered and died. It catches the individual characteristics of people in order to give a prediction of both the individual behavior, and whole evolution of population. They found that both the global and the individual behavior of the disease can be predicted and the simulations that they did give results that agree with empirical predictions regarding the basic role played by the carriers.

Lawi *et al.* [5] presented and analyzed a deterministic model for the dynamics of malaria and meningitis co-infection. They established the basic reproduction number R_{mm}. The analysis showed that the disease free equilibrium of the model may not be globally asymptotically stable whenever $R_{mm} < 1$. The Centre Manifold theory was used to show that the model has a unique endemic equilibrium which is locally asymptotically stable when $R_{mm} < 1$ and unstable when $R_{mm} > 1$. It was deduced further that a reduction in malaria infection cases either through protection or prompt effective treatment, which is dependent on the socio-economic status of a community, would reduce the number of new co-infection cases.

In [6], Opoku *et al.* proposed an epidemiological model to accurately estimate meningitis occurrence and transmission in Ghana. They used optimal control theory to identify the ideal strategies for disease eradication and to study the the impact of vaccination and treatment plans. It was deduced from the numerical simulations that high coverage of susceptible individuals receiving vaccinations, combined with the development of an efficient vaccine, is the best strategy for managing the bacteria.

Tilahun [7] proposed a deterministic model of pneumonia-meningitis coinfection. Firstly, the qualitative behaviours of the model were studied, and then the basic model was extended to optimal control by incorporating four control interventions, such as prevention of pneumonia as well as meningitis and also treatment of pneumonia and meningitis diseases. Their findings showed that each of the listed strategies is effective in minimizing the expansion of pneumonia-only, meningitis-only, and coinfectious population in the specified

period of time.

A mathematical model that governs the epidemiology of cerebrospinal meningitis in Jirapa, Ghana was developed by Wiah and Adetunde [8]. They studied the dynamics of the model where existence of a solution, the stability of equilibria, and bifurcations of the system were investigated. They showed that the epidemic of meningococcal disease was already on the decline when nationwide vaccination campaign was launched. They found that the introduction of the vaccine reduced the incidence of infection to a predicted low of five cases per year, compared with 40 per year with no vaccination.

Yano *et al.* [9] formulated and analyzed a Meningococcal meningitis epidemic model that describes the spreading mechanisms of meningitis in a community with varying population. Using Pontryagin's approach to an optimal problem, their model was extended to include the four control intervention measures: effort to prevent a disease infection, efforts to treat sensitive and resistant strains and immunity control effort. Their optimal control study revealed that the use of these prevention techniques and treatment efforts led to a larger decrease of infections.

The above are a few works regarding mathematically modeling the meningitis disease. One can find more studies dealing with different aspects of meningitis, for instance [10–12]. It worth mentioning that, as can be seen in the above studies, optimal control strategies have not been applied widely in the models describing meningitis. To control the meningitis disease, some models include vaccination as strategies to tackle the evolution of the disease [4, 8, 13]. However, such models did not account for time dependent control strategies, rather fixed parameters values were used.

Optimal control strategies have been applied for various mathematical models of epidemic diseases, for example one can refer to [14–22]. Results obtained in these works as well as in other works are of high interest and can be used to propose and design programs for controlling epidemic diseases.

In this paper, we consider two optimal control strategies applied to a meningitis transmission model developed in [3]. Aiming to reduce the number of individuals developing meningitis, the first control is associated with vaccination to represent the fraction of individuals who are vaccinated and considered as immune individuals, while the second control is associated with the treatment strategy.

The rest of the paper is organized as follows. Section 2 is devoted to the problem statement where the mathematical model along with the set of controls provided. Analysis of the optimal control problem is presented in Section 3. We solve the resulting optimality system numerically in Section 4. A thorough discussion on the results obtained is presented in Section 5.

2. A model for optimal control of meningitis

In this section, we consider the deterministic model presented in [3] where the state system is described by the following nonlinear system of ordinary differential equations

$$\begin{aligned}
\frac{dS}{dt} &= \mu N + \gamma I + \varphi R - \beta(1-u_2)S(C+I) - \mu S - u_1 S,\\
\frac{dC}{dt} &= \beta(1-u_2)S(C+I) - (a+\alpha+\mu)C,\\
\frac{dI}{dt} &= aC - (\rho+\gamma+\mu)I,\\
\frac{dR}{dt} &= \rho I + \alpha C - (\varphi+\mu)R + u_1 S,
\end{aligned} \tag{1}$$

where $N = S+C+I+R$ with initial conditions $S(0) \geq 0, C(0) \geq 0, I(0) \geq 0$ and $R(0) \geq 0$. The host population is divided into susceptible S, an asymptomatic carrier C, ill I, and immune R. The parameters used in the model are defined in [3] as follows. μ : the natural death rate; ρ : the recovery rate; γ : the rate of death from disease; β : the transmission rate; α : the rate of loss of carriage; a : the rate at which carriers become ill; φ : the rate of loss of immunity.

To minimize the carrier individuals and, therefore, to minimize the total number of ill individuals, controls on vaccination and treatment are used. These controls are represented as functions of time and assigned reasonable upper and lower bounds as indicated in the subsequent discussion in this paper. The first control function $u_1(t)$ is inserted into the model to represent the fraction of individuals who are vaccinated and considered as immune individuals, and the second control function $u_2(t)$ is inserted to represent the effectiveness of treatment. Therefore, $(1-u_2(t))$ represents the fraction of individuals developing the disease and hence increasing the value of $u_2(t)$ causes reduction in the number of ill individuals. The functions $u_1(t)$ and $u_2(t)$ are bounded and Lebesgue integrable functions. We define the objective functional as

$$J(u_1,u_2) = \min_{u_1,u_2} \int_0^{t_f} \left(C + \frac{A}{2}u_1^2 + \frac{B}{2}u_2^2 \right) dt, \tag{2}$$

where t_f is the specified and finite final time and the constants A and B are the balancing cost factors. Our goal is to find two optimal controls, u_1^* and u_2^*, such that

$$J(u_1^*,u_2^*) = \min_{\Psi} J(u_1,u_2), \tag{3}$$

where

$$\Psi = \{(u_1,u_2) \in L^1(0,t_f) | a_i \leq u_i \leq b_i, i = 1,2\}, \tag{4}$$

and a_i, b_i; $i = 1,2$, are positive constants representing the bounds on the two controls.

3. Analysis of the optimal control problem

In this section, we use the Pontryagin's Maximum Principle [23] to derive the necessary conditions that an optimal problem must satisfy. This principle is used to convert (1), (2), and (3) into a problem of minimizing a pointwise Hamiltonian, H, with respect to u_1 and u_2:

$$H = C + \frac{A}{2}u_1^2 + \frac{B}{2}u_2^2 + \sum_{i=1}^{4} \lambda_i g_i, \tag{5}$$

where g_i and λ_i, $i = 1, ..., 4$, are the right hand side of the differential equation and the associated adjoint for the i^{th} state variable of system (1). By applying Pontryagin's Maximum Principle [23] and existence result for the optimal control pair from [24], we obtain the following theorem.

Theorem 1. *There exists optimal control pair (u_1^*, u_2^*) and solution (S^*, C^*, I^*, R^*) for the state system (1) that minimizes $J(u_1, u_2)$, given by (2), over Ψ. Furthermore, there exists a vector of adjoint functions, $(\lambda_1(t), ..., \lambda_4(t))$, such that*

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= (\beta(1-u_2)(C^*+I^*)+u_1)\lambda_1 - \beta(1-u_2)(C^*+I^*)\lambda_2 - u_1\lambda_4,\\
\frac{d\lambda_2}{dt} &= -1 - (\mu - \beta(1-u_2)S^*)\lambda_1 - (\beta(1-u_2)S^* - (a+\alpha+\mu))\lambda_2 - a\lambda_3 - \alpha\lambda_4,\\
\frac{d\lambda_3}{dt} &= -(\mu+\gamma-\beta(1-u_2)S^*)\lambda_1 - \beta(1-u_2)S^*\lambda_2 + (\rho+\gamma+\mu)\lambda_3 - \rho\lambda_4,\\
\frac{d\lambda_4}{dt} &= (\phi+\mu)(\lambda_4-\lambda_1),
\end{aligned} \tag{6}$$

with transversality conditions

$$\lambda_i(t_f) = 0, i = 1, ..., 4, \tag{7}$$

and the following characterization

$$\begin{aligned}
u_1^* &= \min\left(\max\left(a_1, \frac{S^*(\lambda_1-\lambda_4)}{A}\right), b_1\right),\\
u_2^* &= \min\left(\max\left(a_2, \frac{\beta S^*(C^*+I^*)(\lambda_2-\lambda_1)}{B}\right), b_2\right).
\end{aligned} \tag{8}$$

Proof. By using a results from [24], we can obtain the existence of an optimal control pair due to the convexity of integrand of J with respect to (u_1, u_2), a *priori* boundedness of the state solutions, and the *Lipschitz* property of the state system with respect to the

state variables. By applying the Pontryagin's Maximum Principle [23], we obtain

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{\partial H}{\partial S}, \ \ \lambda_1(t_f) = 0, \\
\frac{d\lambda_2}{dt} &= -\frac{\partial H}{\partial C}, \ \ \lambda_2(t_f) = 0, \\
\frac{d\lambda_3}{dt} &= -\frac{\partial H}{\partial I}, \ \ \lambda_3(t_f) = 0, \\
\frac{d\lambda_4}{dt} &= -\frac{\partial H}{\partial R}, \ \ \lambda_4(t_f) = 0,
\end{aligned} \tag{9}$$

evaluated at the optimal control pair (u_1^*, u_2^*) and the corresponding states S, C, I, R, which results in the stated adjoint system (6). The characterization (8) can be derived by considering the optimality conditions

$$\frac{\partial H}{\partial u_1} = 0 \ \text{ and } \quad \frac{\partial H}{\partial u_2} = 0, \tag{10}$$

and solving for u_1^* and u_2^*, subject to the constraints (4). The characterization for u_1^* can be obtained from the first equation of (10)

$$\frac{\partial H}{\partial u_1} = Au_1 - S^*\lambda_1 + S^*\lambda_4, \tag{11}$$

by considering three cases:

$$\begin{aligned}
&\frac{\partial H}{\partial u_1} < 0 \implies u_1(t) = a_1 \implies a_1 < \frac{S^*(\lambda_1 - \lambda_4)}{A}, \\
&\frac{\partial H}{\partial u_1} = 0 \implies u_1(t) = \frac{S^*(\lambda_1 - \lambda_4)}{A} \implies a_1 \leq \frac{S^*(\lambda_1 - \lambda_4)}{A} \leq b_1, \\
&\frac{\partial H}{\partial u_1} > 0 \implies u_1(t) = b_1 \implies b_1 > \frac{S^*(\lambda_1 - \lambda_4)}{A},
\end{aligned}$$

and hence,

$$u_1^* = \begin{cases} a_1 \quad ; & \frac{S^*(\lambda_1-\lambda_4)}{A} < a_1, \\ \frac{S^*(\lambda_1-\lambda_4)}{A}; & a_1 \leq \frac{S^*(\lambda_1-\lambda_4)}{A} \leq b_1, \\ b_1 \quad ; & \frac{S^*(\lambda_1-\lambda_4)}{A} > b_1. \end{cases} \tag{12}$$

Therefore, the characterization of u_1^* in compact form can be written as

$$u_1^* = \min\left(b_1, \max\left(a_1, \frac{S^*(\lambda_1 - \lambda_4)}{A}\right)\right). \tag{13}$$

In a similar manner, we can derive the characterization of u_2^* which in compact form as

$$u_2^* = \min\left(b_2, \max\left(a_2, \frac{\beta S^*(C^* + I^*)(\lambda_2 - \lambda_1)}{B}\right)\right). \tag{14}$$

With the existence of the optimal control pair established, we point out that the uniqueness of the optimal control pair follows from the uniqueness of the optimality system the pair must satisfy, which consists of the state system (1) with the its initial conditions, the adjoint system (6) with the transversality conditions (7), and the optimality condition (8). As mentioned in [17], one can obtain the uniqueness of the optimal control for small t_f due to a-*priori* boundedness of the state and adjoint functions and the resulting Lipschitz structure of the ODEs. The finiteness of t_f guarantees the uniqueness of the optimality system. This finiteness restriction on the length on the time interval is due to the opposite time orientations of (1), (6), and (7) where the state problem has initial values and the adjoint problem has final values.

Next, we discuss the numerical solutions of the optimality system and the corresponding results of varying the optimal controls u_1 and u_2 along with the interpretations for different scenarios.

4. Numerical results

In this section, the optimality system consisting of the equations of (1) and (6), is solved iteratively using a fourth order Runge-Kutta method to obtain the optimal strategies regarding the vaccination and treatment. The state system is solved forward in time while the adjoint system is solved backward in time. The two controls are updated at the end of each iteration using (8). The iterations continue until a required convergence is achieved. The readers may note that the main goal of this paper is to design the optimal control strategy and not to find a robust numerical solver. The results obtained by using RK-4 are already convincing and therefore we did not attempt to use variants of RK, e.g, ETDRK or any other methods that we are already familiar with.

By using different combinations of the balancing factors A and B, several vaccination and treatment schedules can be derived. Keeping the bounds for the controls fixed, time period is 90 days, $\beta = 0.24658$, $\alpha = 0.071233$, $a = 0.00054795$, $\phi = 0.00068493$ and rest of the parameters unchanged, we illustrate different scenarios by varying the values of the balancing factors. In the simulations below, we use the following initial conditions, as given in [3], $S(t_0) = 9000, C(t_0) = 996, I(t_0) = 2$, and $R(t_0) = 2$. When $A = 10$ and $B = 10$, the two controls are plotted as functions of time in Figure 1. In Figure 2, we can see the effect of this scenario, the number of the susceptible individuals $S(t)$ is dropped very quickly in the first 10 days when using the two controls as the treated individuals return back to the susceptible class and these individuals will be vaccinated and then removed to the recovered class $R(t)$. This explains the increment in the number of the recovered individuals as indicated in the last simulation in the same figure. Similarly, one can see the sharp decrease in the carrier population $C(t)$. Without using any control strategies, we find that the number of carriers $C(t)$ increases for the first 17 days until it reaches its maximum at 3811 individuals and then it declines until ≈ 84 at the end of the interval. However, when we use the control strategies described above, we can see that starting $C(t)$ with 996 individuals, it drops immediately and continue decreasing without fluctuations until it reaches ≈ 2 individuals indicating the effectiveness of the strategy

used. In the third plot of Figure 2 we notice that starting with $I(t) = 2$ individuals, the number of population in this class increases until it reaches its maximum ≈ 12 by the 23^{rd} day without incorporating the controls. When end of interval reached, the value of $I(t)$ is $\approx$ zero. However, when controls are used, it is shown that the number of infectious individuals increases in the first 7 days, but remains below the curve for the infectious without controls, and then it declines until it reaches $I(t) \approx 0$ by the end of the time interval.

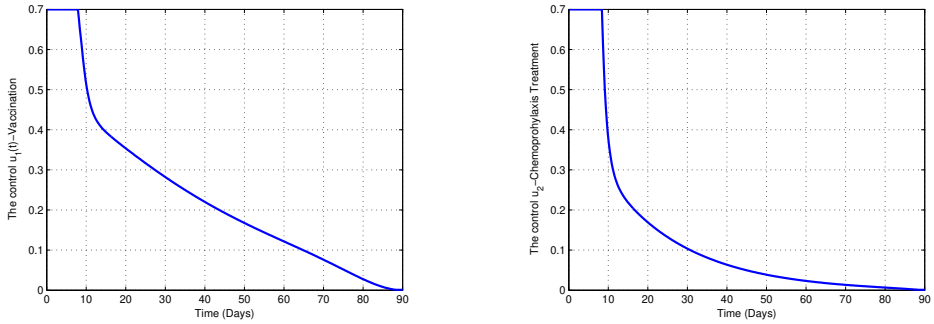

Figure 1: Values of the optimal controls when $A = 10$ and $B = 10$.

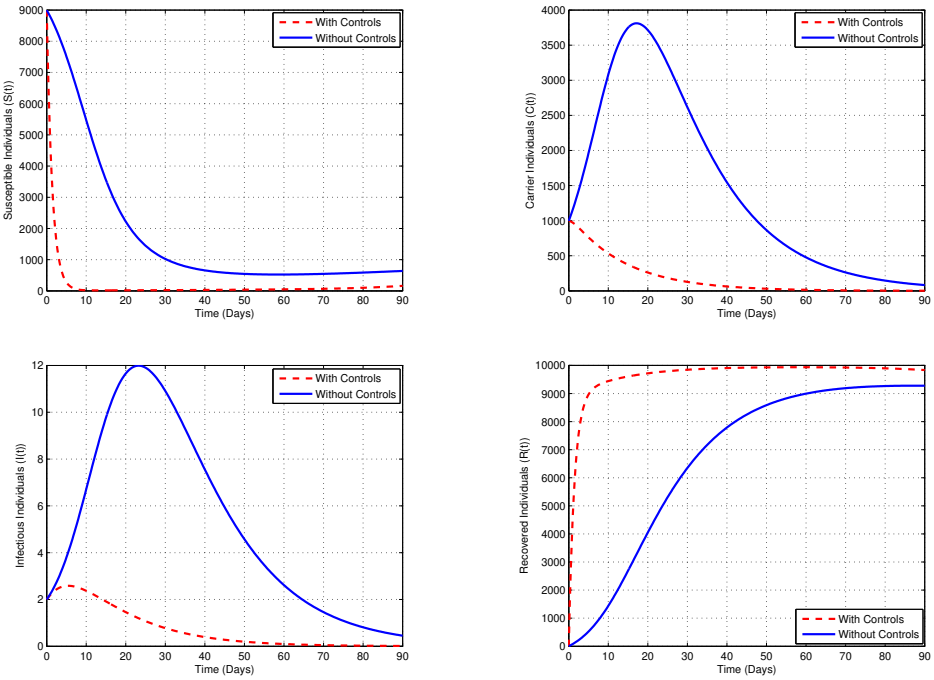

Figure 2: Effect of optimal vaccination and treatment strategies when $A = 10$ and $B = 10$.

Figure 3 shows the different profiles of the two controls u_1 and u_2 for different values of the balancing factors A and B. As expected, increasing the values of these constants reduces the values of the controls and hence their effect is also reduced, whereas decreasing their values causes the controls last longer at their upper bounds before they decrease again but still at larger scales than before.

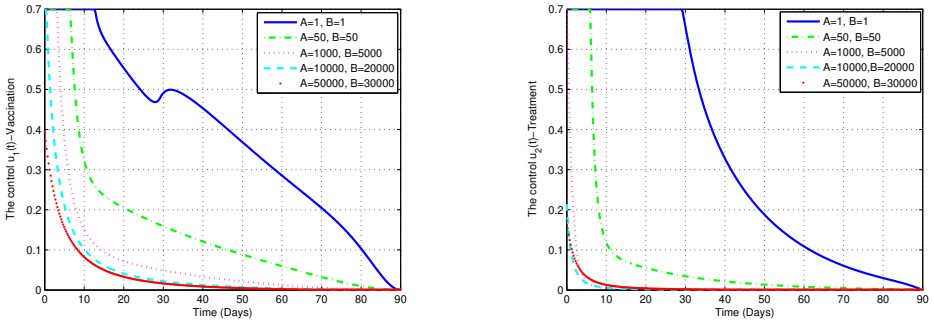

Figure 3: Plots for controls u_1 and u_2 for various values of the balancing factors A and B.

The effects of these controls on other state variables are shown in Figure 4, where we use the same values of A and B used in Figure 3. As can be seen, the simulations verify the fact that increasing the values of the two controls reduces $C(t)$ and $I(t)$ and causes $S(t)$ to decrease and $R(t)$ to increase because in this case more susceptibles are vaccinated and more infectious are successfully treated.

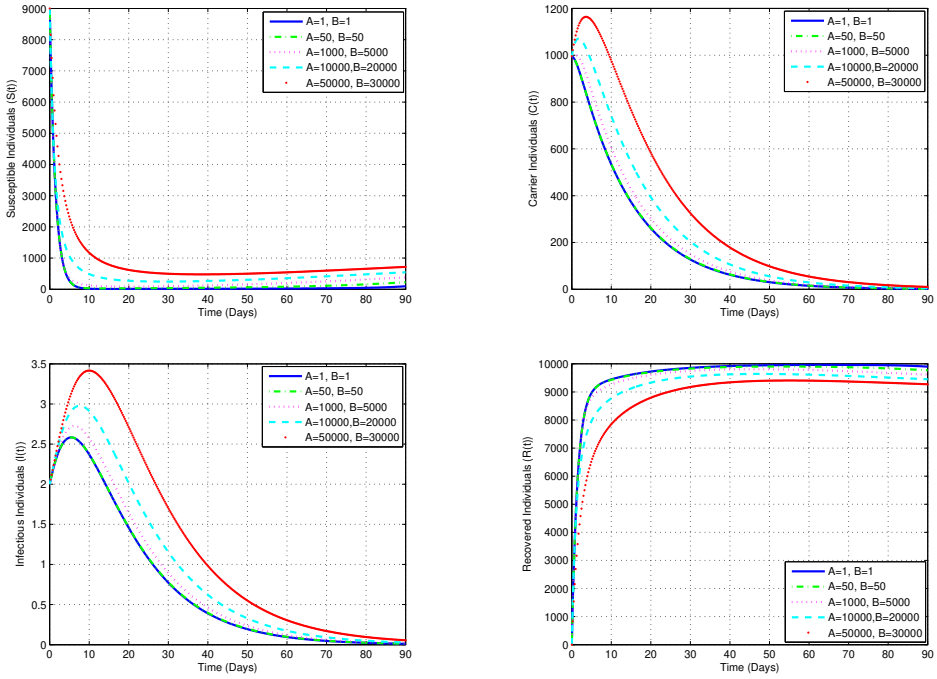

Figure 4: Effect of optimal vaccination and treatment strategies for various values of the balancing factors A and B.

Another scenario is considered to compare the effect of applying the vaccination and treatment together, or applying the vaccination only, or applying the treatment only, on the solutions of the state system (1) when the values for the balancing factors A and B are chosen to be 5000. As can be seen in Figure 5, when $\beta = 0.13699$ using both controls u_1 and u_2 together having the same effect as using the first control u_1 only. We further notice that inserting both controls u_1 and u_2 together is better than using the control u_2 only. This suggests that the effect of vaccination and treatment applied together on the model is the same as applying the vaccination control only. Finally, the use these controls together is better as compared to the use of treatment only control. Therefore, under the conditions given in these simulations, it is better to consider a strategy that depends on the vaccination only.

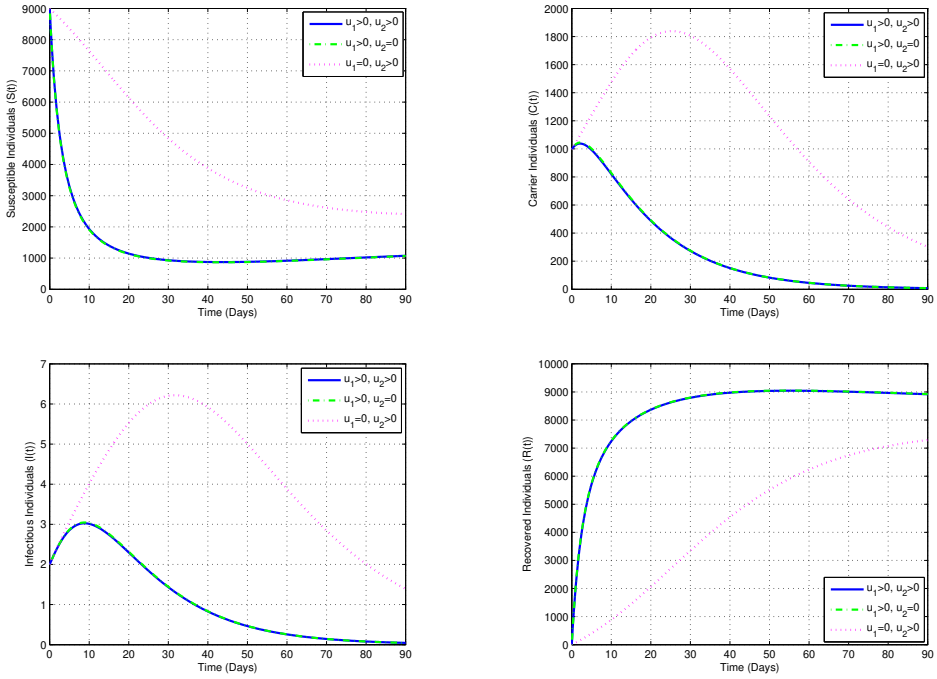

Figure 5: Effect of optimal vaccination and treatment strategies used together as compared to using only vaccination or treatment strategies. Other parameters are taken as $A = 5000$, $B = 5000$ and $\beta = 0.13699$.

To further corroborate this assertion, we consider three other values of β and repeat the simulations, results of which are indicated in Figure 6 (for $\beta = 0.24658$), Figure 7 (for $\beta = 0.35616$) and Figure 8 (for $\beta = 0.54795$). It is clear that using only the second control u_2 does not give better results as compared to using u_1 only or using both of u_1 and u_2.

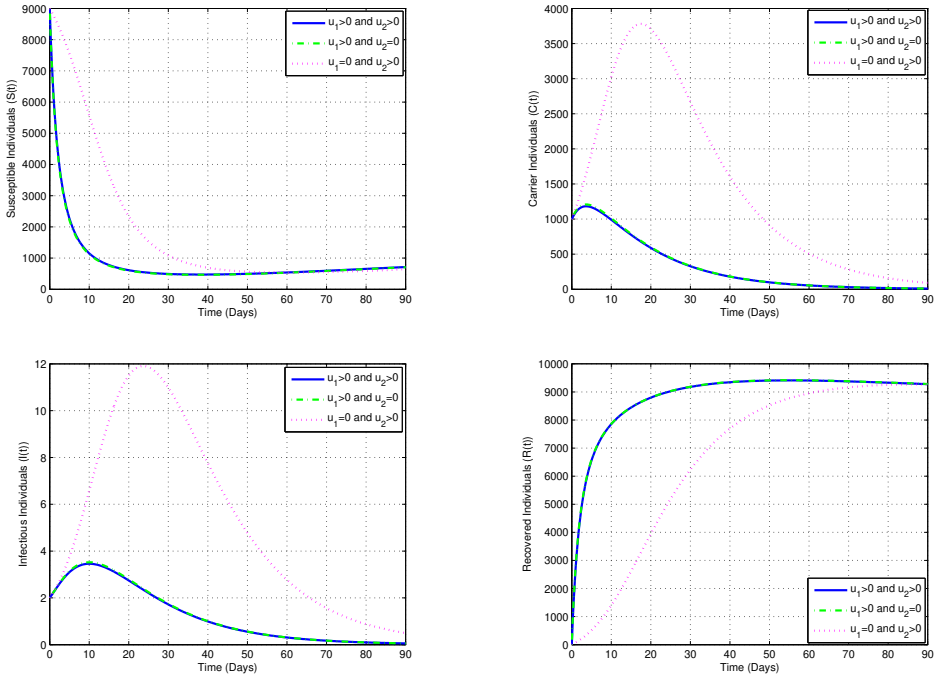

Figure 6: Effect of optimal vaccination and treatment strategies used together as compared to using only vaccination or treatment strategies. Other parameters are taken as $A = 5000$, $B = 5000$ and $\beta = 0.24658$.

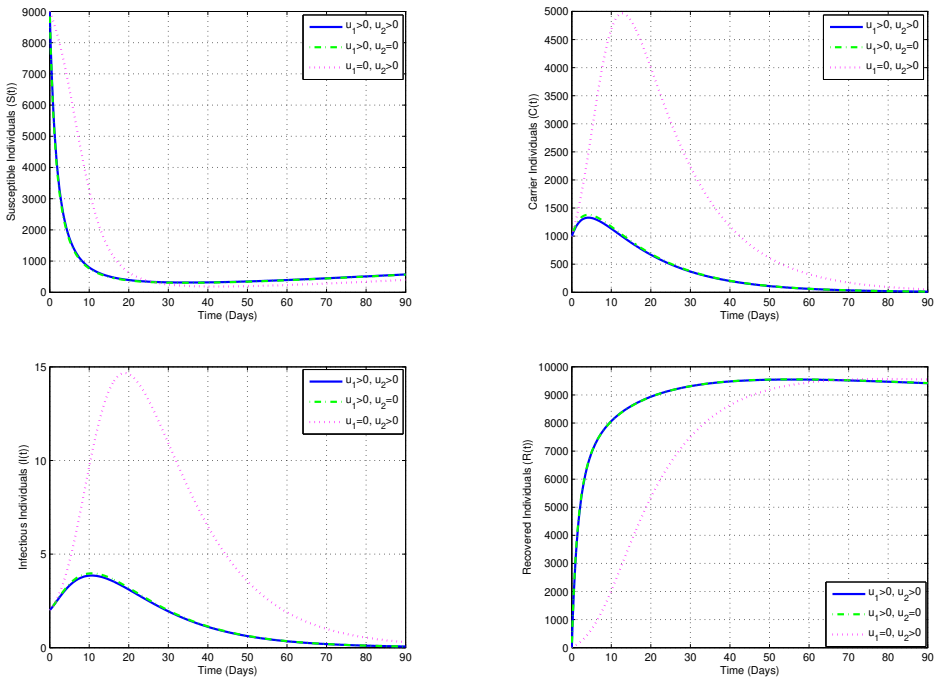

Figure 7: Effect of optimal vaccination and treatment strategies used together as compared to using only vaccination or treatment strategies. Other parameters are taken as $A = 5000$, $B = 5000$ and $\beta = 0.35616$.

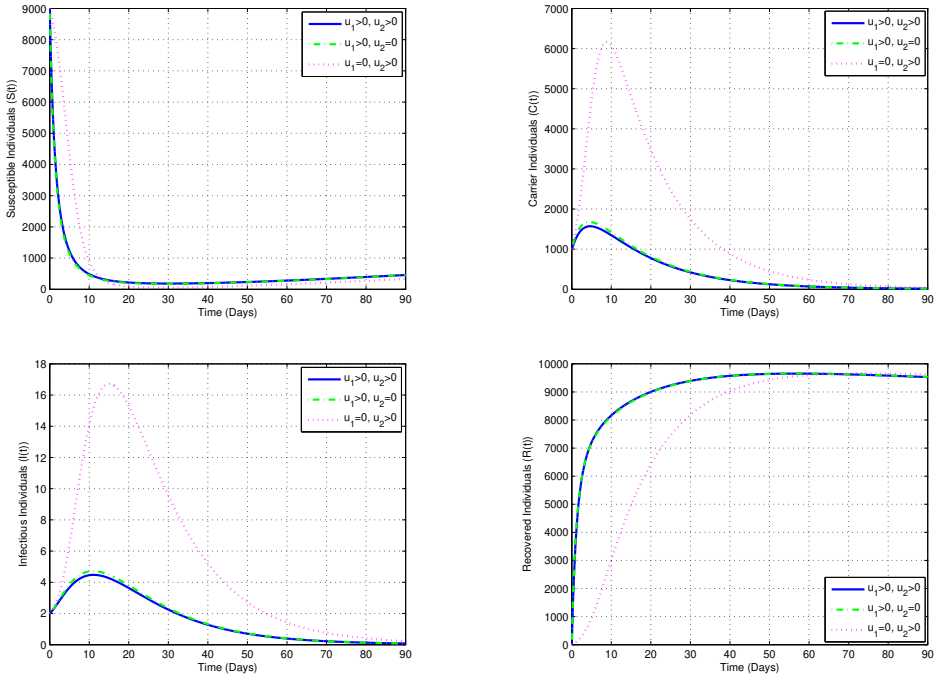

Figure 8: Effect of optimal vaccination and treatment strategies used together as compared to using only vaccination or treatment strategies. Other parameters are taken as $A = 5000$, $B = 5000$ and $\beta = 0.54795$.

5. Conclusion

In this paper, we considered two optimal strategies associated with the vaccination and treatment on a mathematical model of meningitis in order to reduce the numbers of carrier and infectious populations. Several scenarios are dealt with. In the first one, we incorporated the two strategies: vaccination and treatment. We have shown that both controls have great impact on reducing the carriers and infectious individuals and hence on increasing the recovered individuals. In the second scenario it is shown that we can use different combinations of the balancing factors to achieve the results required, and all results obtained numerically were satisfactory. Scenario three involved a comparison of application of a single control vs application of both controls. We found that it is better to apply both vaccination and treatment strategies together than applying only the treatment. On the other hand, for the set of parameters and initial values given for the basic model, we have found that using vaccination and treatment have the same effect as using the vaccination only. From the cost effectiveness aspect, this suggests that one can adopt a single strategy, the vaccination, to effectively reduce the populations of carriers and infectious individuals.

Currently, we are busy investigating the applicability of numerical methods such as

Nonstandard Finite Difference Methods to solve the state and adjoint systems as these methods are convenient when dealing with models describing populations because they preserves the positivity of the solution. This is an essential requirement when modeling epidemic diseases.

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Conflict of interest.

The authors declare no conflict of interest.

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