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On the efficiency of optimal vaccination, environmental sanitation and treatment controls for typhoid fever: a mathematical study approach

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Abstract

Typhoid fever (TF) is a widespread infectious disease caused primarily by contaminated food, inadequate sanitation, and poor hygiene. Our research study has not only developed an optimal control model for the dynamics of TF transmission in the population, but has also provided practical recommendations for its management. The proposed model incorporates four control variables that account for vaccination, sanitation, proper hygiene, treatment, and disinfection and sterilization of the environment. The analytical solution to the optimal control problem is derived using Pontryagin's maximum principle. At the same time, numerical simulations and efficiency analyses have identified a strategy that effectively stops the spread of TF in endemic countries. Combining optimal sanitation and proper hygiene, treatment, disinfection, and sterilization of the environment has proven to be the most effective among the seven strategies examined, offering tangible solutions for policymakers, public health officials, and researchers. However, the combination of all four controls must be taken into account in order to reduce the risk of TF in a population.

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1. Introduction

The spread of infectious diseases has been a significant cause of death throughout history, and still in the modern day. The fourth leading cause of death, according to the World Health Organization (WHO), is lower respiratory infection. According to [35], infectious diseases are ailments that have the potential to spread throughout the populace rapidly, and are brought on by bacteria, viruses, epiphytes and parasites like worms or protozoa. The number of infectious diseases-related deaths is dramatically increasing. According to

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WHO estimates, up to 650,000 people die from severe flu each year, which affects 3-5 million people [3]. Emerging infectious disease epidemics seriously threaten social welfare, the economy, and public health, especially in low-income countries [2]. Infectious disease transmission and management, however, rely on the availability of healthcare facilities and resources [3, 2].

Despite better health services, clean water, and environmental sanitation, TF remains a significant health concern[8]. The prevalence of TF is rising globally, and the effectiveness of antibiotic treatment is decreasing due to increasing resistance to various antibiotics [7, 2, 32]. Though it may be prevented, typhoid fever is an infectious disease that only affects humans, and it has persisted as a public health issue in developing nations with poor sanitation, inadequate personal hygiene standards, and high food contamination areas [13, 10]. TF is caused by various *Salmonella species*, especially *Salmonella paratyphi* A, B, and C and *Salmonella paratyphi*. *Salmonella enterica* is among the most prevalent bacterial infections worldwide, resulting in about 200,000 deaths and 100 million illnesses annually [5]. In a single day, typhoid fever can spread around the world, killing more than 600,000 people each year and infecting 21 million people [16, 4].

The bacteria *Salmonella* in TF is passed from the human body to the intestines and ultimately to the bloodstream through the consumption of faeces-contaminated food or drink [16, 7]. Asymptomatic carriers are thought to be crucial in the development and spread of typhoid fever globally, and their existence makes it much more challenging to eradicate the disease through treatment and vaccine [21, 33]. In chronic cases, high fever and severe diarrhea may accompany TF symptoms, including stomach ache, fever, and abdominal pain [16]. Typically, the incubation phase lasts 10 to 14 days [8]. Without treatment, the mortality rate from typhoid might reach 30% [5]. Although TF is generally managed with antibiotics in low-income and middle-income nations. In high-income countries, the sanitary infrastructure upgrade system essentially controls enteric fever [7].

Quite a number of researchers and mathematicians have carried out research on infectious diseases (for instance, see [40, 39, 38, 35, 18, 6, 36, 22, 27, 26, 19, 20, 23, 1, 29, 30, 31] and some of the references therein). Precisely, [1] formulated a new deterministic model of malaria transmission dynamics. Analytical proof was provided for the existence of steady states. The model has a locally asymptotically stable disease-free equilibrium whenever the reproduction number, \mathcal{R}_0 , satisfies $\mathcal{R}_0 < 1$. Also, when $\mathcal{R}_0 > 1$, a unique globally asymptotically stable endemic equilibrium exists. Pontryagin's maximum principle was used to analyse the optimal control version of the model comprising four time-dependent optimal control variables. The efficiency and cost-effectiveness analyses showed the most efficient and effective combination strategy of the four optimal controls required to reduce the prevalence of malaria in the community.

The study by [40] proposed an algorithm to solve a system of fractional nonlinear equations in Caputo sense to model measles disease. The system stability is evaluated using the Ulam-Hyers approach. Broyden and Haar wavelet collocation methods were used to treat the fractional derivatives. The study emphasizes the importance of modern techniques in understanding measles outbreaks, and suggests their applicability to various mathematical models. The simulation results unequivocally demonstrate the suggested strategy effectiveness and its potential to advance the mathematical modelling of infectious diseases.

Similarly, [20] developed an optimal control problem to stop the current worldwide challenge of the coronavirus pandemic to lessen the disease's burden quickly. As a result, the objective functional of the issue was constructed. The model's optimality system was derived using Pontryagin's maximal principle. Next, a numerical solution to the resulting optimality system is found. The findings show that any control strategies investigated in the work can significantly reduce new cases and the prevalence of the disease cost-effectively. Of these, the combination of all four preventive and control measures is shown to be the most effective in reducing the disease burden in the population.

In addition, the authors in [39] examined a fractional order nonlinear dynamical system of Norovirus disease using a mathematical model consisting of susceptible, exposed, quarantined, infected, and recovered classes. The study uses the Caputo-Fabrizio fractional derivative (CFFD) for qualitative theory and approximate solutions. Fixed point theory, Laplace Transform, and Adomian decomposition approach were used to get approximate results for each compartment. The fixed-point approach established sufficient conditions for the solution's existence and uniqueness. The numerical findings are performed by using Matlab 16.

Mathematical modelling and analysis have helped understand infectious disease transmission dynamics and control management. It dramatically impacts forecasting appropriate management measures, evaluating them, and determining how cost-effective they are [11]. Numerous mathematical models of TF transmission have been developed [9, 10, 11, 12, 13, 21, 14, 15, 37, 4, 25, 16, 17, 7, 5, 2, 3]. Specifically, [16] analyzed a deterministic model for the dynamics of direct and indirect typhoid fever transmission, and by including three control variables that represent the educational campaign, prevention via sanitation and screening along with early treatment, extended the model to an optimal control problem. Using Pontryagin's Maximum Principle, optimal control solutions were put forth and used to complement the existence and uniqueness of the optimal control problem. In order to complement the analytical findings, numerical simulations were carried out on the optimized system. The model's numerical simulation demonstrates that implementing the three proposed controls is most effective when the educational campaigns, prevention via sanitation and screening, and early treatment are combined optimally to prevent the spread of the disease.

Furthermore, the work of [25] developed a mathematical model to describe typhoid fever transmission dynamics, including three optimal control measures. Runge-Kutta of order four was employed for the numerical simulation, and the Pontryagin's maximum principle was utilized to assess each control's effectiveness. Thus, the dynamics of disease transmission in the community were significantly impacted by the deployment of the control(s), whether done singly or simultaneously.

Similarly, the authors in [14] developed and analyzed a model for typhoid disease control. Using Lyapunov theory, the local and global stability of the disease-free equilibrium around the reproduction number were demonstrated. Additionally, the Centre Manifold Theory was used to examine the type of bifurcation exhibited by the model, and it was discovered that the model displays a forward bifurcation. In order to apply three-time dependent controls, the model was re-formulated as an optimum control problem. The optimal control theory was used to determine the circumstances in which disease spread can be stopped and to analyze the effects of various control instruments on the disease

dynamics. According to the numerical simulations and efficiency analysis, treatment must be incorporated into all control strategies to minimize typhoid fever spread drastically.

Interestingly, [38] used the Atangana–Baleanu operator and the Mittag–Leffler function in Caputo sense to analyze the dynamical model of typhoid fever. Local and global stability analysis of the disease-free and endemic equilibrium points of the classical model were examined by constructing appropriate Lyapunov functions. It was found that the typhoid fever model has a unique solution and is locally and globally stable around disease-free and endemic equilibrium points. Adams–Bashforth scheme was employed for the numerical solution of the model. The study reveals that a high interaction rate between the susceptible and infected populations increases the value of the reproduction number, leading to an increasing spread of the disease; conversely, a lower interaction rate results in a lower transmission in the community.

Using a nonlinear system, Lawal *et al.* [34] developed and analysed a mathematical model involving seven distinct compartments that consider medically hygienic individuals and vaccination while analyzing the dynamics of TF transmission in a community. To the extent of our knowledge, however, no publication on existing optimal control models of TF disease has explicitly considered vaccination, sanitation and proper personal hygiene, treatment, and disinfection and sterilization as control interventions. To better understand how these measures affect the management of TF in communities, this study builds on and extends earlier research of [34] by developing a model that incorporates the impacts of four optimal control variables, which are time-dependent, accounting for vaccination, sanitation and proper personal hygiene, treatment, and disinfection and sterilization of the environment. The structure of the paper is as follows: Section 2 briefly presents the non-optimal control TF model. Description and formulation of the optimal control problem is also considered in this section. Section 3 considers the analysis of the optimal control model. Section 4 covers the numerical simulations of the optimality system, results presentation and discussion, and efficiency analysis. Section 5 details the concluding remarks of the study.

2. Description and formulation of typhoid fever model

In this section, we briefly introduce an existing non-optimal control typhoid fever model which incorporates constant control parameters. The model is later extended to an optimal control counterpart which is rigorously analysed in this paper.

2.1. Non-optimal control typhoid fever model

In a previous work, Lawal *et al.* [34] extensively studied a deterministic compartmental model describing the transmission dynamics of typhoid fever in the presence of vaccination, environmental sanitation with proper hygiene, treatment and disinfection and sterilization as controls. The model considers both human population and bacteria concentration in the environment. Seven epidemiological classifications comprise the entire human population: susceptible, vaccinated, exposed, symptomatic, treated, recovered, and medically hygienic individuals. The variable $B_c(t)$ describes the population of bacteria. Consequently, $N(t) = S(t) + E(t) + T(t) + I(t) + R(t) + V(t) + M(t)$.

The system of ordinary differential equations which governs the dynamics of TF model is as given in (2.1).

$$\begin{aligned}
\frac{dS}{dt} &= (1 - \phi)\Lambda + \kappa V + \varepsilon R - \beta S(B_c + \eta I) - (\pi + \mu)S, \\
\frac{dV}{dt} &= \pi S - (1 - m)\beta V(B_c + \eta I) - (\kappa + \mu)V, \\
\frac{dE}{dt} &= \beta(B_c + \eta I)(S + (1 - m)V) - (\alpha + \mu)E, \\
\frac{dI}{dt} &= \alpha E + \xi T - (\gamma + \sigma_1 + \mu + \delta_1)I, \\
\frac{dT}{dt} &= \gamma I - (\xi + \sigma_2 + \mu + \delta_2)T, \\
\frac{dR}{dt} &= \sigma_1 I + (1 - \varphi)\sigma_2 T - (\theta + \varepsilon + \mu)R, \\
\frac{dM}{dt} &= \phi\Lambda + \varphi\sigma_2 T + \theta R - \mu M, \\
\frac{dB_c}{dt} &= \rho I - \mu_1 B_c,
\end{aligned} \tag{2.1}$$

with initial conditions:

$$S(0) > 0, V(0) \geq 0, E(0) \geq 0, I(0) > 0, T(0) \geq 0, R(0) \geq 0, M(0) \geq 0, B_c(0) \geq 0. \tag{2.2}$$

Tables 1 and 2, respectively, present the descriptions of the variables and parameters for model (2.1).

Table 1: Model's variables description

Variable	Description
S	Susceptible human population
V	Vaccinated human population
E	Exposed human population
I	Symptomatic human population
T	Treated population (including drug complaint and non-drug complaint) human
R	Recovered human population
M	Medically hygienic or conscious human population
N	Total human population
B_c	Environmental bacterial concentration

2.2. Optimal control problem formulation

This section is concerned with the extension of the non-optimal control typhoid fever model presented by (2.1) to its optimal control version. In order to develop the optimal control model, we further consider the following four time-dependent control variables:

1. The first control $0 \leq u_1(t) \leq 1$ represents the vaccination control, assuming only the susceptible humans receive the vaccine.

Table 2: Synopsis of the parameters of the model

Parameter	Description
Λ	Rate of human population recruitment
μ	The natural death rate among humans
$1 - \phi$	Proportion of susceptible humans recruitment rate
ϕ	Proportion of the recruitment rate for medically vigilant humans
π	Vaccination rate
ε	Rate of immunity loss per person
β	Rate of effective transmission among humans
η	Humans with symptoms and their relative transmissibility
α	Rate of transition from an exposed state to an infectious state
σ_1	Human symptomatic recovery rate
δ_1	Death by disease in people with symptoms of infection
ξ	Relapse rate in non-drug complaints
δ_2	Disease-related mortality in noncompliant drug users
σ_2	The rate at which drug-compliant humans recover
φ	The rate at which drug-compliant humans join vigilant class
ρ	Rate at which symptomatic humans shed bacteria
μ_1	Decay rate of bacteria from the environment
m	Vaccine efficacy
κ	Vaccine waning rate
θ	Progression rate of recovered individuals to medically hygienic class
α_1	Additional mortality rate of bacteria induced by the chemical intervention
α_2	Proportion of effective treatment for symptomatic infectious individuals

2. The second control, $0 \leq u_2(t) \leq 1$, denotes sanitation and proper hygiene to prevent typhoid fever through contamination of food and water by bacteria. The incidence function is modified to include sanitation and proper hygiene controls, resulting in the modified version of the incidence function in (2.1) as

$$\beta S(B_c + \eta I) = (1 - u_2(t))\beta S(B_c + \eta I) \quad (2.3)$$

3. The third control variable, $0 \leq u_3(t) \leq 1$, represents the treatment efforts, including patient care and proper administration. The efficacy and duration of treatment vary depending on the patient's immune response. Therefore, considering constant treatment rate of symptomatic infectious individuals denoted as γ in the previous model (2.1) as $u_3(t)$, so that the recovery rate of symptomatic infectious individuals, σ_1 , and treated individuals, σ_2 , are modified based on treatment control $u_3(t)$. Thus, recovery rates become

$$\sigma_1 = \sigma_1 + \alpha_1 u_3(t), \quad \sigma_2 = \sigma_2 + \alpha_1 u_3(t),$$

where the proportion of effective treatment for individuals in class I is denoted by α_1 . Following the idea in [14], considering the fact that the proportion of effective treatment decreases disease-induced death of infectious humans with clinical signs,

the disease-induced death rate is modified as

$$\delta_1 = (1 - a_1 u_3(t))\delta_1, \quad \delta_2 = (1 - a_1 u_3(t))\delta_2.$$

Additionally, treatment control makes it possible to reduce the amount of bacteria that infectious people excrete. So,

$$\rho = (1 - a_1 u_3(t))\rho.$$

4. The fourth control, $0 \leq u_4(t) \leq 1$, denotes disinfection and sterilization efforts to prevent typhoid fever through reducing harmful bacteria from surfaces or items or high-touch areas, particularly in toilets, hospitals, schools, markets and homes, contact with infected persons, contamination of vegetables, fruits and food by the bacteria. Thus, following the idea of [41], the incidence function in (2.3) is further modified to explicitly include disinfection and sterilization control. Thus, we are led to a modified incidence function given by

$$\beta S(B_c + \eta I) = [2 - u_2(t) - u_4(t)]\beta S(B_c + \eta I)$$

It is essential to know that this control will increase bacterial decomposition. Consequently, the rate of bacteria decay in model (2.1) becomes

$$\mu_1 = \mu_1 + a_2 u_4(t),$$

where a_2 denotes the additional mortality rate of bacteria induced by chemical intervention.

In view of the above description and assumptions, the optimal control model for typhoid fever dynamics based on the existing model (2.1) is obtained as

$$\begin{aligned} \frac{dS}{dt} &= (1 - \phi)\Lambda + \kappa V + \varepsilon R - (2 - u_2(t) - u_4(t))\beta S(B_c + \eta I) - (u_1(t) + \mu)S, \\ \frac{dV}{dt} &= u_1(t)S - (2 - u_2(t) - u_4(t))(1 - m)\beta V(B_c + \eta I) - (\kappa + \mu)V, \\ \frac{dE}{dt} &= (2 - u_2(t) - u_4(t))\beta(B_c + \eta I)(S + (1 - m)V) - (\alpha + \mu)E, \\ \frac{dI}{dt} &= \alpha E + \xi T - (u_3(t) + \sigma_1 + a_1 u_3(t) + \mu + (1 - a_1 u_3(t))\delta_1)I, \\ \frac{dT}{dt} &= u_3(t)I - (\xi + \sigma_2 + a_1 u_3(t) + \mu + (1 - a_1 u_3(t))\delta_2)T, \\ \frac{dR}{dt} &= (\sigma_1 + a_1 u_3(t))I + (1 - \phi)(\sigma_2 + a_1 u_3(t))T - (\theta + \varepsilon + \mu)R, \\ \frac{dM}{dt} &= \phi\Lambda + \phi(\sigma_2 + a_1 u_3(t))T + \theta R - \mu M, \\ \frac{dB_c}{dt} &= (1 - a_1 u_3(t))\rho I - (\mu_1 + a_2 u_4(t))B_c, \end{aligned} \tag{2.4}$$

with initial conditions:

$$S(0) > 0, V(0) \geq 0, E(0) \geq 0, I(0) > 0, T(0) \geq 0, R(0) \geq 0, M(0) \geq 0, B_c(0) \geq 0. \tag{2.5}$$

Our main goal is to minimize the size of symptomatic infectious human sub-population ($I(t)$) and the number of bacteria ($B_c(t)$) in the community as well as the costs associated with the implementation of vaccination control ($u_1(t)$), sanitation and proper hygiene control ($u_2(t)$), treatment control ($u_3(t)$) and disinfection and sterilization ($u_4(t)$) and maximize the size of medically vigilant and hygienic human sub-population ($M(t)$). Thus, we consider the objective (or cost) functional defined as

$$\mathcal{J}(u_1, u_2, u_3, u_4) = \int_0^{t_f} \left(A_1 I - A_2 M + A_3 B_c + \frac{1}{2} C_1 u_1^2 + \frac{1}{2} C_2 u_2^2 + \frac{1}{2} C_3 u_3^2 + \frac{1}{2} C_4 u_4^2 \right) dt \quad (2.6)$$

subject to the state system (2.4), where A_1 , A_2 , and A_3 represent the positive weight constraints for symptomatic infectious human, medically hygienic individuals and bacteria population and C_i , $i = 1, 2, 3, 4$ stands for the positive weight constants for the optimal control variables, $u_i(t)$, $i = 1, \dots, 4$. the optimal control intervention is implemented over the interval $[0, t_f]$ where the final time interval is denoted by t_f . The non-linearity of the control intervention is characterized by the quadruple control functions. As a result, the nonlinear terms $\frac{1}{2} C_1 u_1^2$, $\frac{1}{2} C_2 u_2^2$, $\frac{1}{2} C_3 u_3^2$ and $\frac{1}{2} C_4 u_4^2$ are used to represent the costs function associated with vaccination, sanitation and proper hygiene, treatment and disinfection and sterilization control strategies. Determining a quadruple control $u^* = (u_1^*, u_2^*, u_3^*, u_4^*)$ which satisfies

$$\mathcal{J}(u^*) = \min\{J(u_1, u_2, u_3, u_4) : (u_1, u_2, u_3, u_4) \in U\} \quad (2.7)$$

is consequently the overall interest, where U is a non-empty Lebesgue measurable set for the controls $0 \leq u_1(t) \leq 1$, $0 \leq u_2(t) \leq 1$, $0 \leq u_3(t) \leq 1$ and $0 \leq u_4(t) \leq 1$ with $t \in [0, t_f]$.

3. Analysis of the optimal control model

The study of the non-autonomous system of model (2.4) is based on the first-order necessary condition of Pontryagin's maximum principle [28] for finding optimal solutions to various control problems.

3.1. Characterization of the optimal control

To characterize the four optimal controls, the key requirements, which must be satisfied by the controls and the corresponding states, are derived from Pontryagin's maximal principle [28]. The Hamiltonian is given by

$$\begin{aligned} H = & A_1 I - A_2 M + A_3 B_c + \frac{1}{2} C_1 u_1^2(t) + \frac{1}{2} C_2 u_2^2 + \frac{1}{2} C_3 u_3^2 + \frac{1}{2} C_4 u_4^2 \\ & + \lambda_1 [(1 - \phi)\Lambda + \kappa V + \epsilon R - (2 - u_2(t) - u_4(t))\beta S(B_c + \eta I) - (u_1 + \mu)S] \\ & + \lambda_2 [u_1 S - (2 - u_2(t) - u_4(t))(1 - m)\beta V(B_c + \eta I) - (\kappa + \mu)V] \\ & + \lambda_3 [(2 - u_2(t) - u_4(t))\beta(B_c + \eta I)(S + (1 - m)V) - (\alpha + \mu)E] \\ & + \lambda_4 [\alpha E + \xi T - (u_3 + \sigma_1 + a_1 u_3 + \mu + (1 - a_1 u_3)\delta_1)I] \\ & + \lambda_5 [u_3 I - (\xi + \sigma_2 + a_1 u_3 + \mu + (1 - a_1 u_3)\delta_2)T] \\ & + \lambda_6 [(\sigma_1 + a_1 u_3)I + (1 - \phi)(\sigma_2 + a_1 u_3)T - (\theta + \epsilon + \mu)R] \\ & + \lambda_7 [\phi\Lambda + \phi(\sigma_2 + a_1 u_3)T + \theta R - \mu M] \end{aligned} \quad (3.1)$$

$$+ \lambda_8[(1 - a_1 u_3)\rho I - (\mu_1 + a_2 u_4)B_c],$$

where, $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8$ are adjoint variable corresponding to the state variables of the model (2.4). Accordingly, the adjoint equations can be derived from

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial x}, \quad (3.2)$$

where $x = (S, V, E, I, T, R, M, B_c)$.

Theorem 3.1. *The adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8$ exist and satisfy the adjoint system for an optimal control quadruple u^* with corresponding solutions S, V, E, I, T, R, M, B_c of the associated state system satisfying (2.7) such that*

$$\begin{aligned} \frac{d\lambda_1}{dt} &= (\lambda_1 - \lambda_3)(2 - u_2 - u_4)\beta(B_c + \eta I) + \lambda_1(u_1 + \mu) - \lambda_2 u_1, \\ \frac{d\lambda_2}{dt} &= -\lambda_1 \kappa + \lambda_2(\kappa + \mu) + (\lambda_2 - \lambda_3)(2 - u_2 - u_4)(1 - m)\beta(B_c + \eta I), \\ \frac{d\lambda_3}{dt} &= \lambda_3(\alpha + \mu) - \lambda_4 \alpha, \\ \frac{d\lambda_4}{dt} &= -A_1 + (\lambda_1 - \lambda_3)[(2 - u_2 - u_4)\beta \eta S] + (\lambda_2 - \lambda_3)[(1 - m)\beta \eta V] \\ &\quad + \lambda_4[(u_3 + \sigma_1 + a_1 u_3 + \mu + (1 - a_1 u_3)\delta_1)] - \lambda_5 u_3 - \lambda_6[(\sigma_1 + a_1 u_3)] - \lambda_8[(1 - a_1 u_3)\rho], \\ \frac{d\lambda_5}{dt} &= -\lambda_4 \xi + \lambda_5(\xi + \sigma_2 + a_1 u_3 + \mu + (1 - a_1 u_3)\delta_2) - \lambda_6(1 - \varphi)(\sigma_2 + a_1 u_3) - \lambda_7 \varphi(\sigma_2 + a_1 u_3) \\ &\quad (3.3) \\ \frac{d\lambda_6}{dt} &= -\lambda_1 \varepsilon + \lambda_6(\theta + \varepsilon + \mu) - \lambda_7 \theta, \quad \frac{d\lambda_7}{dt} = A_2 + \lambda_7 \mu, \\ \frac{d\lambda_8}{dt} &= -A_3 + (\lambda_1 - \lambda_3)(2 - u_2 - u_4)\beta S + (\lambda_2 - \lambda_3)(2 - u_2 - u_4)(1 - m)\beta V + \lambda_8(\mu_1 + a_2 u_4), \end{aligned}$$

with transversality conditions

$$\lambda_i(t_f) = 0, i = 1, 2, \dots, 8 \quad (3.4)$$

and optimal control characterizations given by

$$\begin{aligned} u_1^* &= \min \left\{ 0, \max \left\{ 1, \frac{(\lambda_1 - \lambda_2)S}{C_1} \right\} \right\}, \\ u_2^* &= \min \left\{ 0, \max \left\{ 1, \frac{(\lambda_3 - \lambda_1)\beta S(B_c + \eta I) + (\lambda_3 - \lambda_2)(1 - m)\beta V(B_c + \eta I)}{C_2} \right\} \right\}, \\ u_3^* &= \min \left\{ 0, \max \left\{ 1, \frac{\lambda_4(1 + a_1 - a_1 \delta_1)I + \lambda_5(a_1 - a_1 \delta_2)T - \lambda_5 I - \lambda_6 a_1 I - \lambda_6(1 - \varphi)a_1 T - \lambda_7 \varphi a_1 T + \lambda_8 a_1 \rho I}{C_3} \right\} \right\}, \\ u_4^* &= \min \left\{ 0, \max \left\{ 1, \frac{(\lambda_3 - \lambda_1)\beta S(B_c + \eta I) + (\lambda_3 - \lambda_2)(1 - m)\beta V(B_c + \eta I) + \lambda_8 a_2 B_c}{C_4} \right\} \right\}. \end{aligned} \quad (3.5)$$

Proof. By taking the partial derivative of the Hamiltonian in (3.1) with respect to each of the state variables, S, V, E, I, T, R, M, B_c (in view of (3.2)), the adjoint system of equations

(3.3) is obtained. Additionally, we use the partial differential equation $\frac{\partial H}{\partial u_i} = 0$, $i = 1, 2, 3, 4$, to determine the four optimal control variables as

$$\begin{aligned} u_1^* &= \frac{(\lambda_1 - \lambda_2)S}{C_1}, \quad u_2^* = \frac{(\lambda_3 - \lambda_1)\beta S(B_c + \eta I) + (\lambda_3 - \lambda_2)(1 - m)\beta V(B_c + \eta I)}{C_2}, \\ u_3^* &= \frac{\lambda_4(1 + \alpha_1 - \alpha_1 \delta_1)I + \lambda_5(\alpha_1 - \alpha_1 \delta_2)T - \lambda_5 I - \lambda_6 \alpha_1 I - \lambda_6(1 - \varphi)\alpha_1 T - \lambda_7 \varphi \alpha_1 T + \lambda_8 \alpha_1 \rho I}{C_3}, \\ u_4^* &= \frac{(\lambda_3 - \lambda_1)\beta S(B_c + \eta I) + (\lambda_3 - \lambda_2)(1 - m)\beta V(B_c + \eta I) + \lambda_8 \alpha_2 B_c}{C_4}. \end{aligned} \quad (3.6)$$

Therefore, imposing the bounds on the controls in (3.6) yields the control characterization in (3.5). This completes the proof. \square

4. Numerical simulations, results and efficiency analysis

4.1. Numerical simulation

Here, the study uses numerical simulations to analyze the dynamic behavior of the TF disease model (2.4) with a view to gaining insight into the impact of the four time-dependent control variables under consideration on the population dynamics of TF disease, following the guidelines laid by [34]. The forward-backward sweep method based on Runge-Kutta fourth order scheme is used to solve the optimality system, which combines the state system (2.4) and the adjoint system (3.3). The iterative scheme is implemented in MATLAB. The state system (2.4) is solved forward in time, while the adjoint system (3.3) is solved backward in time. In order to simulate the model for various scenarios of disease outbreaks, the initial conditions of the model variables are taken from [34], while the model parameter values are as given in Table 3. Implementation of the optimality system is carried out under seven different control combination strategies involving the use of at least any one of the four time-dependent control functions. These strategies are defined as follows: Strategy 1, S1 – combination of optimal vaccination (u_1) and treatment (u_3) only, strategy 2, S2 – Combination of optimal sanitation with proper hygiene (u_2) and treatment (u_3) only, strategy 3, S3 – combination of optimal vaccination (u_1), sanitation with proper hygiene (u_2) and treatment (u_3) only, strategy 4, S4 – combination of optimal vaccination (u_1), sanitation with proper hygiene (u_2) and disinfection and sterilization (u_4) only, strategy 5, S5 – combination of optimal vaccination (u_1), treatment (u_3) and disinfection and sterilization (u_4) only, strategy 6, S6, – combination of optimal sanitation with proper personal hygiene (u_2), treatment (u_3) and disinfection and sterilization (u_4) only and strategy 7, S7 – combination of all the four optimal control interventions (u_1, u_2, u_3, u_4).

In what follows, we present the results arising from the implementation of these seven strategies.

4.2. Results

The use of only one control intervention may not be enough to effectively stop the spread of TF in the population, hence the need for the proposed seven combination strategies. Here, the graphical results obtained from the implementation of the strategies are presented.

Table 3: Parameter values of the model

Parameter	Baseline Value	Source	Parameter	Baseline Value	Source
Λ	10726.4451	Estimated from [24]	ξ	9.0×10^{-6}	Assumed
μ	$\frac{1}{55.75 \times 365}$	Estimated from [24]	δ_2	0.001	[25]
ϕ	0.15	Assumed	σ_2	0.1	[25]
ε	9.04×10^{-4}	[14]	φ	0.005	Assumed
β	1.0×10^{-8}	Assumed	ρ	0.50	[16]
η	1.0×10^{-5}	Assumed	μ_1	0.4	[25]
α	0.03	[14]	m	0.95	[14]
γ	0.002	[25]	κ	9.041×10^{-4}	[14]
σ_1	0.75	[16]	α_1	0.7	[14]
δ_1	0.2	[16]	α_2	0.3	[14]

4.2.1. S1 – Combination of optimal vaccination $u_1(t)$ and treatment $u_3(t)$ only

Figures 1–fig:cps1 show the impact of using the combination of optimal vaccination $u_1(t)$ and treatment $u_3(t)$ as the only control measure on the dynamics of typhoid fever transmission in a population. By minimizing the objective functional \mathcal{J} , while the other two controls, u_2 and u_4 , are set to zero, i.e. $u_1, u_3 \neq 0, u_2 = u_4 = 0$, this demonstrates how well the control reduces transmission. In Figure 1, it can be seen that the presence of control has a declining influence on the susceptible population right from day one of the simulation and is significant on the 10th day and by day 60, the susceptible population had been reduced to near zero and maintained throughout the 100 days. Similarly, Figure 2 demonstrates that the vaccination and treatment as control had no discernible impact on the vaccinated compartment until about 93 days after applying the control. After that time, a considerable increase peaked at 96 days and remained through 100 days. Likewise, Figures 3 and 5 show this strategy has a decreasing effect on symptomatic infectious humans and the density of bacteria in the environment. The number of infectious humans is reduced to nearly zero at 80 days and maintained the state throughout the simulation time interval. Additionally, Figure 4 demonstrates that the control intervention has an appreciable impact on the incidence population. There is a drop in the new cases of TF compared to when there is no control, the fall is observed from the 8th day and does not go above 6 cases throughout the entire 100 days of the simulation. Therefore, vaccination as a preventative step and treatment as the curative measure have great positive effects on the spread of TF. Generally speaking, vaccination and treatment are required, especially in regions that are prone to TF. Figure 6 depicts the control profile. It shows that vaccination control is implemented on the 5th day up to 0.37 and maintained this level until 40 days. Thereafter, there was a quick increase at the 40 days of intervention, which maintained the peak. Following this is a rapid decrease in the use of control from 100% to the lower bound at 100th day. The treatment control is nearly not in use except for between the 90th and 100th days of implementation, when it reaches the maximum level of about 90%.

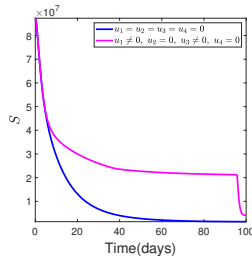


Figure 1: Susceptible humans

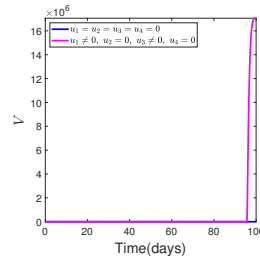


Figure 2: Vaccinated humans

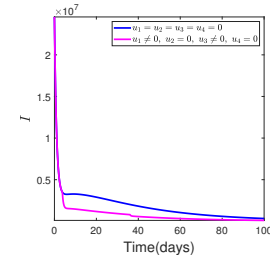


Figure 3: Symptomatic infectious humans

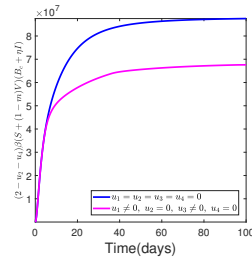


Figure 4: Disease incidence in human population

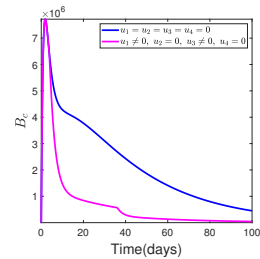


Figure 5: Bacteria population

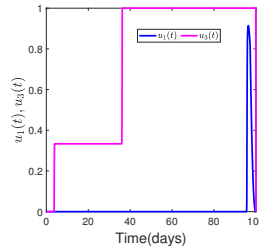


Figure 6: Control profiles

4.2.2. S2 – Combination of optimal sanitation and proper hygiene u_2 and treatment u_3 only

To demonstrate how well the control S2 works in stopping the spread of disease, it is required to optimizing the objective functional \mathcal{J} , such that the optimal controls u_1 and u_4 are set to zero, that is, $(u_2, u_3 \neq 0, u_1 = u_4 = 0)$.

Figure 7 depicts a rapid increase in the population of the susceptible population, which peaked at the initial stage of the simulation and declined gradually till the 16th day, then remained consistent and significantly higher compared to when no control is implemented. Figure 8, 9, 10 and 11 demonstrate declines of exposed humans, symptomatic infectious humans, incidence in human population and environmental bacteria across the period. In addition, the fall is significant in Figure 10 and Figure 11. Moreover, Figure 12 illustrates how sanitation with proper hygiene as control originally has no impact on the disease dynamics but is applied on the 95 to 97 days, while treatment is implemented on the 3rd day and optimally applied between the 40-100 days of the simulation. Therefore, the epidemiological implication is that a combination of sanitation with proper hygiene and treatment is a powerful strategy for reducing the spread of TF in the community when used optimally. It is important to note that the control has a drastic effect on the number of new cases of infection and the bacteria in the environment. There is almost an immediate impact (in terms of reduction) on the incidence of the disease and the bacteria concentration in the population.

4.2.3. S3 – Combination of optimal vaccination u_1 , sanitation with proper hygiene u_2 and treatment u_3 only

Here, we assess how the objective functional \mathcal{J} is being minimized with other control u_4 being set to zero. As shown in Figures 13-16 and 17, this strategy produces better outcomes by reducing both the total number of exposed, infectious, treated, incidence

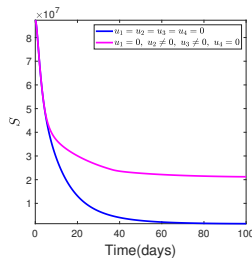


Figure 7: Susceptible humans

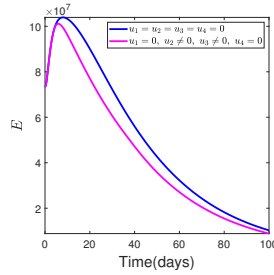


Figure 8: Exposed humans

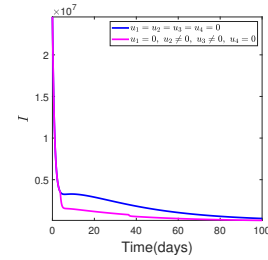


Figure 9: Symptomatic infectious humans

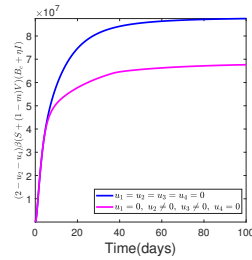


Figure 10: Disease incidence in human population

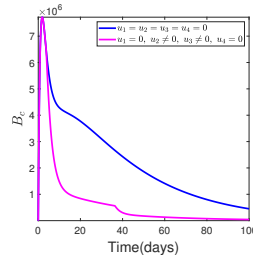


Figure 11: Bacteria population

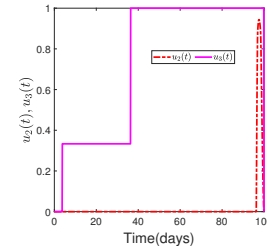


Figure 12: Control profiles

and the total number of bacteria in the environment. Figure 13 shows the exposed group decreasing during the period. Figure 14 demonstrates a sharp decline in the infectious population, especially from day 20. By day 40, the disease has nearly completely disappeared from the community, and by day 60 to 100, after applying the control, TF disease has vanished entirely. In a similar vein, Figure. 15 depicts a decrease in treated persons due to the control intervention. The number of new cases of infection (incidence) has significantly decreased, as seen in Figure 16. In addition, Figure 17 demonstrates that from the first 10 days, the bacteria population, which has peaked, started to decline dramatically, and this trend continued until the bacteria population reached its lowest point between days 60 and 100 after the control is applied. Figure 18 depicts the control profile where treatment control is maximally used until the 95 days when sanitation and vaccination are applied. The implication is that treatment of infectious individuals is necessary to avert further spread and effectively stop TF transmission in the general population.

4.2.4. S4 – Combination of optimal vaccination u_1 , Sanitation and Proper hygiene u_2 and disinfection and sterilization u_4 only

The results of implementing the control combination strategy of vaccination, u_1 , proper hygiene practices and sanitation, u_2 , and disinfection and sterilization, u_4 , are shown in Figures 19–24. Figure 19 demonstrates that the strategy has minimal impact on the susceptible until 50 days when the susceptible population increased. Moreover, Figure 20 depicts that the use of S4 does not impact the vaccinated compartment until around 90 days after the control has been administered, which is followed by a considerable uptick that peaked and lasted for 100 days. Figure 21 shows this strategy has a decreasing effect on infectious individuals, which started to show on the 5th day and declined throughout the interval the control intervention is applied. Comparably, Figure 22 demonstrates that

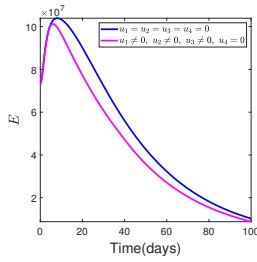


Figure 13: Exposed humans

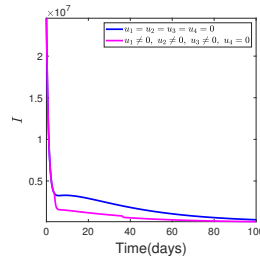


Figure 14: Infectious humans

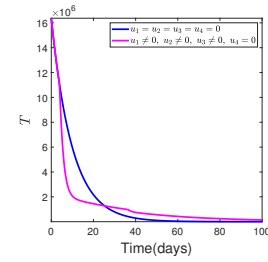


Figure 15: Treated humans

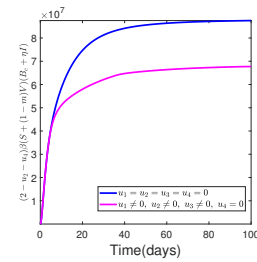


Figure 16: Incidence in human population

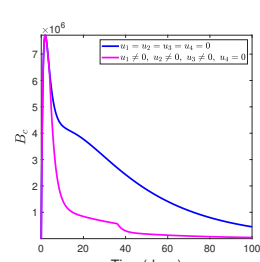


Figure 17: Bacteria population

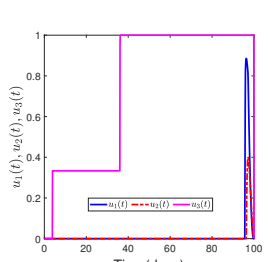


Figure 18: Control profiles

the controls has no significant impact initially until 50th day when the incidence population is decreased by the presence of the control, particularly between 50 and 100 days. Moreover, Figure 23 shows how the presence of S4 significantly affects the bacteria compartment, which initially peaks and then decreases considerably throughout the period. Figure 24 shows no control was applied until day 42 of the simulation, at which disinfection and sterilization as control are maximally applied, and at the 90th day, sanitation and vaccination are put into use where sanitation, and disinfection and sterilization are optimally applied till the 100 days. The implication is that vaccination, sanitation and proper hygiene, disinfection and sterilization are essential preventive techniques in averting the transmission of TF and reducing bacteria in the environment, and will aid in stopping the community spread of TF.

4.2.5. S5 – Combination of optimal vaccination u_1 , treatment u_3 and disinfection and sterilization u_4 only

Figures 25-29 demonstrate how the use of S5 influence the community spread of TF. In this case, we set $u_2 = 0$ and $u_1, u_3, u_4 \neq 0$. Figure 25 demonstrates that the control has an increasing influence on susceptible in the community; Figure 26 reveals an increase in the vaccinated population, especially around the 95-100 days. Likewise Figure 27 depicts a reducing effect on infectious human population, whereas Figure 28 demonstrates significant reduction in the number of new cases of the disease in the population as a result of control intervention. Additionally, Figure 29 shows a considerable decrease in the population of bacteria. From these results, it is noted that vaccination combined with treatment, disinfection and sterilization, enable the reduction in the number of symptomatic infectious individuals, the disease incidence in humans and bacteria in the population, and an increase in the number of susceptible population. This is consistent with the idea that

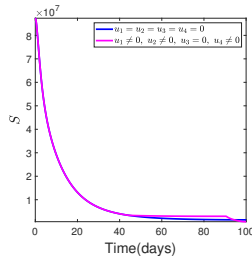


Figure 19: Susceptible humans

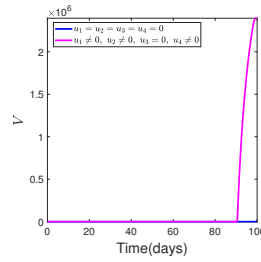


Figure 20: Vaccinated humans

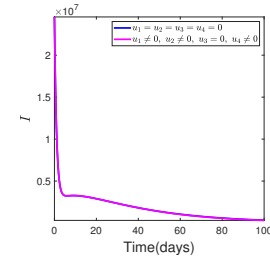


Figure 21: Symptomatic infectious humans

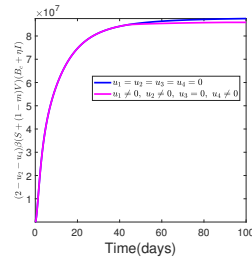


Figure 22: Incidence in human population

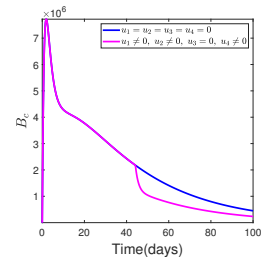


Figure 23: Bacteria population

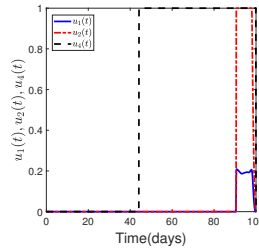


Figure 24: Control profiles

disinfection and sterilization, vaccination and treatments can help to lower the number of bacteria and infected compartments.

4.2.6. *S6 – Combination of optimal sanitation and proper hygiene u_2 , treatment u_3 and disinfection and sterilization u_4 only*

Figures 31–36 illustrate the impact of implementing sanitation and proper hygiene along with treatment disinfection and sterilization to optimize the objective functional \mathcal{J} . As shown in Figures 31–34, when sanitation with proper hygiene, treatment, disinfection and sterilization is adopted, it reduces the number of exposed, infectious, treated humans, and the disease incidence in human population. Additionally, the simultaneous application of the three optimal controls, as depicted in Figure 35, decreases the bacterial population. In conclusion, implementing sanitation with proper hygiene, treatment and disinfection, and sterilization to fight against TF will considerably reduce the disease spread as shown in Figures 31- 35. In addition, Figures 36 show how the controls are applied to obtain this optimal solution.

4.2.7. *S7 – Combination of all the four interventions $u_1(t), u_2(t), u_3(t), u_4(t)$*

This strategy uses all the four optimal controls – vaccination u_1 , sanitation and proper hygiene, u_2 , treatment, u_3 , and disinfection and sterilization, u_4 – concurrently as an intervention to reduce TF in the community. Figures 37–42 demonstrate the outcomes following the application of all the controls, with a sharp increase in the population of susceptible human and a drop in the population of vaccinated individual, infectious individual, the disease incidence in the human population, as well as bacteria concentration in the environment. Compared to the case when there is no control, Figures 39 and 40 illustrate how the infection transmission and new cases of infection decrease steadily.

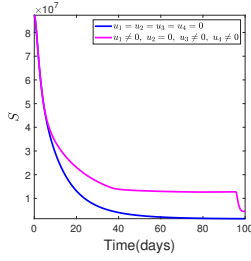


Figure 25: Susceptible humans

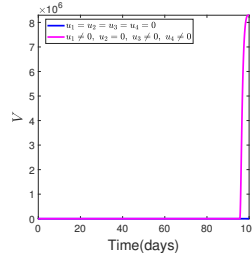


Figure 26: Vaccinated humans

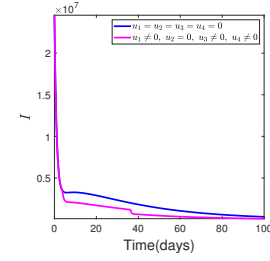


Figure 27: Infectious humans

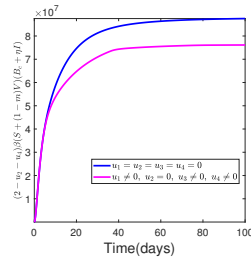


Figure 28: Disease incidence in human population

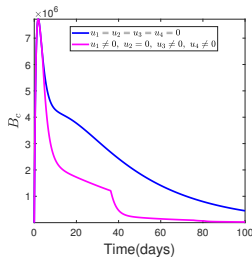


Figure 29: Bacteria population

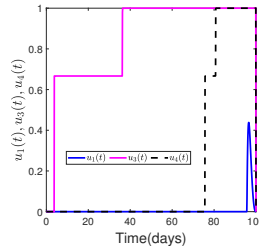


Figure 30: Control profiles

Therefore, it is concluded that using all the four optimal control interventions is more efficient in containing TF in the communities susceptible to it throughout a given period. The control profiles in Figure 42 illustrate the best time to apply the controls.

4.3. Efficiency analysis

In this subsection, efficiency indices of the seven different control combination strategies are calculated to identify the most efficient intervention that could be implemented to avert the highest infections in the population. Thus, efficiency index (EI) is defined mathematically as [1, 19]

$$EI = \frac{\text{Total infection averted by the control intervention}}{\text{Total infection without any control intervention}} \times 100 \quad (4.1)$$

Table 4.3 shows that S4 has the lowest EI (0.5897), while S1 has the highest EI (50.4074),

Table 4: Efficiency indices of Si, i = 1, 2, ..., 7

Strategy	Total infection averted	EI
S1	9.3411×10^8	50.4074
S2	9.3410×10^8	50.4072
S3	9.3219×10^8	50.3038
S4	1.0928×10^7	0.5897
S5	7.5120×10^8	40.5372
S6	7.5125×10^8	40.5396
S7	7.5027×10^8	40.4869

followed by S2 with EI of 50.4072. Therefore, S1 is the most efficient strategy to reduce the spread of TF in the population, even though the strategy uses fewer control combinations and averted the highest number of cases when compared to S7, in particular.

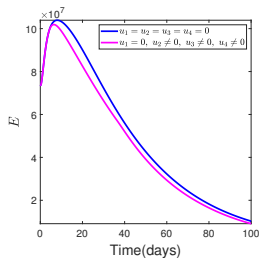


Figure 31: Exposed humans

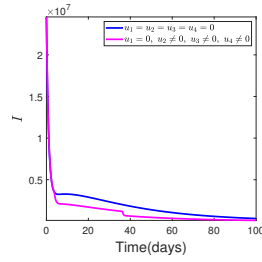


Figure 32: Symptomatic infectious humans

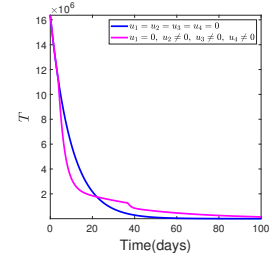


Figure 33: Treated humans

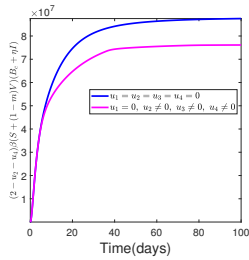


Figure 34: Disease incidence in human population

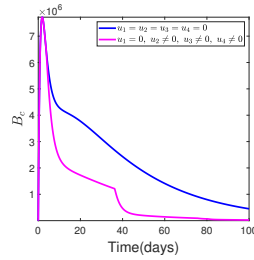


Figure 35: Bacteria population

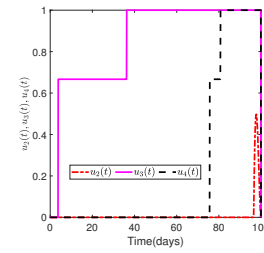


Figure 36: Control profiles

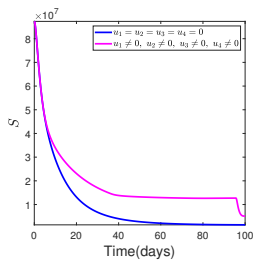


Figure 37: Susceptible humans

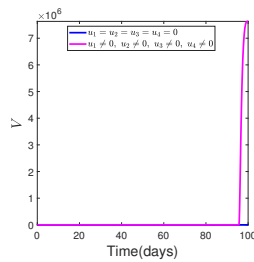


Figure 38: Vaccinated humans

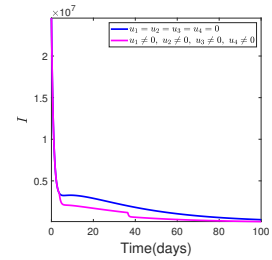


Figure 39: Symptomatic infectious humans

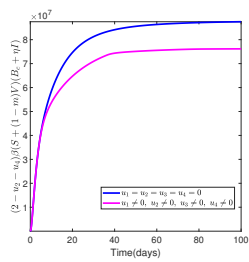


Figure 40: Incidence in human population

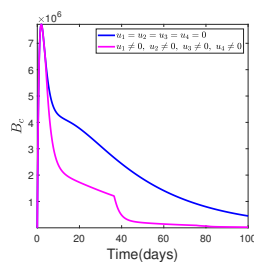


Figure 41: Bacteria population

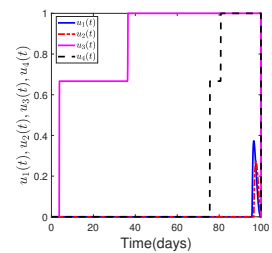


Figure 42: Control profiles

Figure 43: Simulation showing the dynamics of the states variables of model (2.1) with profile for optimal vaccination, sanitation and proper hygiene, treatment, and disinfection and sterilization

5. conclusion

This study reformulated a non-optimal control mathematical model of TF transmission dynamics as an optimal control problem. In order to investigate the effects of four time-dependent control variables, which are vaccination, sanitation with proper hygiene, treatment, and disinfection and sterilization based on different combination of these four controls, analysis of the model based on optimal control theory with the aid of the well-known Pontryagin's maximum principle was carried out. The four optimal controls were combined to create seven distinct strategies that significantly decreased TF cases. It was found that when the control strategies are implemented, the incidence of TF spread in the population declines more noticeably compared to the case without optimal control strategies. In addition, numerical simulations and efficiency analysis were used to determine the strategy that avert the most significant number of TF cases. Consequently, the findings indicated that strategy 1 (combination of vaccination and treatment only) is the most efficient in controlling the spread of TF in the community. In contrast, strategy 4 (combination of vaccination, sanitation with proper hygiene and disinfection and sterilization only) is the least efficient strategy. As a result of this study, it is recommended that any control approach considering the timely treatment of the individuals who exhibit typhoid symptoms and vaccination of the susceptible population be used to avert the continuous spread of the disease. To complement this, resources like clean toilets, portable water, a clean environment, medical facilities, and money for medications, sterilization, and disinfection should be easily accessible.

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