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Research Article

Modelling and Optimal Control of Typhoid Fever Disease with Cost-Effective Strategies

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We propose and analyze a compartmental nonlinear deterministic mathematical model for the typhoid fever outbreak and optimal control strategies in a community with varying population. The model is studied qualitatively using stability theory of differential equations and the basic reproductive number that represents the epidemic indicator is obtained from the largest eigenvalue of the next-generation matrix. Both local and global asymptotic stability conditions for disease-free and endemic equilibria are determined. The model exhibits a forward transcritical bifurcation and the sensitivity analysis is performed. The optimal control problem is designed by applying Pontryagin maximum principle with three control strategies, namely, the prevention strategy through sanitation, proper hygiene, and vaccination; the treatment strategy through application of appropriate medicine; and the screening of the carriers. The cost functional accounts for the cost involved in prevention, screening, and treatment together with the total number of the infected persons averted. Numerical results for the typhoid outbreak dynamics and its optimal control revealed that a combination of prevention and treatment is the best cost-effective strategy to eradicate the disease.

1. Introduction

According to [1], "infectious diseases are those diseases caused by viruses, bacteria, epiphytes, and parasites such as protozoans or worms that have a potential to spread into the population easily." Typhoid fever is one of the common infectious diseases in human beings that is caused by different species of Salmonella. The most common species of Salmonella that cause typhoid fever are *Salmonella paratyphi A, B, and C* and *Salmonella paratyphi D* [WHO [2]]. "Most of the time typhoid fever is caused by lack of sanitation in which the disease causing bacteria is transmitted by ingestion of contaminated food or water" WHO, 2003. The bacteria are released from the infectious individuals or carriers and then contaminate food or drinking water as a consequence of unsatisfactory hygiene practices. Due to this, typhoid fever is a common disease in developing countries. The data taken from Ethiopia for that past seven years (2009–2015), in Figure 1, indicate that in each year the disease is increasing in alarming rate. Mathematical models have great benefits for describing the dynamics of infectious disease. Moreover, it plays a significant role in predicting suitable control strategies and analyzing and ranking their cost-effectiveness (for example, see Okosun and Makinde [3–7]). Very essential research results on the transmission dynamics of typhoid have come out in the last decade; for instance, see Adetunde [8], Mushayabasa and Bhunu [9], Moffat et al. (2014), Steady et al. (2014), Adeboye and Haruna [10], Omame et al. [11], Khan et al. [12], and Akinyi et al. [13]. All of the above studies reveal an important result for typhoid fever dynamics by considering different countries situation. But we have identified that till now there is no study that has been done to investigate the typhoid fever dynamics with the application of optimal control methods and cost-effectiveness analysis of the applied control strategies.

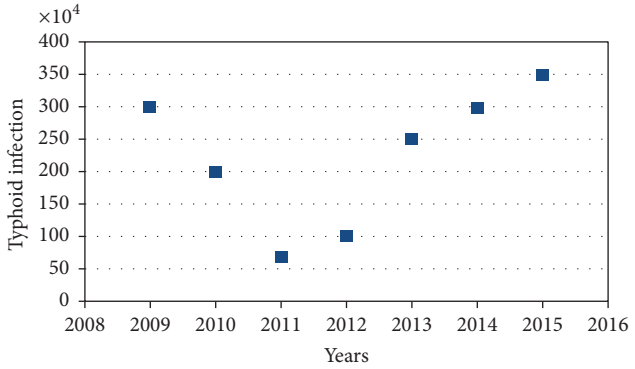


Figure 1: Reported cases of typhoid in Ethiopia for the past seven years.

In view of the above, we developed a deterministic mathematical model to investigate the dynamics of typhoid fever with optimal control strategies and also we investigated the cost-effectiveness of the implemented control strategies.

2. Model Description and Formulation

The model considers human population as well as bacteria population (B_c). The human population at time t is divided into four subclasses. *Susceptible* (S): this class includes those individuals who are at risk for developing an infection from typhoid fever disease. *Infected* (I): this class includes all individuals who are showing the symptom of the disease. *Carrier* (C): this is a person who is colonized by the bacterium *Salmonella typhi* without showing any obvious signs of disease and who is a potential source of infection to others by contaminating foods and water carelessly during preparation and handling. *Recovered* (R): this class includes all individuals that have recovered from the disease and got temporary immunity. The susceptible class is increased by birth or emigration at a rate of Λ and also from recovered class by losing temporary immunity with δ rate. Susceptible individuals will get typhoid causing bacteria when they take foods or waters which is contaminated by Salmonella bacteria. The force of infection of the model is $\lambda = B_c v/(K + B_c)$, where v is ingestion rate, K is the concentration of Salmonella bacteria in foods or waters, and $B_c/(K + B_c)$ is the probability of individuals in consuming foods or drinks contaminated with typhoid causing bacteria. After the susceptible individuals got the typhoid causing bacteria, they have probability of joining carrier with ρ rate or being a member of infective with $1 - \rho$ rate. The infected subclass is increased from carrier subclass by θ screening rate. Those individuals in the infected subclass can get treatment and join recovered subclass with a rate of β. The recovered subclass also increases with individuals who came from carrier class by getting natural immunity with a rate of ϕ. In all human subclasses, μ is the natural death rate of individuals, but in the infective class α is the disease causing death rate. The model assumed the bacteria population in contaminated foods and waters, where carriers and infectives can contribute to increasing the number of bacteria population in foods and waters without proper sanitation with a discharge rate of σ_1 and σ_2, respectively. We consider μ_b to be the death rate of Salmonella bacteria and all the described parameters are nonnegative.

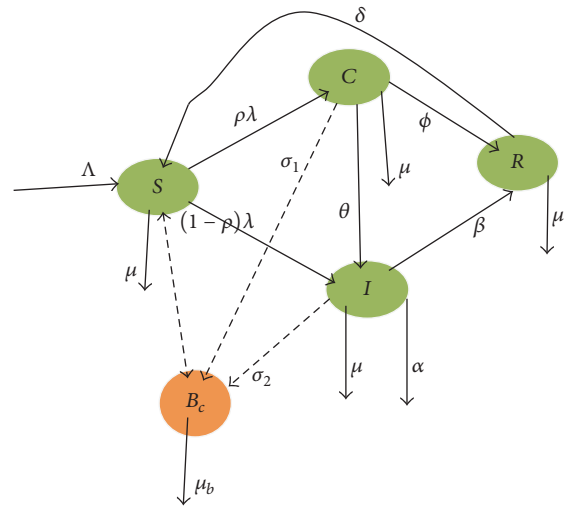


Figure 2: Flow diagram of the model.

The above model description is represented Figure 2.

Figure 2 can be written in five systems of differential equations.

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda + \delta R - (\mu + \lambda) S, \\
\frac{dC}{dt} &= \rho\lambda S - (\sigma_1 + \theta + \mu + \phi) C, \\
\frac{dI}{dt} &= (1 - \rho)\lambda S + \theta C - (\sigma_2 + \beta + \mu + \alpha) I, \\
\frac{dR}{dt} &= \beta I + \phi C - (\mu + \delta) R, \\
\frac{dB_c}{dt} &= \sigma_1 C + \sigma_2 I - \mu_b B_c,
\end{aligned} \tag{1}$$

where $\lambda = B_c v/(K + B_c)$, with initial condition $S(0) = S_0$, $C(0) = C_0$, $I(0) = I_0$, $R(0) = R_0$, and $B_c(0) = B_{c0}$.

3. The Model Analysis

3.1. Invariant Region. We obtained the invariant region, in which the model solution is bounded. To do this, first we considered the total human population (N), where $N = S + C + I + R$.

Then, differentiating N both sides with respect to t leads to

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dC}{dt} + \frac{dI}{dt} + \frac{dR}{dt}. \tag{2}$$

By combining (1) and (2), we can get

$$\frac{dN}{dt} = \Lambda - \mu N - \alpha I. \tag{3}$$

In the absence of mortality due to typhoid fever disease ($\alpha = 0$), (3) becomes

$$\frac{dN}{dt} \leq \Lambda - \mu N. \tag{4}$$

Integrating both sides of (4),

$$\begin{gathered} \int \frac{dN}{\Lambda - \mu N} \leq \int dt \Longleftrightarrow \\ \frac{-1}{\mu} \ln\left(\Lambda - \mu N\right) \leq t + c \end{gathered} \tag{5}$$

which simplifies into

$$\Lambda - \mu N \geq Ae^{-\mu t}, \tag{6}$$

where A is constant. By applying the initial condition $N(0) = N_0$ in (6), we get $A = \Lambda - \mu N_0$ which upon substitution in (6) yields

$$\Lambda - \mu N \geq \left(\Lambda - \mu N_0\right) e^{-\mu t}. \tag{7}$$

Then by rearranging (7), we can get

$$N \leq \frac{\Lambda}{\mu} - \left[\frac{\Lambda - \mu N_0}{\mu}\right] e^{-\mu t}. \tag{8}$$

As $t \to \infty$ in (8), the population size $N \to \Lambda/\mu$ which implies that $0 \leq N \leq \Lambda/\mu$. Thus, the feasible solution set of the system equation of the model enters and remains in the region:

$$\Omega = \left\{(S, I, C, R) \in \mathfrak{R}_+^4 : N \leq \frac{\Lambda}{\mu}\right\}. \tag{9}$$

Therefore, the basic model is well posed epidemiologically and mathematically. Hence, it is sufficient to study the dynamics of the basic model in Ω.

3.2. Positivity of the Solutions. We assumed that the initial condition of the model is nonnegative, and now we also showed that the solution of the model is also positive.

Theorem 1. *Let* $\Omega = \{(S, C, I, R, B_c) \in \mathfrak{R}_+^5 : S_0 > 0,\ I_0 > 0,\ C_0 > 0,\ R_0 > 0,\ B_{c_0} > 0\}$*; then the solutions of* $\{S, C, I, R, B_c\}$ *are positive for* $t \geq 0$.

Proof. From the system of differential equation (1), let us take the first equation:

$$\begin{gathered} \frac{dS}{dt} = \Lambda + \delta R - \left(\mu + \lambda\right) S \Longrightarrow \\ \frac{dS(t)}{dt} \geq -\left(\mu + \lambda\right) S(t) \Longrightarrow \\ \frac{dS(t)}{S(t)} \geq -\left(\mu + \lambda\right) d(t) \Longrightarrow \\ \int \frac{dS(t)}{S(t)} \geq -\int \left(\mu + \lambda\right) d(t). \end{gathered} \tag{10}$$

Then by solving using separation of variable and applying condition, we obtained

$$S(t) \geq S_0 e^{-(\mu+\lambda)t} \geq 0. \tag{11}$$

And also by taking the second equation of (1), that is,

$$\frac{dC}{dt} = \rho\lambda S - \left(\sigma_1 + \theta + \mu + \phi\right) C, \tag{12}$$

it is true that

$$\begin{gathered} \frac{dC}{dt} \geq -\left(\sigma_1 + \theta + \mu + \phi\right) C \Longrightarrow \\ \frac{dC}{C} \geq -\left(\sigma_1 + \theta + \mu + \phi\right) d(t) \Longrightarrow \\ \int \frac{dC}{C} \geq -\int \left(\sigma_1 + \theta + \mu + \phi\right) dt. \end{gathered} \tag{13}$$

Then by solving using separation of variable and applying initial condition gives;

$$\therefore C(t) \geq C_0 e^{-(\mu+\phi)t} \geq 0. \tag{14}$$

Similarly we took the third equation of (1) which is;

$$\frac{dI(t)}{dt} = \left(1 - \rho\right)\lambda S + \theta C - \left(\sigma_2 + \beta + \mu + \alpha\right) I \tag{15}$$

it is true that

$$\begin{gathered} \frac{dI}{dt} \geq -\left(\sigma_2 + \beta + \mu + \alpha\right) I \Longrightarrow \\ \frac{dI}{I} \geq -\left(\sigma_2 + \beta + \mu + \alpha\right) d(t) \Longrightarrow \\ \int \frac{dI}{I} \geq -\int \left(\sigma_2 + \beta + \mu + \alpha\right) d(t). \end{gathered} \tag{16}$$

After solving using technique of separation of variable and then applying initial condition, the following is obtained:

$$\therefore I(t) \geq I_0 e^{-(\sigma_2+\beta+\mu+\alpha)t} \geq 0. \tag{17}$$

We took the fourth equation of (1) which is

$$\begin{gathered} \frac{dR}{dt} = \beta I + \phi C - \left(\mu + \delta\right) R \Longrightarrow \\ \frac{dR}{dt} \geq -\left(\mu + \delta\right) R \Longrightarrow \end{gathered}$$

$$\frac{dR}{R} \geq -(\mu+\delta)\,d(t) \Longrightarrow$$
$$\int \frac{dR}{R(t)} \geq -\int (\mu+\delta)\,d(t)$$
$$\therefore R(t) \geq R_0 e^{-(\mu+\delta)t} \geq 0. \tag{18}$$

Finally we took the fifth equation of (1),

$$\frac{dB_c}{dt} = \sigma_1 C + \sigma_2 I - \mu_b B_c \Longrightarrow$$
$$\frac{dB_c}{dt} \geq -\mu_b B_c \Longrightarrow$$
$$\frac{dB_c}{B_c(t)} \geq -(\mu_b)\,d(t) \Longrightarrow \tag{19}$$
$$\int \frac{dB_c}{B_c} \geq -\int (\mu_b)\,d(t)$$
$$\therefore B_c \geq B_{c_0} e^{-(\mu_b)t} \geq 0.$$

This completes the proof of the theorem. □

Therefore, the solution of the model is positive.

3.3. The Disease-Free Equilibrium (DFE). To find the disease-free equilibrium (DFE), we equated the right hand side of model (1) to zero, evaluating it at $C = I = 0$ and solving for the noninfected and noncarrier state variables. Therefore, the disease-free equilibrium $E_0 = (\Lambda/\mu, 0, 0, 0, 0)$.

3.4. The Basic Reproductive Number ($\mathfrak{R}_0$). In this section, we obtained the threshold parameter that governs the spread of a disease which is called the basic reproduction number which is determined. To obtain the basic reproduction number, we used the next-generation matrix method so that it is the spectral radius of the next-generation matrix [15].

The model equations are rewritten starting with newly infective classes:

$$\frac{dC}{dt} = \rho\lambda S - (\sigma_1 + \theta + \mu + \phi)\,C,$$
$$\frac{dI}{dt} = (1-\rho)\,\lambda S + \theta C - (\sigma_2 + \beta + \mu + \alpha)\,I, \tag{20}$$
$$\frac{dB_c}{dt} = \sigma_1 C + \sigma_2 I - \mu_b B_c.$$

Then by the principle of next-generation matrix, we obtained

$$f = \begin{bmatrix} \rho\left(\dfrac{B_c \nu}{K + B_c}\right) S \\ (1-\rho)\left(\dfrac{B_c \nu}{K + B_c}\right) S \end{bmatrix},$$
$$\nu = \begin{bmatrix} (\sigma_1 + \theta + \mu + \phi)\,C \\ (\sigma_2 + \beta + \mu + \alpha)\,I - \theta C \\ -(\sigma_1 C + \sigma_2 I - \mu_b B_c) \end{bmatrix}. \tag{21}$$

The Jacobian matrices of f and ν evaluated at DFE are given by F and V, respectively, such that

$$F = \begin{bmatrix} 0 & 0 & \rho\dfrac{\Lambda\nu}{\mu K} \\ 0 & 0 & (1-\rho)\dfrac{\Lambda\nu}{\mu K} \\ 0 & 0 & 0 \end{bmatrix},$$
$$V = \begin{bmatrix} (\sigma_1 + \theta + \mu + \phi) & 0 & 0 \\ -\theta & (\sigma_2 + \beta + \mu + \alpha) & 0 \\ -\delta_1 & -\delta_2 & \mu_b \end{bmatrix}. \tag{22}$$

The inverse of V is obtained and given by

$$V^{-1} = \begin{bmatrix} \dfrac{1}{k_1} & 0 & 0 \\ \dfrac{\theta}{k_1 k_2} & \dfrac{1}{k_2} & 0 \\ \dfrac{\theta\sigma_2 + \sigma_1 k_2}{k_1 k_2 \mu_b} & \dfrac{\sigma_2}{k_2 \mu_b} & \dfrac{1}{\mu_b} \end{bmatrix}, \tag{23}$$

where $k_1 = (\sigma_1 + \theta + \mu + \phi)$ and $k_2 = (\sigma_2 + \beta + \mu + \alpha)$.

Then,

$$FV^{-1} = \begin{bmatrix} \dfrac{\rho\Lambda\nu(\theta\sigma_2 + \sigma_1 k_2)}{\mu K k_1 k_2 \mu_b} & \dfrac{\rho\Lambda\nu\sigma_2}{\mu K k_2 \mu_b} & \dfrac{\rho\Lambda\nu}{\nu K \mu_b} \\ \dfrac{(1-\rho)\Lambda\nu(\theta\sigma_2 + \sigma_1 k_2)}{\mu K k_1 k_2 \mu_b} & \dfrac{(1-\rho)\Lambda\nu\sigma_2}{\mu K k_2 \mu_b} & \dfrac{(1-\rho)\Lambda\nu}{\nu K \mu_b} \\ 0 & 0 & 0 \end{bmatrix}. \tag{24}$$

The characteristic equation of FV^{-1} is obtained as

$$\lambda^2 \left(\rho\frac{\Lambda\nu(\theta\sigma_2 + \sigma_1 k_2)}{\mu K k_1 k_2 \mu_b} + (1-\rho)\right)\frac{\Lambda\nu\sigma_2}{\mu K k_2 \mu_b} = 0. \tag{25}$$

The eigenvalues of FV^{-1} are

$$\lambda_1 = \lambda_2 = 0,$$
$$\lambda_3 = \rho\frac{\Lambda\nu(\theta\sigma_2 + \sigma_1 k_2)}{\mu K k_1 k_2 \mu_b} + (1-\rho)\frac{\Lambda\nu\sigma_2}{\mu K k_2 \mu_b}. \tag{26}$$

The dominant eigenvalue of FV^{-1} is λ_3.

Therefore, the basic reproduction number ($\mathfrak{R}_0$) after substituting k_1 and k_2 is given by

$$\mathfrak{R}_0 = \left[\rho\frac{(\theta\sigma_2 + \sigma_1(\sigma_2 + \beta + \mu + \alpha))}{(\sigma_1 + \theta + \mu + \phi)} + (1-\rho)\sigma_2\right] \cdot \frac{\Lambda\nu}{\mu K(\sigma_2 + \beta + \mu + \alpha)\mu_b}. \tag{27}$$

3.5. Local Stability of Disease-Free Equilibrium

Proposition 2. *The disease-free equilibrium point is locally asymptotically stable if $\mathfrak{R}_0 < 1$ and unstable if $\mathfrak{R}_0 > 1$.*

Proof. To proof this theorem first we obtain the Jacobian matrix of system (1) at the disease-free equilibrium E_0 as follows:

$$J_{E_0} = \begin{bmatrix} -\mu & 0 & 0 & \delta & \frac{\nu\Lambda}{K\mu} \\ 0 & -(\sigma_1 + \theta + \mu + \phi) & 0 & 0 & \frac{\rho\nu\Lambda}{\mu K} \\ 0 & \theta & -(\sigma_2 + \beta + \mu + \alpha) & 0 & \frac{(1-\rho)\nu\Lambda}{\mu K} \\ 0 & \phi & \beta & -(\mu + \delta) & 0 \\ 0 & \sigma_1 & \sigma_2 & 0 & -\mu_b \end{bmatrix}. \tag{28}$$

From the Jacobian matrix of (28), we obtained a characteristic polynomial:

$$(-\lambda - \mu)(-\lambda - (\mu + \delta))\left(\lambda^3 + L_1\lambda^2 + L_2\lambda + L_3\right) = 0, \tag{29}$$

where

$$\begin{aligned} L_1 &= \sigma_2 + \beta + 2\mu + \alpha + \sigma_1 + \phi + \theta + \mu_b, \\ L_2 &= \mu_b(\sigma_2 + \beta + 2\mu + \alpha + \sigma_1 + \phi + \theta) \\ &\quad + (\sigma_2 + \beta + \mu + \alpha)(\sigma_1 + \mu + \phi + \theta) \\ &\quad - (\rho\sigma_1 + (1-\rho)\sigma_2)\frac{\nu\Lambda}{\mu K}, \\ L_3 &= \mu_b(\sigma_2 + \beta + \mu + \alpha)(\sigma_1 + \mu + \phi + \theta)(1 - \mathfrak{R}_0). \end{aligned} \tag{30}$$

From (29) clearly, we see that

$$\begin{aligned} -\lambda - \mu &= 0, \\ \text{or } -\lambda - (\mu + \delta) &= 0, \\ \text{or } \lambda^3 + L_1\lambda^2 + L_2\lambda + L_3 &= 0 \\ &\Downarrow \\ \lambda_1 &= -\mu < 0, \\ \lambda_2 &= -(\mu + \delta) < 0. \end{aligned} \tag{31}$$

For the last expression, that is,

$$\lambda^3 + L_1\lambda^2 + L_2\lambda + L_3 = 0, \tag{32}$$

we applied Routh-Hurwitz criteria. By the principle of Routh-Hurwitz criteria, (32) has strictly negative real root if and only if $L_1 > 0$, $L_3 > 0$, and $L_1L_2 > L_3$.

Obviously we see that L_1 is positive because it is a sum of positive variables, but L_3 to be positive $1 - \mathfrak{R}_0$ must be positive, which leads to $\mathfrak{R}_0 < 1$. Therefore, DFE will be locally asymptotically stable if and only if $\mathfrak{R}_0 < 1$. □

3.6. Global Stability of DFE

Theorem 3. *The disease-free equilibrium is globally asymptotically stable in the feasible region Ω if $\mathfrak{R}_0 < 1$.*

Proof. To proof this theorem, we first developed a Lyapunov function, technically.

$$L = \left[\frac{\theta\sigma_2 + \sigma_1k_2}{k_1}\right]C + \sigma_2I + k_2B_c, \tag{33}$$

where $k_1 = \sigma_1 + \theta + \mu + \phi$ and $k_2 = \sigma_2 + \beta + \mu + \alpha$

Then differentiating L both sides leads to

$$\frac{dL}{dt} = \left[\frac{\theta\sigma_2 + \sigma_1k_2}{k_1}\right]\frac{dC}{dt} + \sigma_2\frac{dI}{dt} + k_2\frac{dB_c}{dt}. \tag{34}$$

Substituting expression for dC/dt, dI/dt, and dB_c/dt from (1) to (34) results in

$$\begin{aligned} \frac{dL}{dt} &= \left[\frac{\theta\sigma_2 + \sigma_1k_2}{k_1}\right]\rho\lambda S - (\sigma_1 + \theta + \mu + \phi)C \\ &\quad + \sigma_2((1-\rho)\lambda S + \theta C - (\sigma_2 + \beta + \mu + \alpha)I) \\ &\quad + k_2(\sigma_1C + \sigma_2I - \mu_bB_c). \end{aligned} \tag{35}$$

By collecting like terms of (35),

$$\begin{aligned} \frac{dL}{dt} &= \left[\rho\frac{\theta\sigma_2 + \sigma_1k_2}{k_1} + (1-\rho)\sigma_2\right]\lambda S \\ &\quad + (\theta\sigma_2 - \theta\sigma_2 - \sigma_1k_2)C - \sigma_2k_2I \\ &\quad + k_2(\sigma_1C + \sigma_2I - \mu_bB_c). \end{aligned} \tag{36}$$

Equation (36) can be simplified as

$$\frac{dL}{dt} = \left[\rho\frac{\theta\sigma_2 + \sigma_1 k_2}{k_1} + (1-\rho)\sigma_2\right]\lambda S - k_2\mu_b B_c). \quad (37)$$

Equation (37) can be written as interims of $\mathfrak{R}_0$,

$$\frac{dL}{dt} = \left(\mathfrak{R}_0\mu_b k_2\frac{\mu K}{\Lambda\nu}\right)\lambda S - k_2\mu_b B_c). \quad (38)$$

At $S = S_0 = \Lambda/\mu$, (38) becomes

$$\frac{dL}{dt} \le (\mathfrak{R}_0 - 1)\, k_2\mu_b B_c. \quad (39)$$

So $dL/dt \le 0$ if $\mathfrak{R}_0 \le 1$. Furthermore, $dL/dt = 0 \Leftrightarrow B_c = 0$ which leads to $C = I = 0$ or $\mathfrak{R}_0 = 1$.

Hence, L is Lyapunov function on Ω and the largest compact invariant set in $\{(S, C, I, R, B_c) \in \Omega,\ dL/dt = 0\}$ is the singleton $(S_0, 0, 0, 0, 0)$.

Therefore, by LaSalle's invariance principle (LaSalle [16]), every solution to equations of model (1) with initial conditions in Ω which approaches the disease-free equilibrium at t (time) tends to infinity ($t \to \infty$) whenever $\mathfrak{R}_0 \le 1$. Hence, the disease-free equilibrium is globally asymptotically stable. □

3.7. The Endemic Equilibrium. The endemic equilibrium is denoted by $E^* = (S^*, C^*, I^*, R^*, B_c^*)$ and it occurs when the disease persists in the community. To obtain it, we equate all the model equations (1) to zero. Then we obtain

$$\begin{aligned}
S^* &= \frac{\Lambda(\sigma_2+\mu+\alpha+\beta)(\sigma_1+\mu+\theta+\phi)(\mu+\delta)}{(\mu+\lambda^*) - \beta\lambda^*\delta((1-\rho)(\sigma_1+\mu+\theta+\phi)+\rho\theta) - \delta\phi\rho\lambda^*(\sigma_2+\mu+\beta+\alpha)},\\
C^* &= \frac{\rho\lambda^*\Lambda(\sigma_2+\mu+\alpha+\beta)(\mu+\delta)}{(\mu+\lambda^*) - \beta\lambda^*\delta((1-\rho)(\sigma_1+\mu+\theta+\phi)+\rho\theta) - \delta\phi\rho\lambda^*(\sigma_2+\mu+\beta+\alpha)},\\
I^* &= \frac{(\mathfrak{R}_0 K(\sigma_1+\mu+\theta+\phi)(\sigma_2+\mu+\beta+\alpha)\mu\mu_b - \sigma_1\rho\Lambda\nu(\sigma_2+\mu+\beta+\alpha))(\mu+\delta)}{\mu K\sigma_2 + \nu\sigma_2 - \beta\delta\mathfrak{R}_0 K(\sigma_1+\mu+\theta+\phi)(\sigma_2+\mu+\beta+\alpha)\mu\mu_b + \beta\delta\sigma_1(\sigma_2+\mu+\beta+\alpha)\Lambda\nu - \delta\sigma_2\phi\rho\nu(\sigma_2+\mu+\beta+\alpha)},\\
R^* &= \frac{\beta I^* + \phi C^*}{\mu+\delta},\\
B_c^* &= \frac{\lambda^*\Lambda(\mu+\lambda^*)[\sigma_1\rho(\sigma_2+\mu+\alpha+\beta)+\sigma_2(1-\rho)(\sigma_1+\mu+\theta+\phi)+\rho\theta]}{\mu_b[\mu+\lambda^*) - \beta\lambda\delta((1-\rho)(\sigma_1+\mu+\theta+\phi)+\rho\theta) - \delta\phi\rho\lambda^*(\sigma_2+\mu+\beta+\alpha)]}.
\end{aligned} \quad (40)$$

When we substitute the expression for B_c^* into the force of infection, that is, $\lambda^* = B_c^*\nu/(K + B_c^*)$, we obtained a characteristic polynomial of force of infection,

$$p(\lambda^*) = D_1\lambda^{*2} + D_2\lambda^* = 0, \quad (41)$$

where $D_1 = 1+\mathfrak{R}_0(\sigma_2+\mu+\alpha+\beta)(\sigma_1+\mu+\theta+\phi)(\mu+\delta)\mu\mu_b K + (\beta\delta((1-\rho)(\sigma_1+\mu+\theta+\phi)+\rho\theta) + \delta\phi\rho(\sigma_2+\mu+\alpha+\beta))$, $D_2 = (1-\mathfrak{R}_0)(\mu+\delta)\mu$.

Clearly, $D_1 > 0$ and $D_2 \ge 0$. Whenever $\mathfrak{R}_0 < 1$, $\lambda^* = -D_1/D_2 \le 0$. From this, we see that, for $\mathfrak{R}_0 < 1$, there is no endemic equilibrium for this model.

Therefore, this condition shows that it is not possible for backward bifurcation in the model if $\mathfrak{R}_0 < 1$. When we plot I^* over $\mathfrak{R}_0$ by using the expression for I^* and estimated parameters in Table 2, we got a forward bifurcation (Figure 3).

Lemma 4. *A unique endemic equilibrium point E^* exists and is positive if $\mathfrak{R}_0 > 1$.*

4. Sensitivity Analysis of Model Parameters

On the basic parameters, we carried out sensitivity analysis. This helped us to check and identify parameters that can impact the basic reproductive number. To carry out sensitivity analysis, we followed the technique outlined by [17, 18]. This technique develops a formula to obtain the sensitivity index of all the basic parameters, defined as $\Delta_x^{\mathfrak{R}_0} = (\partial\mathfrak{R}_0/\partial x)(x/\mathfrak{R}_0)$, for x represents all the basic parameters.

For example, the sensitivity index of $\mathfrak{R}_0$ with respect to ν is $\Delta_\nu^{\mathfrak{R}_0} = (\partial\mathfrak{R}_0/\partial\nu)(\nu/R_{\text{eff}}) = 1$. And with respect to the remaining parameters, $\Delta_K^{\mathfrak{R}_0}$, $\Delta_{\sigma_1}^{\mathfrak{R}_0}$, $\Delta_{\sigma_2}^{\mathfrak{R}_0}$, $\Delta_\rho^{\mathfrak{R}_0}$, $\Delta_\mu^{\mathfrak{R}_0}$, $\Delta_{\mu_b}^{\mathfrak{R}_0}$, $\Delta_\alpha^{\mathfrak{R}_0}$, $\Delta_\theta^{\mathfrak{R}_0}$, $\Delta_\beta^{\mathfrak{R}_0}$, and $\Delta_\phi^{\mathfrak{R}_0}$ are obtained and evaluated at $\Lambda = 100$, $\phi = 0.0003$, $\sigma_1 = 0.9$, $\sigma_2 = 0.8$, $\beta = 0.0002$, $\rho = 0.3$, $\mu = 0.0247$, $\mu_b = 0.0001$, $\alpha = 0.052$, $\theta = 0.2$, $\nu = 0.9$, and $K = 50{,}000$. Their sensitivity indices are in Table 1.

4.1. Interpretation of Sensitivity Indices. The sensitivity indices of the basic reproductive number with respect to main parameters are arranged orderly in Table 1. Those

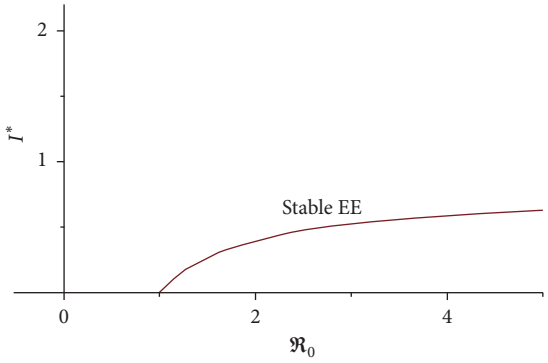


Figure 3: Forward bifurcation of typhoid fever model.

Table 1: Sensitivity indices table.

Parameter symbol	Sensitivity indices
ν	1
K	0.999
σ_1	0.26
σ_2	0.03
ρ	0.00506
μ	−1.028
μ_b	−1
α	−0.0592
θ	0.009
β	−0.00017
ϕ	−0.000089

parameters that have positive indices (ν, K, σ_1, σ_2, and ρ) show that they have great impact on expanding the disease in the community if their values are increasing. Due to the reason that the basic reproduction number increases as their values increase, it means that the average number of secondary cases of infection increases in the community. And also those parameters in which their sensitivity indices are negative (μ, μ_b, α, θ, β, and ϕ) have an influence of minimizing the burden of the disease in the community as their values increase while the others are left constant. And also as their values increase, the basic reproduction number decreases, which leads to minimizing the endemicity of the disease in the community.

5. Extension of the Model into an Optimal Control

In this section, the basic model of typhoid fever is generalized by incorporating three control interventions. The controls are prevention (u_1) (sanitation and proper hygiene controls), treatment (u_2) (treating individuals who developed symptoms of the disease), and screening of carriers (u_3) which helps them to get proper treatment if they are aware of their status.

After incorporating the controls into the basic model of typhoid fever, we get the following state equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda + \delta R - (1-u_1)\lambda S - \mu S,\\
\frac{dC}{dt} &= (1-u_1)\rho\lambda S - (\theta + u_3)C - (\sigma_1 + \phi + \mu)C,\\
\frac{dI}{dt} &= (1-u_1)(1-\rho)\lambda S + (1-u_3)\theta C - (u_2+\beta)I\\
&\quad - (\sigma_2 + \mu + \alpha)I,\\
\frac{dR}{dt} &= (u_2+\beta)I + \phi C - (\mu+\delta)R,\\
\frac{dB_c}{dt} &= \sigma_1 C + \sigma_2 I - \mu_b B_c,
\end{aligned} \tag{42}$$

where $\lambda = B_c\nu/(K + B_c)$.

$\{0 \le u_1 < 1,\ 0 \le u_2 < 1,\ 0 \le u_3 < 1, 0 \le t \le T\}$ is Lebesgue measurable. Our main objective is to obtain the optimal levels of the controls and associated state variables that optimize the objective function. The form of the objective function is taken from [19] and given by

$$J = \min_{u_1,u_2,u_3} \int_0^{t_f} \left(b_1 C + b_2 I + \frac{1}{2}\sum_{i=1}^{3} w_i u_i^2 \right) dt. \tag{43}$$

The coefficients associated with state variables (b_1 and b_2) and with controls (w_i) are positive. Due to the fact that cost is not linear in its condition, we make the cost expression $((1/2)w_i u_i^2)$ quadratic.

As objective function (43) shows, we aimed to minimize the number of carriers, infectives, and costs. That is, we want to get an optimal triple (u_1^*, u_2^*, u_3^*) such that

$J(u_1^*, u_2^*, u_3^*) = \min\{J(u_1, u_2, u_3) \mid u_i \in U\}$, where $U = \{(u_1, u_2, u_3) \mid \text{each } u_i \text{ is measurable with } 0 \le u_i < 1 \text{ for } 0 \le t \le t_f\}$ is the set of acceptable controls.

5.1. Existence of an Optimal Control. The existence of the optimal control can be showed by using an approach of [20]. We have already justified the boundedness of the solution of the basic typhoid fever model. This result can be used to prove the existence of optimal control. For detailed proof, see [20] [Theorem 4.1, p68-69].

5.2. The Hamiltonian and Optimality System. To obtain the Hamiltonian (H), we follow the approach of [21] such that

$$H = \frac{dJ}{dt} + \lambda_1\frac{dS}{dt} + \lambda_2\frac{dC}{dt} + \lambda_3\frac{dI}{dt} + \lambda_4\frac{dR}{dt} + \lambda_5\frac{dB_c}{dt}. \tag{44}$$

That is,

$$\begin{aligned}
H(S, C, I, R, B_c, t) &= L(C, I, u_1, u_2, u_3, t) + \lambda_1\frac{dS}{dt}\\
&\quad + \lambda_2\frac{dC}{dt} + \lambda_3\frac{dI}{dt} + \lambda_4\frac{dR}{dt}\\
&\quad + \lambda_5\frac{dB_c}{dt},
\end{aligned} \tag{45}$$

Table 2: Parameter values for typhoid fever model.

Parameter symbol	Parameter description	Value	Source
ν	Salmonella ingestion rate	0.9	Assumed
K	Concentration of Salmonella bacteria in foods and water	50000	[14]
μ	Human beings natural death rate	0.0247	Assumed
α	Typhoid induced death rate	0.052	Estimated
β	Treatment rate of infectious diseases	0.002	Estimated
σ_1	Discharge rate of Salmonella from carriers	0.9	Gosh et al., 2006
σ_2	Discharge rate of Salmonella from infective	0.8	Assumed
δ	Removal rate from recovered subclass to susceptible subclass	0.000904	Adetunde, 2008
θ	Screening rate of carriers	0.2	Assumed
ϕ	Removal of carriers by natural immunity	0.0003	Assumed
ρ	Probability of susceptible joining carrier state	0.3	Assumed
μ_b	Natural/drug induced death rate of bacteria	0.001	Gosh et al., 2006
Λ	Recruitment of human beings	100	Assumed

where $L(C, I, u_1, u_2, u_3, t) = b_1 C + b_2 I + (1/2)\sum_{i=1}^{3} w_i u_i^2$, λ_1, $\lambda_2, \lambda_3, \lambda_4$, and λ_5 are the adjoint variable functions. To obtain the adjoint variables, we followed the classical result of [21].

Theorem 5. *There exist an optimal control set of u_1, u_2, and u_3 and corresponding solution, S, C, I, R, and B_c, that minimize $J(u_1, u_2, u_3)$ over U. Furthermore, there exist adjoint functions $\lambda_1, \ldots, \lambda_5$ such that*

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= -\lambda_1\left(-\mu - \frac{B_c\nu(1-u_1)}{K+B_c}\right) \\
&\quad - \frac{\lambda_2(1-\rho)(1-u_1)B_c\nu}{K+B_c} - \frac{\lambda_3(1-u_1)\rho\nu B_c}{K+B_c}, \\
\frac{d\lambda_2}{dt} &= -b_1 - \lambda_2(-\theta-u_3) - \lambda_3(1-u_3)\theta - \lambda_4\phi \\
&\quad - \lambda_5(\sigma_1+\phi+\mu), \\
\frac{d\lambda_3}{dt} &= -b_2 - \lambda_3(-u_2-\beta-\sigma_2) - \lambda_4(u_2+\beta) \\
&\quad - \lambda_5(\sigma_2+\mu+\alpha), \\
\frac{d\lambda_4}{dt} &= -\lambda_1\delta - \lambda_4(-\mu-\delta), \\
\frac{d\lambda_5}{dt} &= -\frac{\lambda_1 B_c\nu(1-u_1)s}{(k+B_c)^2} - \lambda_2\left(\frac{(1-u_1)\rho\nu S}{K+B_c}\right. \\
&\quad \left. - \frac{(1-u_1)\rho\nu B - cS}{(K+B_c)^2}\right) - \lambda_3\left(\frac{(1-\rho)(1-u_1)\nu S}{K+B_c}\right. \\
&\quad \left. - \frac{(1-\rho)(1-u_1)B_c\nu S}{(K+B_c)^2}\right) + \lambda_5\mu_b,
\end{aligned} \tag{46}$$

with transversality conditions,

$$\lambda_i(t_f) = 0, \quad i = 1, \ldots, 5. \tag{47}$$

And the characterized control set of (u_1^*, u_2^*, u_3^*) is

$$\begin{aligned}
u_1^*(t) &= \max\left\{0, \right. \\
&\quad \left. \min\left(1, \frac{S(\lambda_2\rho\nu B_c - B_c\rho\nu\lambda_3 + B_c\nu\lambda_3 - \lambda_1 B_c\nu)}{(K+B_c)w_1}\right)\right\}, \\
u_2^*(t) &= \max\left\{0, \min\left(1, \frac{I(\lambda_3-\lambda_4)}{w_2}\right)\right\}, \\
u_3^*(t) &= \max\left\{0, \min\left(1, \frac{C(\lambda_3\theta+\lambda_2)}{w_3}\right)\right\}.
\end{aligned} \tag{48}$$

Proof. To prove this theorem, we used the classical result of [21]. Accordingly, to get the system of adjoint variables, we differentiate the Hamiltonian (45) with respect to each state as follows:

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{dH}{dS} = -\lambda_1\left(-\mu - \frac{B_c\nu(1-u_1)}{K+B_c}\right) \\
&\quad - \frac{\lambda_2(1-\rho)(1-u_1)B_c\nu}{K+B_c} - \frac{\lambda_3(1-u_1)\rho\nu B_c}{K+B_c}, \\
\frac{d\lambda_2}{dt} &= -\frac{dH}{dC} = -b_1 - \lambda_2(-\theta-u_3) - \lambda_3(1-u_3)\theta \\
&\quad - \lambda_4\phi - \lambda_5(\sigma_1+\phi+\mu), \\
\frac{d\lambda_3}{dt} &= -\frac{dH}{dI} = -b_2 - \lambda_3(-u_2-\beta-\sigma_2) - \lambda_4(u_2 \\
&\quad + \beta) - \lambda_5(\sigma_2+\mu+\alpha), \\
\frac{d\lambda_4}{dt} &= -\frac{dH}{dR} = -\lambda_1\delta - \lambda_4(-\mu-\delta),
\end{aligned}$$

$$\frac{d\lambda_5}{dt} = -\frac{dH}{dB_c} = -\frac{\lambda_1 B_c \nu (1-u_1) S}{(K+B_c)^2} - \lambda_2 \left(\frac{(1-u_1)\rho\nu S}{K+B_c} - \frac{(1-u_1)\rho\nu B_c S}{(K+B_c)^2} \right) - \lambda_3 \left(\frac{(1-\rho)(1-u_1)\nu S}{K+B_c} - \frac{(1-\rho)(1-u_1) B_c \nu S}{(K+B_c)^2} \right) + \lambda_5 \mu_b. \tag{49}$$

And also for characterization of the optimal control, we used the following partial differential equation:

$$\frac{\partial H}{\partial u_i} = 0 \quad \text{at } u_i = u_i^*, \tag{50}$$

where $i = 1, 2, 3$.

For $i = 1$,

$$\frac{\partial H}{\partial u_1} = 0 \quad \text{at } u_1^* \Downarrow u_1^* = \frac{S(\lambda_2 \rho \nu B_c - B_c \rho \nu \lambda_3 + B_c \nu \lambda_3 - \lambda_1 B_c \nu)}{(K+B_c) w_1}. \tag{51}$$

For $i = 2$,

$$\frac{\partial H}{\partial u_2} = 0 \quad \text{at } u_2^* \Downarrow u_2^* = \frac{I(\lambda_3 - \lambda_4)}{w_2}. \tag{52}$$

For $i = 3$,

$$\frac{\partial H}{\partial u_3} = 0 \quad \text{at } u_3^* \Downarrow u_3^* = \frac{C(\lambda_3 \theta + \lambda_2)}{w_3}. \tag{53}$$

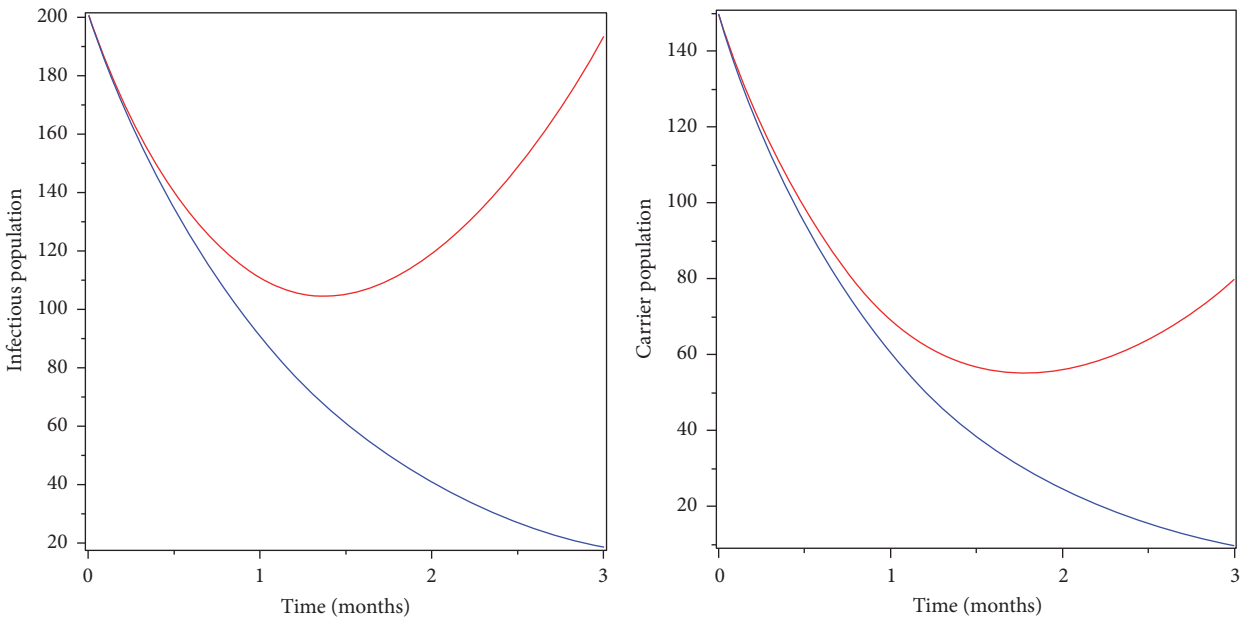
Since $0 < u_i^* < 1$, we can write in a compact notation:

$$u_1^* = \max\left\{0, \min\left(1, \frac{S(\lambda_2 \rho \nu B_c - B_c \rho \nu \lambda_3 + B_c \nu \lambda_3 - \lambda_1 B_c \nu)}{(K+B_c) w_1}\right)\right\},$$
$$u_2^* = \max\left\{0, \min\left(1, \frac{I(\lambda_3 - \lambda_4)}{w_2}\right)\right\},$$
$$u_3^* = \max\left\{0, \min\left(1, \frac{C(\lambda_3 \theta + \lambda_2)}{w_3}\right)\right\}. \tag{54}$$

□

5.3. The Optimality System. It is a system of states (42) and adjoint (46) incorporating with the characterization of the optimal control and initial and transversality conditions. Then we have the following optimality system:

$$\frac{dS}{dt} = \Lambda + \delta R - (1-u_1^*)\lambda S - \mu S,$$
$$\frac{dC}{dt} = (1-u_1{}^*)\rho\lambda S - (\theta + u_3^*) C - (\sigma_1 + \phi + \mu) C,$$
$$\frac{dI}{dt} = (1-u_1^*)(1-\rho)\lambda S + (1-u_3^*)\theta C - (u_2^* + \beta) I - (\sigma_2 + \mu + \alpha) I,$$
$$\frac{dR}{dt} = (u_2^* + \beta) I + \phi C - (\mu + \delta) R,$$
$$\frac{dB_c}{dt} = Q + \sigma_1 C + \sigma_2 I - \mu_b B_c,$$
$$\frac{d\lambda_1}{dt} = -\lambda_1 \left(-\mu - \frac{B_c \nu (1-u_1^*)}{k+B_c} \right) - \frac{\lambda_2 (1-\rho)(1-u_1^*) B_c \nu}{K+B_c} - \frac{\lambda_3 (1-u_1^*)\rho\nu B_c}{K+B_c},$$
$$\frac{d\lambda_2}{dt} = -b_1 - \lambda_2(-\theta - u_3^*) - \lambda_3(1-u_3^*)\theta - \lambda_4\phi - \lambda_5\sigma_1,$$
$$\frac{d\lambda_3}{dt} = -b_2 - \lambda_3(-u_2^* - \beta - (\sigma_2 + \mu + \alpha)) - \lambda_4(u_2^* + \beta) - \lambda_5\sigma_2,$$
$$\frac{d\lambda_4}{dt} = -\lambda_1\delta - \lambda_4(-\mu - \delta),$$
$$\frac{d\lambda_5}{dt} = -\frac{\lambda_1 B_c \nu (1-u_1^*) S}{(K+B_c)^2} - \lambda_2 \left(\frac{(1-u_1^*)\rho\nu S}{K+B_c} - \frac{(1-u_1^*)\rho\nu B - cS}{(K+B_c)^2} \right) - \lambda_3 \left(\frac{(1-\rho)(1-u_1^*)\nu S}{K+B_c} - \frac{(1-\rho)(1-u_1^*) B_c \nu S}{(K+B_c)^2} \right) + \lambda_5 \mu_b, \tag{55}$$
$$\lambda_i(t_f) = 0, \quad i = 1, 2, 3, 4, 5,$$
$$S(0) = S_0,$$
$$C(0) = C_0,$$
$$I(0) = I_0,$$
$$R(0) = R_0,$$
$$B_c(0) = B_{c_0}.$$



(a) Prevention impact on infectious population

(b) Prevention impact on carrier population

FIGURE 4: Simulations of typhoid fever model with prevention control only.

5.4. Uniqueness of the Optimality System. Since the state and adjoint variables are bounded and also the obtained ordinary differential equations have Lipschitz in their structure, it is possible to show the uniqueness, hence the following theorem.

Theorem 6. *For $t \in [0, t_f]$, the bounded solutions to the optimality system are unique.*

Proof. See [22] for the proof of this theorem. □

6. Numerical Simulations

We perform numerical simulation of the optimality system by using the parameter values given in Table 2.

To obtain optimal solution, we apply iterative technique. By using an advantage of the initial conditions of the state system, we used a forward fourth-order Runge-Kutta method to solve it and also due to the final conditions for the adjoint system, we used a backward fourth-order Runge-Kutta method to solve it. To solve the state initial guess of controls is used and the solution of the state system and the initial guess helps to solve the adjoint system. Each control continues to be updated by combining its previous and characterization values. To repeat the solutions, the updated controls are used. This situation continues until two consecutive iterations are close enough [23].

To examine the impact of each control on eradication of typhoid fever disease, we used the following strategy:

(i) Applying prevention only (u_1) as intervention

(ii) Applying treatment only (u_2) as intervention

(iii) Applying screening only (u_3) as intervention

(iv) Implementing prevention (u_1) and treatment (u_2) intervention

(v) Implementing prevention (u_1) and screening (u_3) intervention

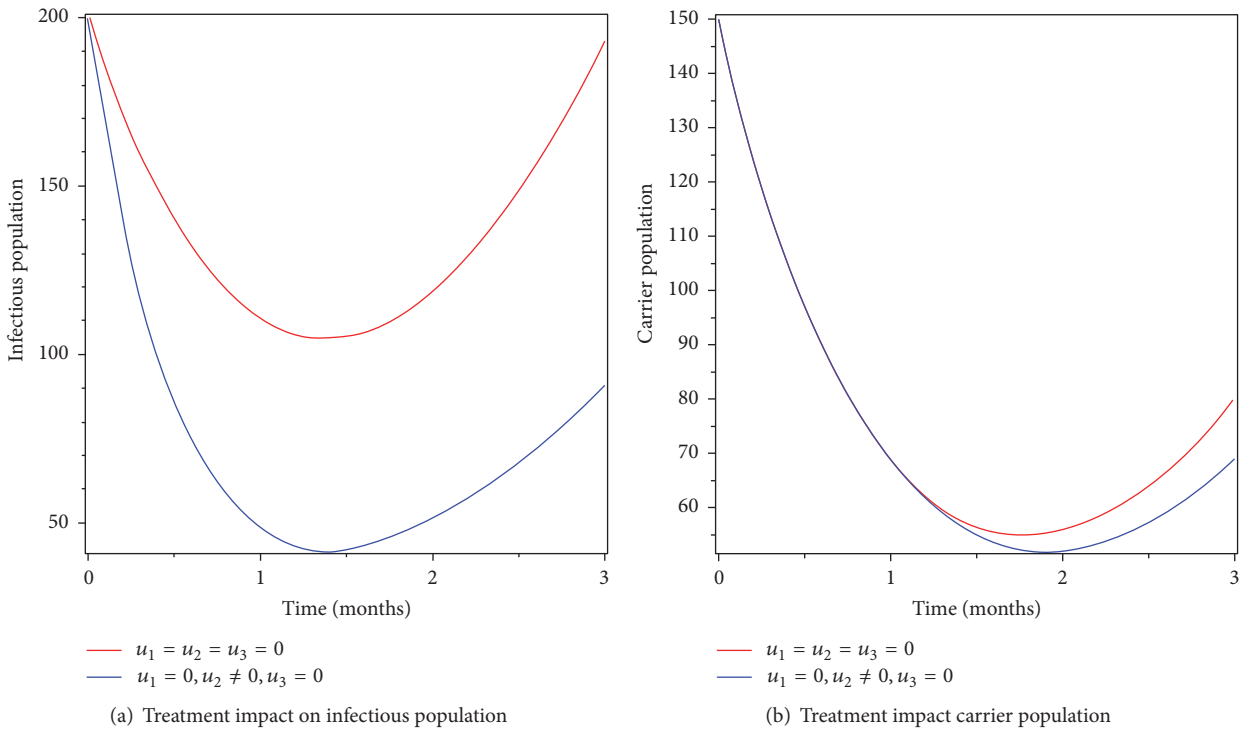
(vi) Implementing treatment (u_2) and screening (u_3) intervention

(vii) Using all the three controls: prevention effort u_1, treatment effort u_2, and also screening u_3

Initial values that we used for simulation of the optimal control are $S(0) = 1000$, $C(0) = 150$, $I(0) = 200$, $R(0) = 300$, and $B_c(0) = 200$ and also coefficients of the state and controls that we used are $b_1 = 25$, $b_2 = 25$, $w_1 = 4$, $w_2 = 3$, and $w_3 = 5$.

6.1. Control with Prevention Only. We simulated the optimality system by incorporating prevention intervention only. Figures 4(a) and 4(b) show the decrease of infectious and carrier population in the specified time. We conclude that prevention that includes sanitation and other techniques is a vital method to reduce typhoid fever infection. The number of individuals who have been with typhoid fever disease before implementation of prevention control has gone down due to disease induced and natural deaths. Therefore, applying optimized prevention control can eradicate typhoid fever disease in the community.

6.2. Control with Treatment Only. We applied treatment only as intervention that is treating individuals who develop



(a) Treatment impact on infectious population

(b) Treatment impact carrier population

FIGURE 5: Simulations of typhoid fever model with treatment control only.

disease symptom. From Figures 5(a) and 5(b), we understand that the number of infectious individuals and carriers decreased when treatment intervention is applied. The number of infectious individuals and carriers did not go to zero over the period of implementation of this intervention strategy. The reason is that due to lack of prevention susceptible individuals still get infected. Therefore, we conclude that applying optimized treatment only as control intervention decreases the burden of the disease but it cannot eradicate typhoid fever disease in the community.

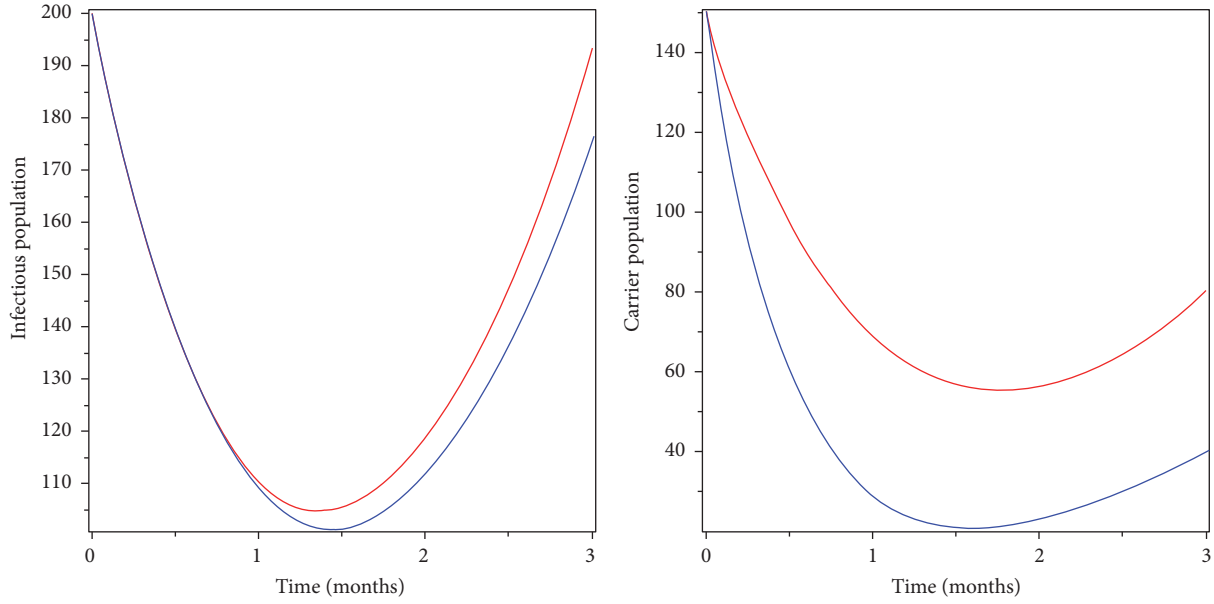
6.3. Control with Screening Only. As we know screening helps carriers to identify their status as they are leaving with the bacteria or not. Therefore, Figures 6(a) and 6(b) show that the infectious and carrier population goes down by screening effort but their number cannot be zero. New infection always appears in the community because the diseases are not prevented and individuals who develop the symptom of the disease are not getting treatment. Therefore, control with screening only reduces the burden in some extent but it is not helpful to eradicate typhoid fever disease totally from the community.

6.4. Control with Prevention and Treatment. We simulate the model using a combination of prevention and treatment as intervention strategy for control of typhoid fever disease in the community. Figures 7(a) and 7(b) clearly show that the infectious and carrier population has gone to zero at the end of the implementation period. Therefore, we conclude that this strategy is effective in eradicating the disease from the community in a specified period of time.

6.5. Control with Prevention and Screening. We simulated the model by incorporating optimized prevention and screening as disease control strategy. Figures 8(a) and 8(b) show that the infectious and carrier population goes to zero at the end of the implementation of intervention time. From this, we can conclude that applying prevention and screening can eradicate the disease even if without treating individuals that have disease symptom. Therefore, applying optimized prevention and screening as intervention strategy will eradicate typhoid fever disease from the community.

6.6. Control with Treatment and Screening. In this strategy, we applied treatment and screening as intervention to control typhoid fever disease. Figures 9(a) and 9(b) show that optimized intervention by treating infectious individuals and screening of carriers decreases the number of infectious and carrier populations but did not go to zero. Therefore, this strategy is not 100% effective in eradicating the disease in the specified period of time.

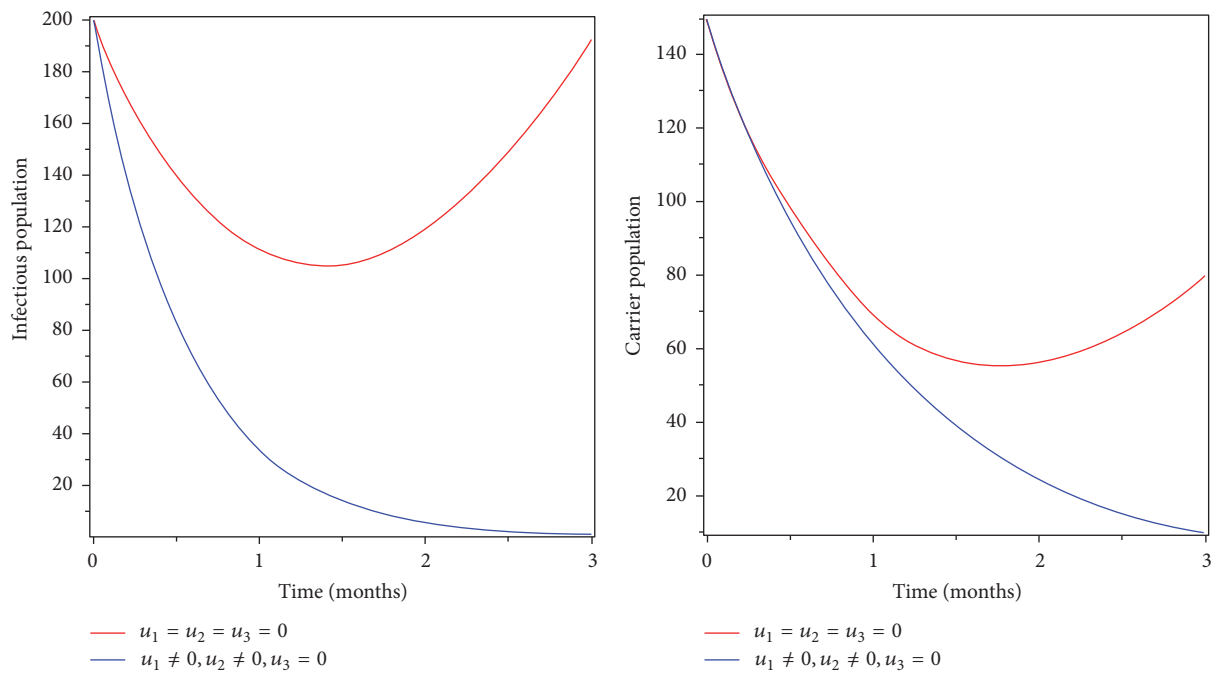
6.7. Control with Prevention, Treatment, and Screening. In this strategy, we implemented all the three controls (prevention, treatment, and screening) as intervention to eradicate typhoid fever from the community. Figures 10(a) and 10(b) show that the number of infectious individuals and carriers goes to zero at the end of the implementation period. Moreover, Figure 11 shows that the number of Salmonella bacteria population decreased after the implementation of the strategy. Therefore, applying this strategy is effective in eradicating typhoid fever disease form the community in a specified period of time.



(a) Screening impact on infectious population

(b) Screening only impact on carrier population

Figure 6: Simulations of typhoid fever model with screening control only.



(a) Prevention and treatment impact on infectious individuals

(b) Prevention and treatment impact on carrier

Figure 7: Simulations of typhoid fever model with prevention and treatment controls.

7. Cost-Effectiveness Analysis

In this section, we identified a strategy which is cost-effective compared to other strategies. To achieve this, we used incremental cost-effectiveness ratio (ICER), which is done dividing the difference of costs between two strategies to the difference of the total number of their infections averted. We estimated the total number of infections averted for each strategy by subtracting total infections with control from without control. To get the total cost of each strategy, we used

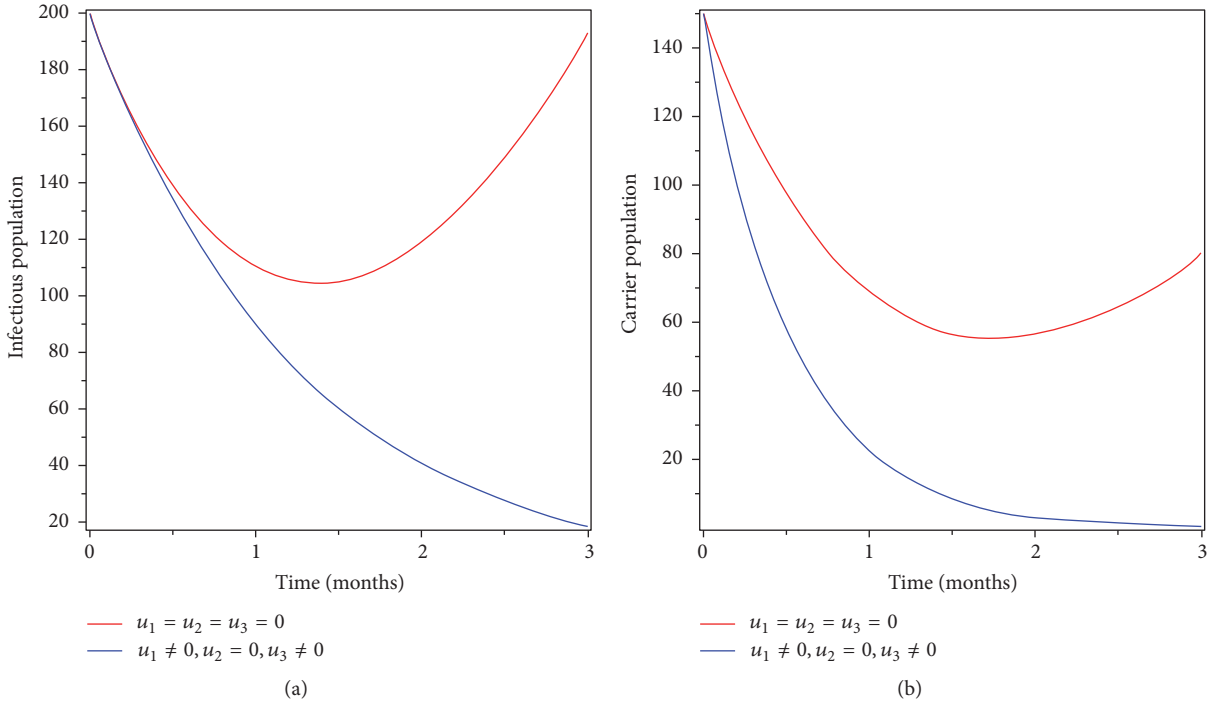


FIGURE 8: Simulations of the typhoid fever model with prevention and screening controls.

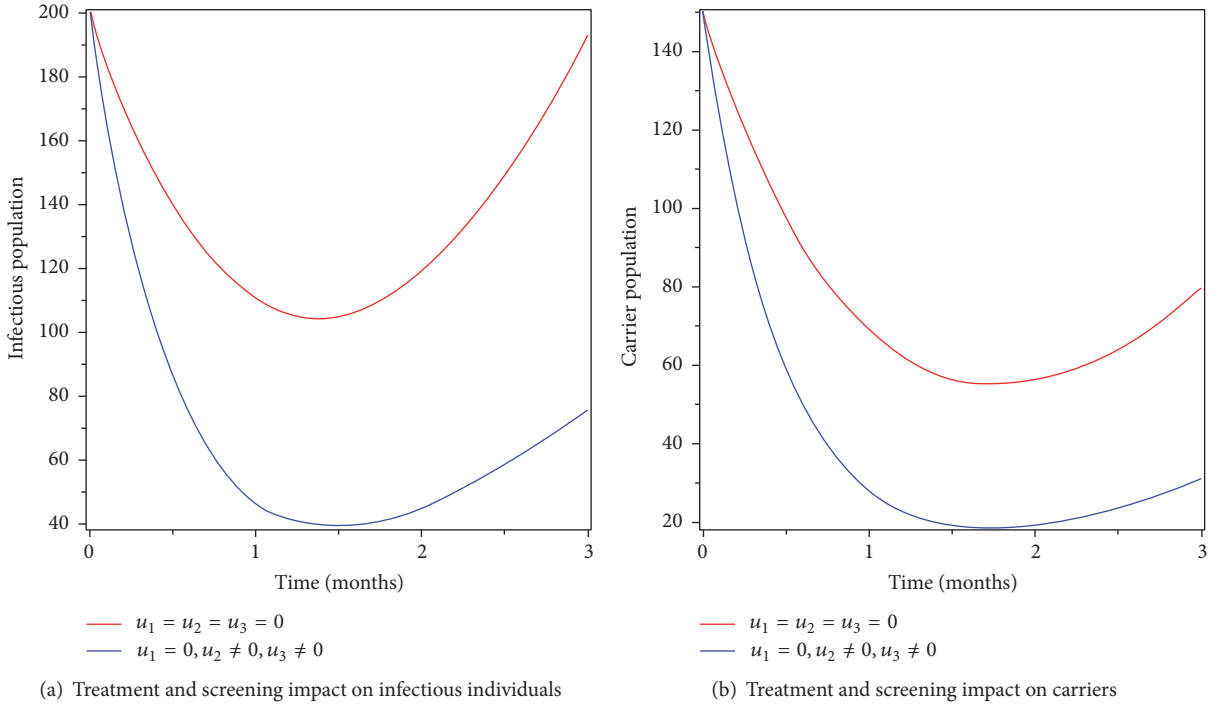
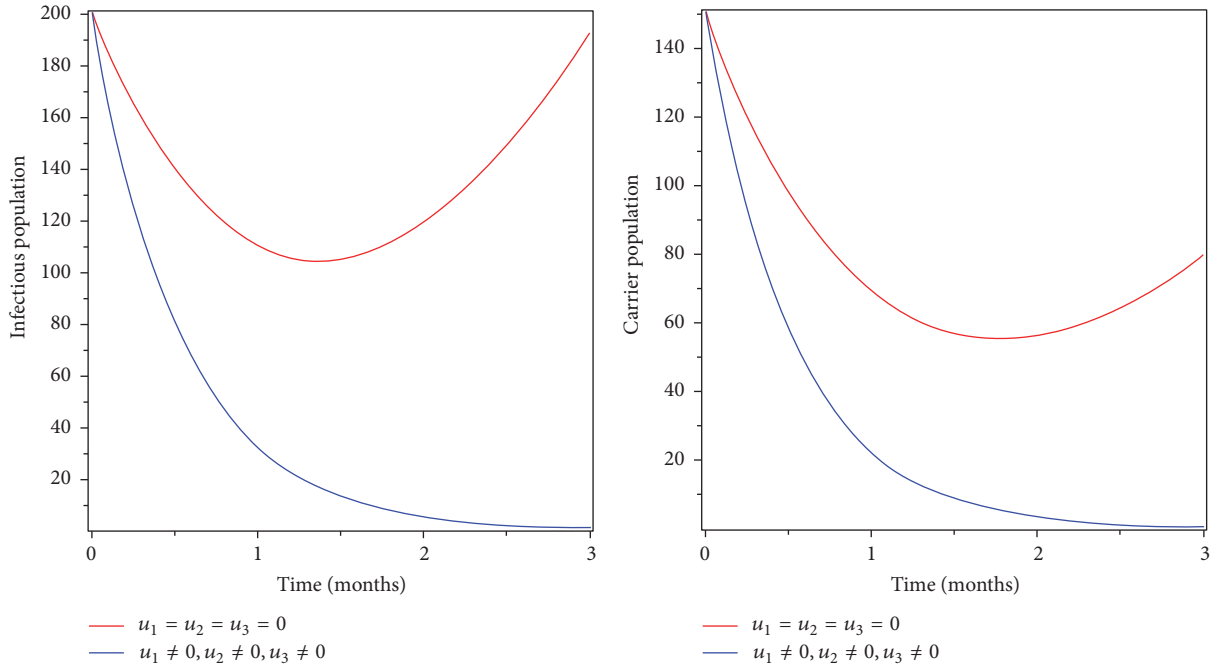


FIGURE 9: Simulations of the typhoid fever model with treatment and screening controls.

their respective cost function ($(1/2)w_1u_1^2$, $(1/2)w_2u_2^2$, and $(1/2)w_3u_3^2$) to calculate over the time of intervention. We did not consider strategies that implement one intervention only, due to the reason that one intervention only is not guaranteed to eradicate the disease totally from the community. Those strategies which incorporate more than one intervention are ordered below to be compared pairwise:

Strategy A (prevention and screening)

Strategy B (treatment and screening)



(a) Prevention, treatment, and screening impact on infectious individuals

(b) Prevention, treatment, and screening impact on carriers

Figure 10: Simulations of the typhoid fever model with prevention, treatment, and screening controls.

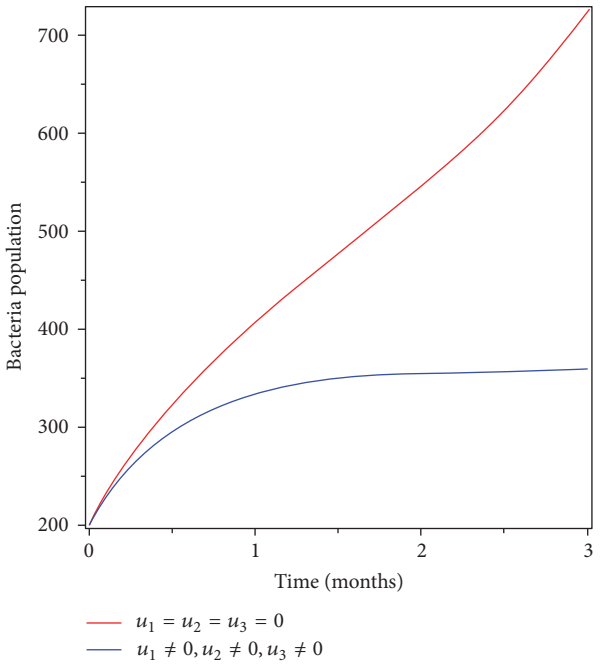


Figure 11: Simulations of the typhoid fever model with prevention, treatment, and screening controls on Salmonella bacteria populations.

Table 3: Number of infections averted and total cost of each strategy.

Strategies	Description	Total infections averted	Total cost (USD)
A	Prevention and screening	11,977	733.07
B	Treatment and screening	13,805	800
C	Prevention and treatment	19,699	531.19
D	Prevention, treatment, and screening	19,987	1104.5

We used parameter values in Table 2 to estimate the total cost and total infections averted in Table 3.

First we compared the cost-effectiveness of strategies A and B: ICER(A) = 733.07/11,977 = 0.06, ICER(B) = (733.07 − 800)/(11,977 − 13,805) = 0.037.

This shows that strategy B is cheaper than strategy A by saving 0.037. That means strategy A needs higher money than strategy B. Therefore, we exclude strategy A and continue to compare strategies B and C.

$$\text{ICER (B)} = \frac{800}{13{,}805} = 0.058,$$
$$\text{ICER (C)} = \frac{800 - 573.19}{13{,}805 - 19{,}699} = -0.039. \tag{56}$$

Strategy C (prevention and treatment)

Strategy D (prevention, treatment, and screening)

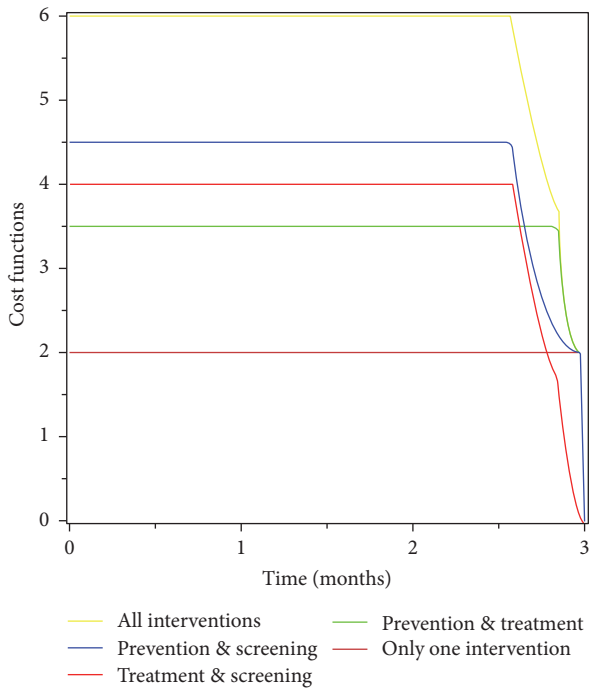


FIGURE 12: Cost function of the intervention strategies for the period of 3 months.

Similarly, this comparison indicates that strategy C is cheaper than strategy B by saving 0.039. Therefore, strategy B is rejected and continues to compare strategy C with the last strategy which is D.

$$\text{ICER (C)} = \frac{573.19}{19{,}699} = 0.029,$$
$$\text{ICER (D)} = \frac{573.19 - 1{,}104.5}{19{,}699 - 19{,}987} = 1.845. \quad (57)$$

Finally, the comparison result reveals that strategy C is cheaper than strategy D by saving 0.029. Therefore, strategy C (combination of prevention and treatment) is the best strategy from all compared strategies due to its cost-effectiveness and healthy benefit.

Moreover, Figure 12 shows that applying only one intervention is cheapest. But we do not consider this because a single intervention is not effective in eradicating the disease. A combination of prevention and treatment strategy is the cheapest of all other combined intervention strategies. The combination of all the three interventions (prevention, treatment, and screening) is the most expensive strategy compared to other strategies.

8. Discussions and Conclusions

In this study, a deterministic model for the dynamics of typhoid fever disease is proposed. The qualitative analysis of the model shows that the solution of the model is bounded and positive and also the equilibria points of the model are obtained and their local as well as global stability condition is established. The study also obtained the basic reproduction number and it reveals that for $\mathfrak{R}_0 < 1$ there is no possibility of having backward bifurcation. In Section 4, sensitivity analysis of the reproductive number has been carried out. Results from the sensitivity analysis of the reproductive number suggest that an increase in ν, K, σ_1, and σ_2 has the greatest influence on increasing the magnitude of the associated reproductive number which results in the endemicity of typhoid fever.

In Section 5, using Pontryagin's maximum principle, the optimal control problem is formulated and the conditions for optimal control of the disease are analyzed with effective preventive measures (sanitation and proper hygiene controls), treatment regime, and screening. Existence conditions for optimal control are established and the optimality system is developed. Seven intervention strategies are proposed for examining each strategy on the eradication of typhoid. In Section 6, the proposed strategies are investigated numerically and their results are displayed graphically. Cost-effectiveness analysis of the main strategies is done in Section 7, and the results indicate that prevention and the cost put into treatment have a strong impact on the disease control. Effective treatment only without prevention is not the best option in controlling the spread of typhoid fever. Therefore, this finding conclude that adequate control measures which adhered to these control strategies (preventive and treatment) would be a very effective way for fighting the disease and also for cost-effectiveness.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

[1] World Health Organization, "Typhoid fever fact sheet," 2000, http://www.who.int/mediacentre/factsheets/.

[2] World Health Organization (WHO), *The Diagnosis,Treatment and Prevention of Typhoid Fever*, 2003.

[3] O. D. Makinde and K. O. Okosun, "Impact of chemo-therapy on optimal control of malaria disease with infected immigrants," *BioSystems*, vol. 104, no. 1, pp. 32–41, 2011.

[4] K. O. Okosun and O. D. Makinde, "On a drug-resistant malaria model with susceptible individuals without access to basic amenities," *Journal of Biological Physics*, vol. 38, no. 3, pp. 507–530, 2012.

[5] K. O. Okosun and O. D. Makinde, "Optimal control analysis of malaria in the presence of non-linear incidence rate," *Applied and Computational Mathematics. An International Journal*, vol. 12, no. 1, pp. 20–32, 2013.

[6] K. O. Okosun and O. D. Makinde, "Optimal control analysis of hepatitis C virus with acute and chronic stages in the presence of treatment and infected immigrants," *International Journal of Biomathematics*, vol. 7, no. 2, Article ID 1450019, 23 pages, 2014.

[7] K. O. Okosun and O. D. Makinde, "A co-infection model of malaria and cholera diseases with optimal control," *Mathematical Biosciences*, vol. 258, pp. 19–32, 2014.

[8] I. A. Adetunde, "Mathematical models for the dynamics of typhoid fever in kassena-nankana district of upper east region of Ghana," *Modern Mathematics and Statistics*, 2008.

[9] S. Mushayabasa and C. P. Bhunu, "Prostitution and drug (alcohol) misuse: the menacing combination," *Journal of Biological Systems*, vol. 20, no. 2, Article ID 1250005, pp. 177–193, 2013.

[10] K. R. Adeboye and M. Haruna, "A mathematical model for the transmission and control of malaria and typhoid co-infection using sirs approach," *Nigeria Research Journal of Mathematics*, 2015.

[11] A. Omame, R. A. Umana, N. O. Iheonu, and S. Chioma, "On the existence of a stochastic model of typhoid fever," *Mathematical Theory and Modeling*, vol. 5, no. 8, 2015.

[12] M. A. Khan, M. Parvez, S. Islam, I. Khan, S. Shafie, and T. Gul, "Mathematical analysis of typhoid model with saturated incidence rate," *Advanced Studies in Biology*, vol. 7, pp. 65–78, 2015.

[13] O. C. Akinyi, J. Y. T. Mugisha, A. Manyonge, and C. Ouma, "A model on the impact of treating typhoid with anti-malarial: Dynamics of malaria concurrent and co-infection with typhoid," *International Journal of Mathematical Analysis*, vol. 9, no. 9-12, pp. 541–551, 2015.

[14] M. Gosh, P. Chandra, P. Sinha, and J. B. Shukla, "Modelling the spread of bacterial infectious disease with environmental effect in a logistically growing human population," *Non-linear - Analysis: Real World Applications*, vol. 7, pp. 341–363, 2006.

[15] P. van den Driessche and J. Watmough, "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission," *Mathematical Biosciences*, vol. 180, pp. 29–48, 2002.

[16] J. P. LaSalle, *The Stability of Dynamical Systems*, SIAM, Philadelphia, Pa, USA, 1976.

[17] N. Chitnis, J. M. Cushing, and J. M. Hyman, "Bifurcation analysis of a mathematical model for malaria transmission," *SIAM Journal on Applied Mathematics*, vol. 67, no. 1, pp. 24–45, 2006.

[18] S. M. Blower and H. Dowlatabadi, "Sensitivity and Uncertainty Analysis of Complex Models of Disease Transmission: an HIV Model as an Example," *International Statistical Institute, Great-Britain*, vol. 62, pp. 229–243, 1994.

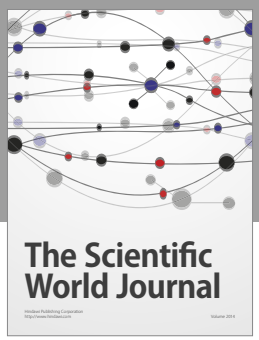
[19] S. Baba and O. D. Makinde, "Optimal control of HIV/AIDS in the workplace in the presence of careless individuals," *Computational and Mathematical Methods in Medicine*, vol. 2014, Article ID 831506, 2014.

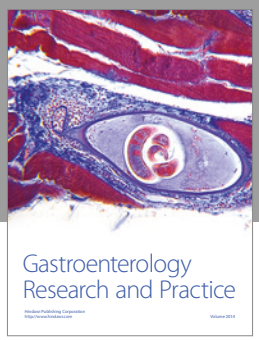
[20] W. H. Fleming and R. W. Rishel, *Deterministic and Stochastic Optimal Control*, vol. 1, Springer, New York, NY, USA, 1975.

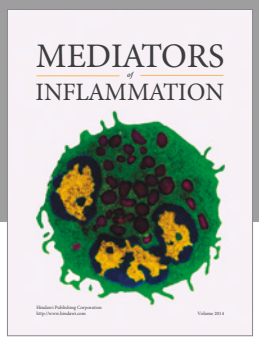
[21] L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze, and E. F. Mishchenko, *The Mathematical Theory of Optimal Processes*, John Wiley & Sons, London, UK, 1962.

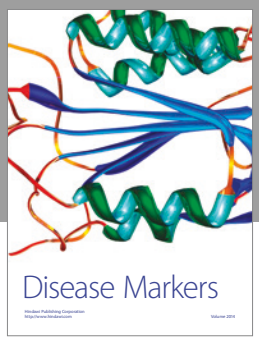
[22] K. R. Fister, S. Lenhart, and J. S. McNally, "Optimizing chemotherapy in an HIV model," *Electronic Journal of Differential Equations*, vol. 1998, 12 pages, 1998.

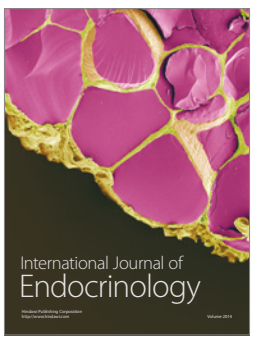
[23] S. M. Lenhart and J. T. Workman, *Optimal Control Applied to Biological Models*, CRC Press, 2007.

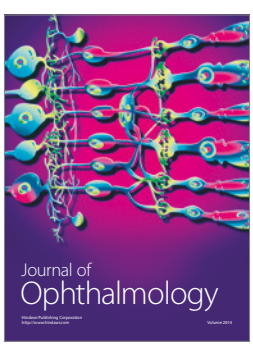


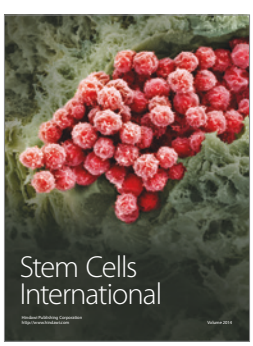


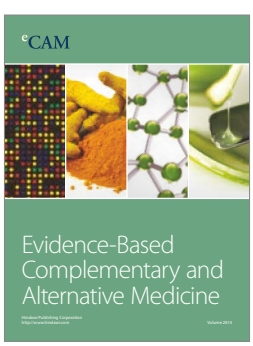


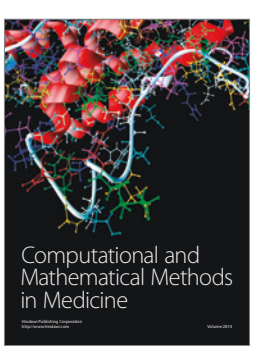


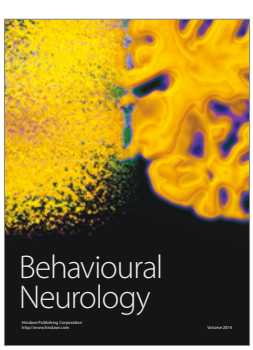


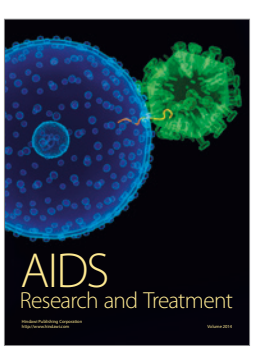


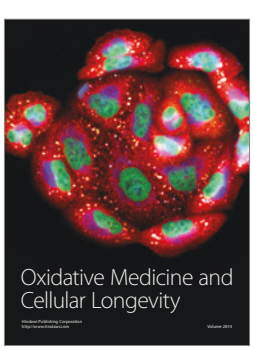










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