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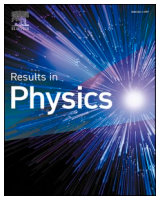

Direct and indirect transmission of typhoid fever model with optimal control

Olumuyiwa James Peter [a,*], Mohammed Olanrewaju Ibrahim [a], Helen Olaronke Edogbanya [b], Festus Abiodun Oguntolu [c], Kayode Oshinubi [d], Abdullahi Adinoyi Ibrahim [e], Tawakalt Abosede Ayoola [f], John Oluwasegun Lawal [a]

[a] Department of Mathematics, University of Ilorin, Ilorin, Kwara State, Nigeria
[b] Department of Mathematical Sciences, Federal University Lokoja, Kogi State, Nigeria
[c] Department of Mathematics, Federal University of Technology, Minna, Nigeria
[d] School of Foundation Studies, Lagos State University, Lagos State, Nigeria
[e] Department of Mathematical Sciences, Baze University Abuja, Nigeria
[f] Department of Mathematics, Osun State University Oshogbo, Nigeria

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ABSTRACT

In this paper, a model for direct and indirect transmission dynamics of typhoid fever with three control interventions is analyzed. Optimal control strategies are proposed to minimize both the disease burden and the intervention cost. We proved the existence and uniqueness of optimal control paths and obtained these optimal paths analytically using Pontryagin's Maximum Principle. We analyzed our results numerically to compare various strategies of proposed controls. It is observed that the implementation of the three controls among all strategies is most successful. Thus, we conclude that in order to reduce typhoid fever threat, all the three controls must be taken into consideration concurrently.

Introduction

Typhoid fever is an infection that is limited to humans and is endemic in the world's least developed countries. Despite advances in medical science and recent advances in water and environmental management, the disease remains a major health crisis. There are more than 16 million cases of typhoid worldwide each year and more than 600 000 deaths [1]. The typhoid fever bacterium Salmonella is transmitted by ingestion of contaminated water or food. When the bacterium enters the body, it travels in the intestines of human body and then enters the bloodstream [2]. The symptoms of this disease are abdominal pain, fever, stomach pain and either constipation or diarrhea. When the disease gets worse, high fever and severe diarrhea occurs. The incubation period is usually ten to fourteen days [3,4]. Some mathematical models have been formulated on the transmission of typhoid fever [5–19]. Other studies on infectious disease can be found in [20–24]. To the best of our knowledge, this is the first work on optimal control of typhoid fever model that has considered educational campaign, prevention via sanitation and screening along with early treatment as control intervention. This studies aims to extend and compliment previous work of [19] by formulating a model that captures the following controls; educational campaign, prevention via sanitation and screening along with early treatment and the application of optimal control theory to the model. The paper is arranged as follows: section two is devoted to describing the transmission of typhoid fever and the control variables. Section three, the analysis of the optimal control is discussed; section four contains numerical simulation of the optimal control of the model. Section five deals with the discussion of results for the optimal control. Finally, section six contains the conclusion of the study.

Materials and methods

The model subdivides the human population into four compartments: susceptible class $S(t)$, infected carrier class $I_c(t)$, infected class $I(t)$, and recovered class $R(t)$. Although typhoid is primarily contracted from environmental bacteria through contaminated food or water, it can also be contracted through direct person to person contact. To incorporate this real biological phenomenon, we consider an additional

* Corresponding author.
E-mail address: peterjames4real@gmail.com (O.J. Peter).

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Table 1
Descriptions of parameters.

Parameter	Initial Value	Source
μ_2	$0.2day^{-1}$	[1]
μ_1	$0.142\ day^{-1}$	[1]
μ_3	$0.2\ day^{-1}$	[1]
μ_4	$0.142\ day^{-1}$	[1]
ρ	0.5	Assumed
β_1	0.02	Assumed
β_2	0.01	Assumed
β_3	0.01	Assumed
δ	0.75	Assumed
θ	$10^6\ day^{-1}$	[6]
ε_1	0.4	Estimated
ε_2	0.5	Estimated
φ	0.3	Assumed
μ_b	$0.01\ day^{-1}$	[8]

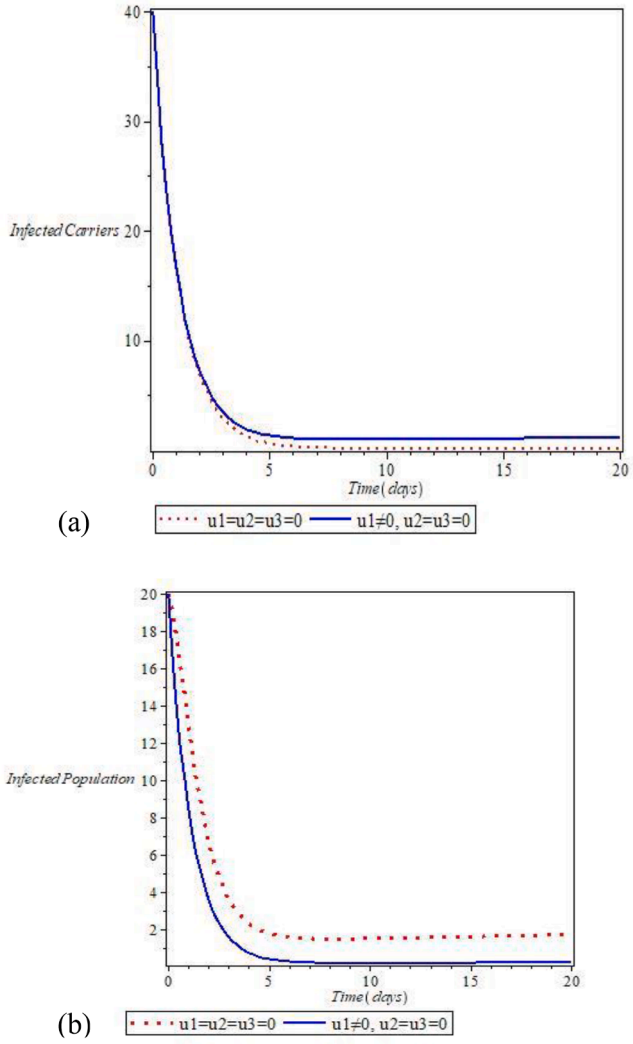


Fig. 1. Simulation result showing effect of using optimal educational campaign as the only control strategy.

compartment, *W(t),* which represents bacteria in the environment. We assume that susceptible individuals get infected with typhoid at a rate proportional to the susceptible population, *S(t)*. We incorporate additional parameter, φ which represents the progression rate from infected

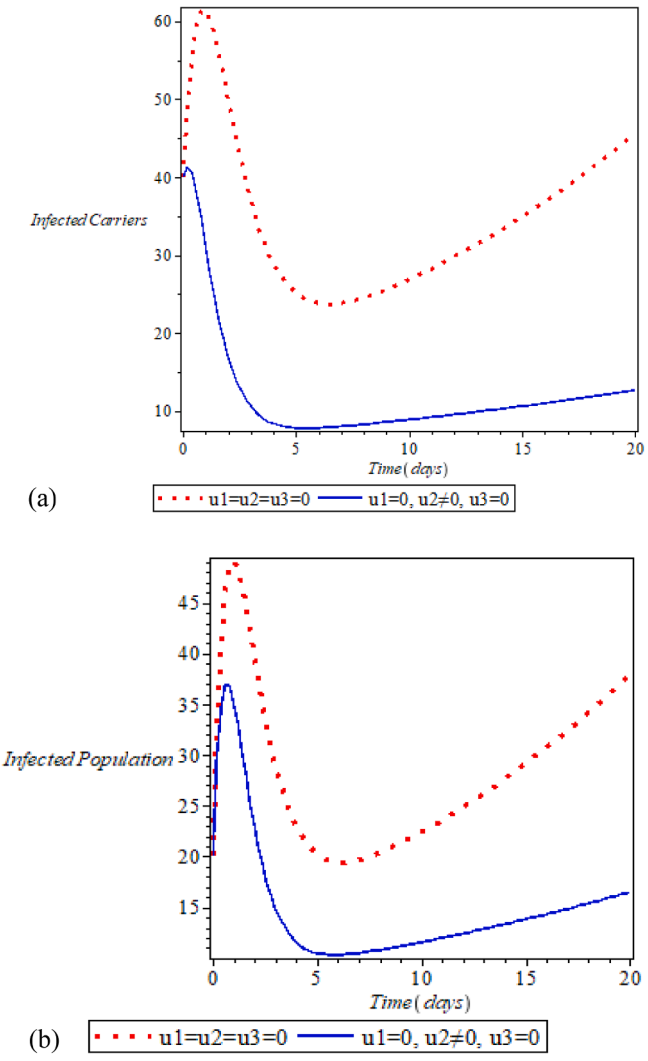


Fig. 2. Simulation result showing effect of using optimal prevention via sanitation as the only control strategy.

carrier class to infected class. individuals in the infected class, can recover from typhoid fever at a rate δ. The infected carrier and infected individuals both excrete bacteria into the environment. However, the rate of excretion by the infectious group ε_2 is higher than that of the carrier group ε_1 this is because infectious carriers do not show any signs of infection. The constant recruitment rate into the susceptible human population is represented by θ, the natural death rate of susceptible individuals, infected carrier individuals, infected individuals and recovered individuals is represented by μ_1, μ_2, μ_3 and μ_4 respectively, while the natural death rate of bacteria is represented by μ_b. The progression rate from infected carrier to infected class is denoted by φ. The following set of nonlinear ordinary differential equations in (1) is obtained from the above illustrations.

$$\left.\begin{aligned} S' &= \theta - \mu_1 S - S(\beta_1 I_c + \beta_2 I + \beta_3 W) \\ I_c' &= \rho S(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_2 + \varepsilon_1 - \varphi) I_c \\ I' &= (1-\rho) S(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_3 + \delta + \varepsilon_2) I + \varphi I_c \\ R' &= \delta I - \mu_4 R \\ W' &= \varepsilon_1 I_c + \varepsilon_2 I - \mu_b W \end{aligned}\right\} \quad (1)$$

Extension of the model into optimal control

In this section, we extend the model in (1) which comprises direct

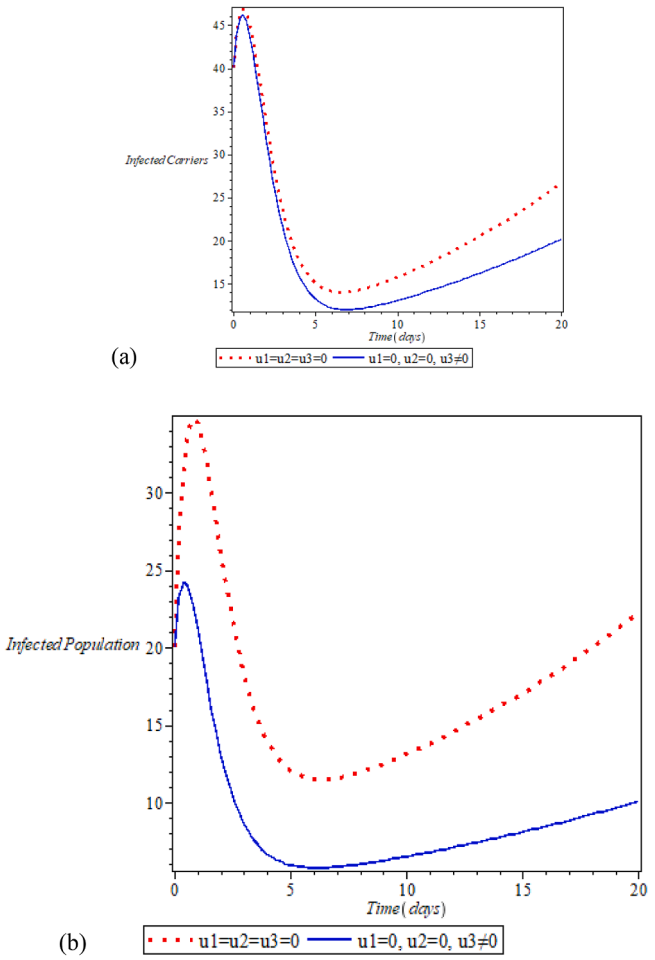


Fig. 3. Simulation result showing effect of using optimal screening along with early treatment as the only control strategy.

and indirect transmission of typhoid fever by incorporating three control strategies: namely, educational campaign, prevention via sanitation and screening along with early treatmentu_1, $u_2$andu_3 respectively. Furthermore, $0\leqslant, u_1(t), u_2(t), u_3(t)\leqslant 1$. When the control is zero this means that there is no effort invested in controlling the spread of typhoid fever that is, no control and when it is unity, maximum control is implemented. After incorporating the following assumptions and controls into the basic model, the model equations with controls are given as

$$\begin{aligned}
\frac{dS}{dt} &= \theta - \mu_1 S - S(\beta_1 I_c + \beta_2 I + \beta_3 W)(1-u_1)\\
\frac{dIc}{dt} &= \rho S(1-u_1)(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_2+\varepsilon_1) I_c - (\varphi + u_2) I_c\\
\frac{dI}{dt} &= (1-\rho)(1-u_1) S(\beta_1 I_c + \beta_2 I + \beta_3 W) + (1-u_2)\varphi I_c - (u_3+\delta) I - (\varepsilon_2+\mu_3) I\\
\frac{dR}{dt} &= (\mu_3+\delta) I - \mu_4 R\\
\frac{dW}{dt} &= \varepsilon_1 I_c + \varepsilon_2 I - \mu_b W
\end{aligned} \tag{2}$$

$S\geqslant 0$, $I_c\geqslant 0$, $I\geqslant 0$, $R\geqslant 0$, $W\geqslant 0$.The objective function is used to minimized the total number of carrier infected *Ic(t)* as well as infected individuals *I(t)* with typhoid fever and the cost associated with the control variables u_1^*, u_2^*, u_3^*. The objective function is defined as

$$J(u_1,u_2,u_3) = \int_0^{t_f} (A_1 I_c + A_2 I + K_1\frac{u_1^2}{2} + K_1\frac{u_2^2}{2} + K_1\frac{u_3^2}{2})dt \tag{3}$$

The state Eq. in (2) where A_1 and $A_2$are non-negative weighted constant of infected carrier *Ic(t)* and infected individuals *I(t)*. K_1, K_2 and K_3 are costs associated with educational campaign, prevention with sanitation and screening with early treatment. Our main target is to find the optimal control function (u_1^*, u_2^*, u_3^*) such that, $J(u_1^*, u_2^*, u_3^*) = min\{J(u_1,u_2,u_3) \mid (u_1,u_2,u_3)\in \Omega\}$where $\Omega = \{u = ((u_1,u_2,u_3)) : u_i(t)\ is\ Lebesque\ Measurable\ on\ [0,t_f], 0\leqslant u_i\leqslant 1, i = 1,\ 2,\ 3\}$ is the control set.

Existence of the optimal control

The essential conditions are derived from Pontryagin's Maximum Principle to be fulfilled by the controls and the corresponding states [25]. Using the differential equations of the state variables in (2), the Hamiltonian H as defined by [26–30] is given as

$H = \frac{dJ}{dt} + \lambda_1\frac{dS}{dt} + \lambda_2\frac{dI_c}{dt} + \lambda_3\frac{dI}{dt} + \lambda_4\frac{dR}{dt} + \lambda_5\frac{dW}{dt}$ that is,

$$\begin{aligned}
H(S,I_c,I,R,W) = &\left(A_1 I_c + A_2 I + K_1\frac{u_1^2}{2} + K_1\frac{u_2^2}{2} + K_1\frac{u_3^2}{2}\right)\\
&+\lambda_1(\theta - \mu_1 S - S(\beta_1 I_c + \beta_2 I + \beta_3 W)(1-u_1))\\
&+\lambda_2(\rho S(1-u_1)(\beta_1 I_c + \beta_2 I + \beta_3 W) - (\mu_2+\varepsilon_1) I_c - (\varphi+u_2) I_c)\\
&+\lambda_3((1-\rho)(1-u_1) S(\beta_1 I_c + \beta_2 I + \beta_3 W) + (1-u_2)\varphi I_c - (u_3+\delta) I - (\varepsilon_2+\mu_3) I)\\
&+\lambda_4((u_3+\delta) I - \mu_4 R)\\
&+\lambda_5(\varepsilon_1 I_c + \varepsilon_2 I - \mu_b W)
\end{aligned} \tag{4}$$

where $\lambda_1,\ \lambda_2, \lambda_3, \lambda_4, \lambda_5$ are adjoint variable functions.

Theorem 1: There exist an optimal control with the corresponding solution (S, I_c, I, R, W) corresponding to the state Eq. in (2) and the adjoint variables $\lambda_1(t)$, $\lambda_2(t)$, $\lambda_3(t)$, $\lambda_4(t)$, $\lambda_5(t)$ such that,

$$\begin{aligned}
\lambda_1' = &-\lambda_1(-\mu_1 - (\beta_1 I_c + \beta_2 I + \beta_3 W)(1-u_1)) - \lambda_2(\rho(1-u_1)(\beta_1 I_c + \beta_2 I + \beta_3 W))\\
&-\lambda_3((1-\rho)(1-u_1) S(\beta_1 I_c + \beta_2 I + \beta_3 W)),
\end{aligned}$$

$$\begin{aligned}
\lambda_2' = &-\lambda_1(-(1-u_1)\beta_2 S) - \lambda_2((1-u_1)\rho\beta_1 S - (\mu_2+\varepsilon_1) - (\varphi+u_2))\\
&-\lambda_3((1-\rho)(1-u_1)(\beta_1 S + (1-u_2)\varphi - \lambda_5\varepsilon_1 - A_1,
\end{aligned}$$

$$\begin{aligned}
\lambda_3' = &-\lambda_1(-(1-u_1)\beta_2 S) - \lambda_2(1-u_1)\rho\beta_2 S - \lambda_3((1-\rho)(1-u_1)(\beta_2 S - (\mu_3+\varepsilon_2)\\
&-(u_3+\delta)) - \lambda_4(u_3+\delta) - \lambda_5\varepsilon_2 - A_2,
\end{aligned}$$

$$\lambda_4' = -\lambda_4(-\mu_4),$$

$$\lambda_5' = -\lambda_5\mu_b - \lambda_1((1-u_1)\beta_3 S,$$

With boundary conditions

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = 0$$

Therefore, the optimal u_1^*, u_2^*, u_3^* are given by,

$$u_1^* = max\left\{0,\ min\left(1,\ \frac{S(\beta_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1-\rho) + \rho\lambda_2 - \lambda_1}{K_1}\right)\right\}$$

$$u_2^* = max\left\{0,\ min\left(1,\ \frac{(\lambda_2 + \lambda_3\varphi) I_c}{K_2}\right)\right\}$$

$$u_3^* = max\left\{0,\ min\left(1,\ \frac{(\lambda_3 - \lambda_4) I}{K_3}\right)\right\}$$

Proof. Using the results of Fleming and Rishel, [23] accordingly to obtain the adjoint variables, we differentiate the Hamiltonian H in (4) with respect to each variables that is, $S(t)$, $I_c(t)$, $I(t)$, $R(t)$, $W(t)$ such that,

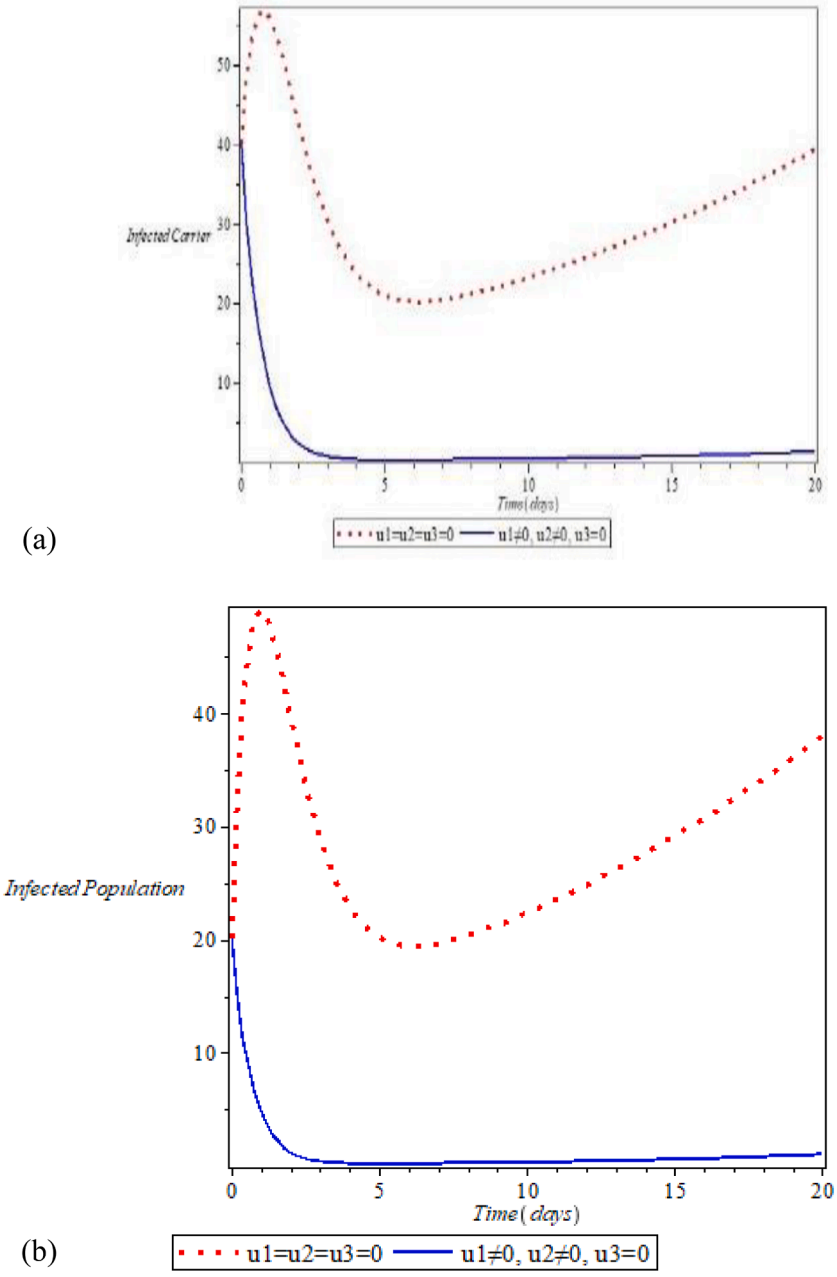


Fig. 4. Simulation result showing effect of using optimal educational campaign and prevention with sanitation as control strategy.

$$\frac{d\lambda_1}{dt} = \frac{-\partial H}{\partial S} = -\lambda_1(-\mu_1 - (\beta_1 I_c + \beta_2 I + \beta_3 W)(1-u_1)) - \lambda_2(\rho(1-u_1)(\beta_1 I_c + \beta_2 I + \beta_3 W)) - \lambda_3((1-\rho)(1-u_1)S(\beta_1 I_c + \beta_2 I + \beta_3 W))$$

$$\frac{d\lambda_2}{dt} = \frac{-\partial H}{\partial I_c} = -\lambda_1(-(1-u_1)\beta_2 S) - \lambda_2((1-u_1)\rho\beta_1 S - (\mu_2 + \varepsilon_1) - (\varphi + u_2)) - \lambda_3((1-\rho)(1-u_1)(\beta_1 S + (1-u_2)\varphi - \lambda_5\varepsilon_1 - A_1$$

$$\frac{d\lambda_3}{dt} = \frac{-\partial H}{\partial I} = -\lambda_1(-(1-u_1)\beta_2 S) - \lambda_2(1-u_1)\rho\beta_2 S - \lambda_3((1-\rho)(1-u_1)(\beta_2 S - (\mu_3 + \varepsilon_2) - (u_3 + \delta)) - \lambda_4(u_3 + \delta) - \lambda_5\varepsilon_2 - A_2$$

$$\frac{d\lambda_4}{dt} = \frac{-\partial H}{\partial R} = -\lambda_4(-\mu_4)$$

$$\frac{d\lambda_5}{dt} = \frac{-\partial H}{\partial W} = -\lambda_5\mu_b - \lambda_1((1-u_1)\beta_3 S$$

Also, to find the optimal control of the control variables set u_1, u_2, u_3using partial differential equation

$$\frac{\partial H}{\partial u_i} = 0 : i = 1, 2, 3$$

For u_1^*

$$\frac{\partial H(S, I_c, I, R, W)}{\partial u_1} = 0$$

Therefore

$$u_1^* = \frac{S(\beta_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1-\rho) + \rho\lambda_2 - \lambda_1}{K_1}$$

For u_2^*

$$\frac{\partial H(S, I_c, I, R, W)}{\partial u_2} = 0$$

$$u_2^* = \frac{(\lambda_2 + \lambda_3\varphi)I_c}{K_2}$$

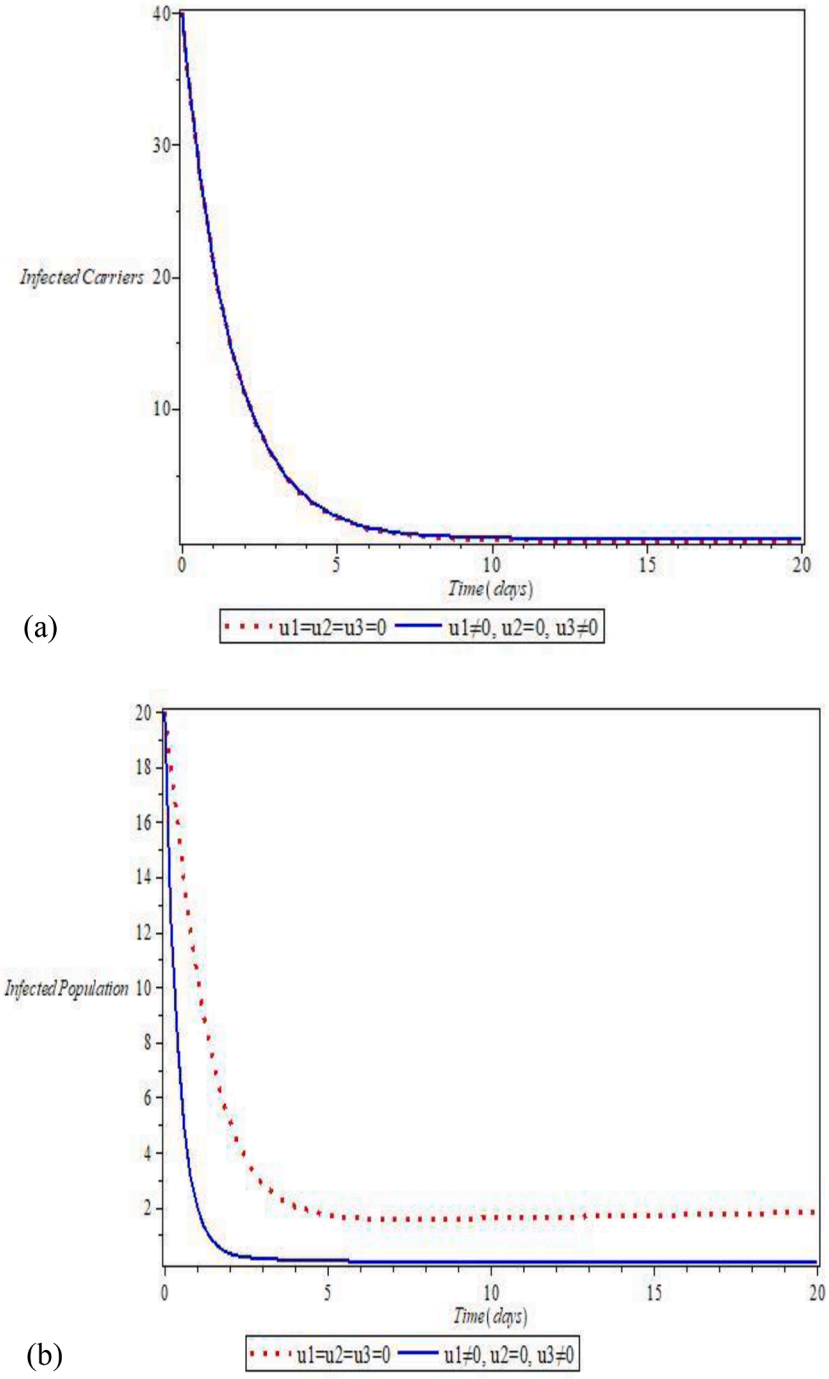


Fig. 5. Simulation result showing effect of using optimal educational campaign and screening with early treatment as control strategies on carriers population.

For u_3^*

$$\frac{\partial H(S, I_c, I, R, W)}{\partial u_3} = 0$$

$$u_3^* = \frac{(\lambda_3 - \lambda_4)I}{K_3}$$

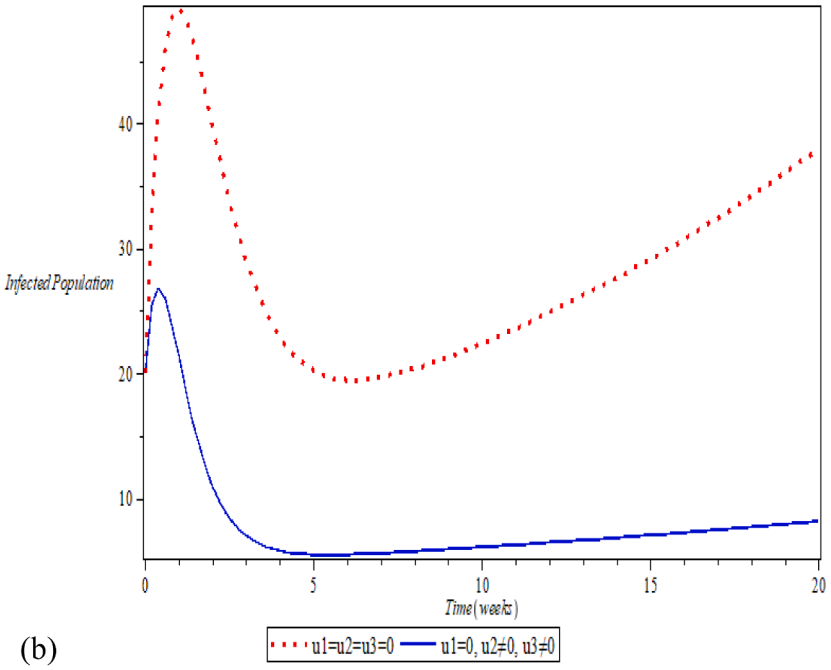
Therefore,

$$u_1^* = max\left\{0, min\left(1, \frac{S(\beta_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1-\rho) + \rho\lambda_2 - \lambda_1}{K_1}\right)\right\}$$

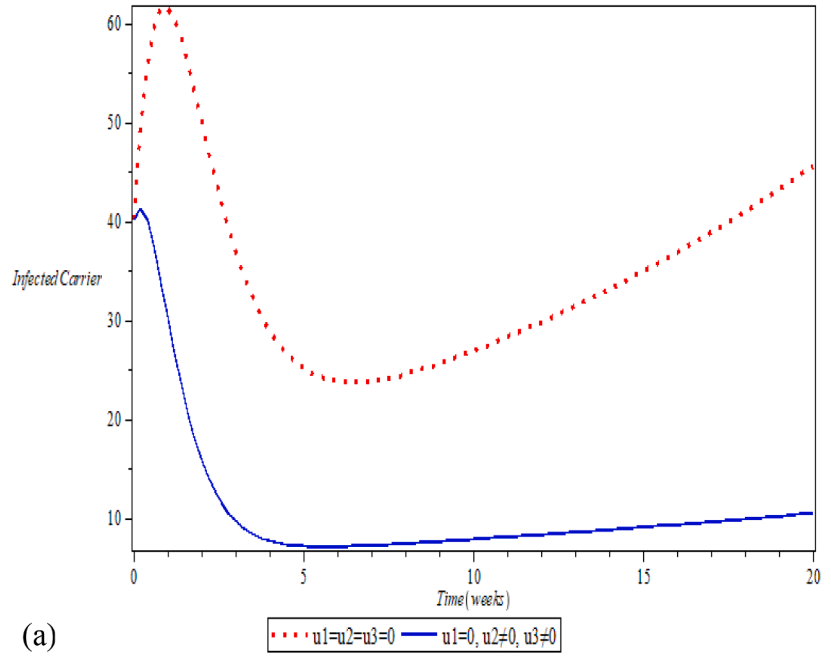
$$u_2^* = max\left\{0, min\left(1, \frac{(\lambda_2 + \lambda_3\varphi)I_c}{K_2}\right)\right\}$$

$$u_3^* = max\left\{0, min\left(1, \frac{(\lambda_3 - \lambda_4)I}{K_3}\right)\right\}$$

Based on the prior boundedness of the state and adjoint variables, the uniqueness of the optimal control has been established. By standard control arguments which involves the bound on the control, we can say that



(b)



(a)

Fig. 6. Simulation result showing effect of using optimal prevention with sanitation and early treatment with screening as control strategies on carriers' population.

$$u_1^* = \begin{cases} 0 & if \quad \dfrac{S(\beta_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1-\rho) + \rho\lambda_2 - \lambda_1}{K_1} < 0 \\ (0,\ 1) & if \quad \dfrac{S(\beta_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1-\rho) + \rho\lambda_2 - \lambda_1}{K_1} \leqslant 1 \\ 1 & if \quad \dfrac{S(\beta_1 I_c + \beta_2 I + \beta_3 W)(\lambda_3(1-\rho) + \rho\lambda_2 - \lambda_1}{K_1} > 1 \end{cases}$$

$$u_2^* = \begin{cases} 0 & if \quad \dfrac{(\lambda_2 + \lambda_3\varphi)I_c}{K_2} < 0 \\ (0,\ 1) & if \quad \dfrac{(\lambda_2 + \lambda_3\varphi)I_c}{K_2} \leqslant 1 \\ 1 & if \quad \dfrac{(\lambda_2 + \lambda_3\varphi)I_c}{K_2} > 1 \end{cases}$$

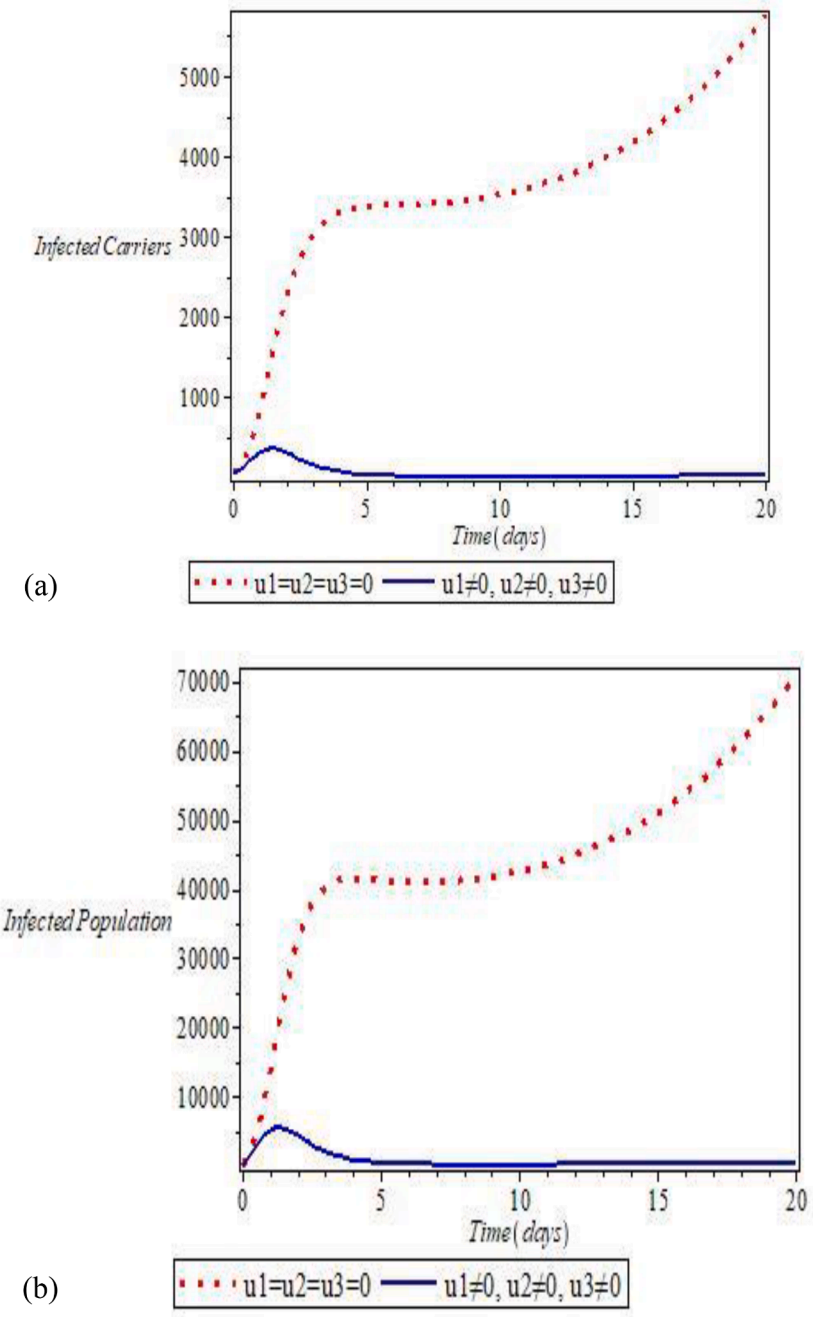


Fig. 7. Figure simulation result showing effect of using optimal educational campaign, prevention via sanitation and screening along with early treatment control strategies on infected population.

$$u_3^* = \begin{cases} 0 & if \quad \dfrac{(\lambda_3 - \lambda_4)I}{K_3} < 0 \\ (0,\ 1) & if \quad \dfrac{(\lambda_3 - \lambda_4)I}{K_3} \leqslant 1 \\ 1 & if \quad \dfrac{(\lambda_3 - \lambda_4)I}{K_3} > 1 \end{cases}$$

Numerical Simulation of the optimal control

We solve for the optimized system by using the values in the Table 1. The optimality system which consists of the state and adjoint equations. We use the forward-backwards sweep method and solve for the optimized system numerically. The simulation was carried out by using the values in table 1 and with the help of Maple 18 software. The following values for the coefficients for the states and controls are used. $A_1 = 1$, $A_2 = 1.5$, $K_1 = 1.5$, $K_2 = 0.02$, $K_3 = 0.15$.

To examine the effect of the control interventions, we considered the following strategies

(i) Applying educational campaign as the only control intervention u_1
(ii) Applying prevention via sanitation as the only control intervention u_2
(iii) Applying screening with early treatment as the only control intervention u_3
(iv) Applying educational campaign and prevention via sanitation as control intervention u_1 and u_2

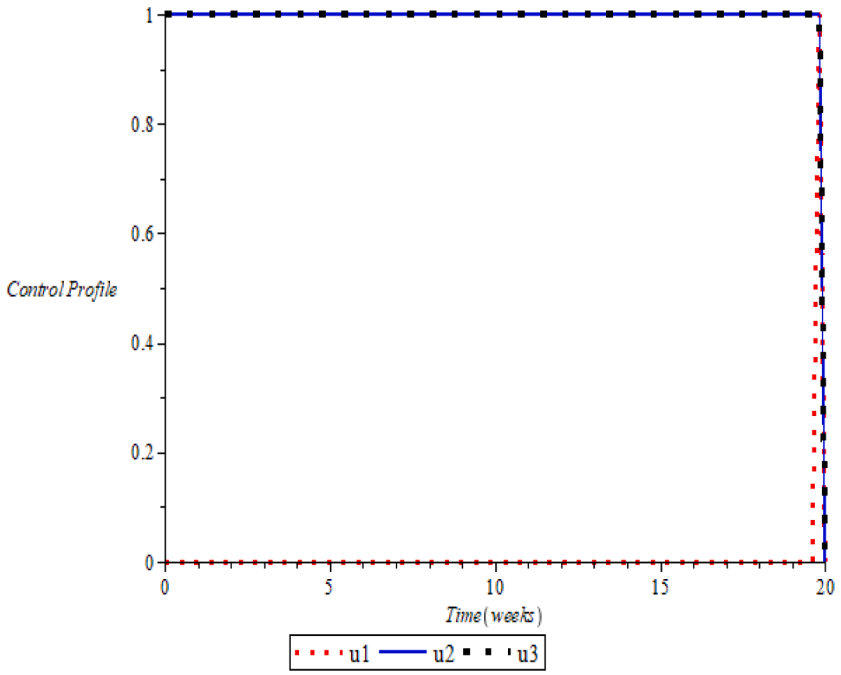


Fig. 8. Figure showing control profile for educational campaign, prevention with sanitation and screening with early treatment with screening.

(v) Applying educational campaign and screening along with early treatment as control intervention $u_1$and u_3
(vi) Applying prevention via sanitation and screening along with early treatment as control intervention $u_2$and u_3
(vii) Applying educational campaign, prevention via sanitation and screening along with early treatment as control intervention u_1, u_2, $u_3$respectively

Discussion of results for the optimal control

Control with prevention and sanitation

In Fig. 1a and b, we applied the educational campaign intervention $u_1 \neq 0$ as the only control on the infected carrier and infected population while we set the other controls$u_2$and u_3 to zero. We observed that this strategy has a positive effect on the infected carrier and infected population by decreasing the population of both classes. Thus, there should be a need for public awareness mostly in typhoid fever prone communities.

Prevention with sanitation

We incorporate prevention with sanitation as the only intervention which includes, provision of safe drinking water, improved toilet facilities, personal hygiene that is,$u_2 \neq 0$ while we set other controls to zero that is,$u_1$and u_3 Fig. 2a and b shows the rapid decrease in the population of the infected carrier and infected population. We conclude that, when prevention is combined with sanitation, this will reduce typhoid fever infection.

Screening along with early treatment

We applied screening with early treatment in this strategy to control the spread of typhoid fever. Fig. 3a and b show optimized screening with early treatment. Screening helps the asymptomatic carrier and the symptomatic infected individuals to know their status and when this is done and early treatment is implemented, this will drastically reduce the population of the asymptomatic carrier and the symptomatic infected population as shown in Fig. 3a and b.

Control with educational campaign and prevention via sanitation

In these strategies, we applied educational campaign and prevention combined with sanitation. Fig. 4a and b shows the effect of these controls. Public awareness is a vital tool in controlling the spread of infectious disease. When this is combined with sanitation as in the case of typhoid fever, this will have a positive impact in controlling the spread of typhoid fever.

Control with educational campaign and screening with early treatment

Fig. 5a and b show the effect of educating the carrier infected and infected populations and how an individual could prevent carriers from contracting typhoid fever together with screening of asymptomatic carrier of typhoid and early treatment of infected individuals will reduce the spread of typhoid fever.

Prevention with sanitation and screening with early treatment

Fig. 6a and b show the effect of applying prevention with sanitation and screening with early treatment. In this case we set $u_2 = u_3 \neq 0$ as control intervention. We conclude that applying prevention with sanitation and screening of asymptomatic individuals will reduce the infected carrier population. Also, when early treatment is implemented, on the infected individuals, this will reduce the infected population.

Control with educational campaign, prevention via sanitation and screening along with early treatment

In this strategy, we implemented all the three controls that is, control with educational campaign, control with prevention combined sanitation and screening with early treatmentu_1, u_2, $u_3$respectively as an intervention to control typhoid fever. Fig. 7a and b shows that after the implementation of the control, we achieved a better result as the population of the infected carrier and infected individuals reduced drastically. Therefore, we conclude that applying all three strategies is more effective in the control and containment of typhoid fever in typhoid fever prone communities over a given time period. Fig. 8 represents the control profile.

Conclusion

In this paper, we analysed a deterministic model on typhoid fever. We further extend the model in (1) to optimal control problems by adding three control variables which are educational campaign, prevention via sanitation and screening along with early treatment. By using the Pontryagin's Maximum Principle, we formulate the optimal control problem by analysing the conditions for the optimal control of the disease spread. The optimized system is solved numerically; the corresponding uncertain problem is solved by proposing new techniques. Numerical simulations are carried out to illustrate the analytical results. The numerical simulation of the model show that possible optimal control strategies become more effective in the control and containment of typhoid fever when educational campaign, prevention via sanitation and screening along with early treatment are combined optimally, these would reduce the spread of the disease.

Authors' contributions

All authors have read and approved the final manuscript.

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Author contribution statement

Olumuyiwa James Peter, conceived the idea, Mohammed Olanrewaju Ibrahim, Helen Olaronke Edogbanya, Festus Abiodun Oguntolu and Kayode Oshinubi did the simulation writing-original draft, Review Editing, Abdullahi Adinoyi Ibrahim, Tawakalt Abosede Ayoola, John Oluwasegun Lawal formulated the model, Olumuyiwa James Peter, and Kayode Oshinubi wrote the coding aspect.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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