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On mathematical modelling of optimal control of typhoid fever with efficiency analysis

Omowumi F. Lawal¹^{a,b,*}, Tunde T. Yusuf^a, Afeez Abidemi²

^aDepartment of Mathematical Sciences, Federal University of Technology Akure, P.M.B. 704, Ondo State, Nigeria ^bDepartment of Mathematical Sciences, Bamidele Olumilua University of Education, Science, and Technology, Ikere-Ekiti, P.M.B. 250, Ekiti State, Nigeria

Abstract

Typhoid fever is a fatal infectious disease that is endemic in most parts of the world, accounting for millions of cases and thousands of deaths from the disease annually. Despite several mathematical models for control of the disease, typhoid fever remains a threat, especially in Africa, South and Southeast Asia, South America and the Indian subcontinent, necessitating the need to propose an optimal control strategy for the transmission dynamics of typhoid fever. Thus, this research formulates an optimal control model for the transmission dynamics of typhoid fever by including a medically hygienic compartment in the model. To reduce the spread of the disease, the study incorporates environmental sanitation with personal hygiene practices and medical treatment as control strategies to examine their combined impact on typhoid fever prevention and control. The necessary conditions for the existence of the optimal solution to the formulated optimal control problem were derived based on Pontryagin's Maximum Principle. The resulting optimality system was then solved numerically using the fourth-order Runge-Kutta-based scheme. Also, the finding simulation demonstrated the effectiveness of the proposed control strategies in preventing the spread of the disease. In addition, an efficiency analysis was carried out to determine which combinations of the control strategies would be most effective in controlling the alarming spread of the disease. The findings from our study indicate that a combination of environmental sanitation with personal hygiene and treatment was the most efficient in controlling the spread of typhoid fever.

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Keywords: Typhoid fever, Medically hygienic, Optimal control, Efficiency analysis

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1. Introduction

Typhoid fever (TF) is an enteric fever and endemic disease caused by enterica *Salmonella serovar Typhi* [1–3]. TF is fatal in the poorest and most vulnerable countries of Africa, Asia, and Latin America [2–4]. The disease is a threat among pop-

ulations lacking typhoid-specific immunity with high transmission rates and detrimental impacts on both health and socioeconomic situations [4]. More often, TF is caused by povertystricken conditions and continues to be one of the most prevalent bloodstream infections and fevers [4]. TF symptoms, particularly in its early stages, can closely resemble the symptoms of malaria, which can result in a great misdiagnosis and ineffective treatment [5]. These symptoms include headache, nausea, high fever, loss of appetite, weight loss, constipation, diarrhoea, abdominal and general body pain, dry cough, and itching or

^{*}Corresponding author: Tel.: +234-803-520-2740.

Email address: lawal.fatimah@bouesti.edu.ng (Omowumi F. Lawal^(D))

rashes, while severe cases of TF can result in death in human [6, 7]. There are over 145,000 typhoid-related deaths annually, and more than 16 million cases are recorded [2, 7] with an estimated incubation period of ten to fourteen days [8]. Children are most susceptible to TF infection [9].

Globally, TF increases morbidity and death rates, especially in low- and middle-income countries [8, 10]. Moreover, the disease is commonly found in the Continents of Africa, South Asia and some regions of Oceania ([4, 11]. Almost all sub-Saharan Africa have high incidence rates except Southern and North Africa, especially in Central and Western Africa [12]. The incidence of TF is influenced by socio-demographic characteristics, including age and gender, while humans are still the exclusive source of these bacteria [9, 12, 13]. TF infections are spread through direct transmission from humans to humans and indirect transmission of the environment to humans, making it spread similar to that of cholera [2, 8]. TF is caused by drinking contaminated water, ingestion of water polluted by the excrement of an acutely infected, recovering or chronically asymptomatic carrier as well as previous contacts with chronic carriers as well as consumption of raw fruits and vegetables fertilized with human waste without proper washing, living in poverty and poor hygiene [5, 12]. During the rainy season, environmental problems such as open sewages, poisonous water bodies, and low-lying areas can also cause TF [11].

Many African centres still need to rely on clinical diagnosis and serodiagnosis utilizing the Wilda test due to a lack of resources and affordability [12]. Also, it is simple and requires essential equipment and low competence. Nevertheless, research concerning this test has shown alarming patterns about the apparent increase in TF infections in Nigerian and other African healthcare facilities [12, 14, 15]. Antibiotics treat TF [7, 12, 16]. Furthermore, the commercially available vaccines for TF prevention are the injectable Vi polysaccharide vaccine (ViCPS or Vi) based on the purified Vi antigen with efficacy of 55% for children aged two years and above, the live oral attenuated Ty21a vaccine in capsule form with efficacy of 51% for individuals five years of age and older. Equally, an injectable typhoid conjugate vaccine (TCV) is the most widely recommended of the three vaccines due to its increased immunological properties and ability to be administered to individuals of all ages [7, 12, 17, 18]. The disadvantage of using the vaccines is the short lifetime of immunity produced by typhoid vaccinations, which reduces within the first three years of use.

TF can be prevented in the infected populations by treatment and public health initiatives such as giving away free water chlorination products, educating residents about water treatment, and setting up secure alternate water sources [12]. In summary, improved drinking water sources, poverty alleviation programs, proper hygiene and sanitation, being medically conscious, and safe food should be the cornerstones of long-term TF prevention measures [5, 12]. In addition, frequent checkups, considerate care, drinking lots of water, and maintaining a healthy diet [19, 20] are ways to stay healthy with minimal health challenges. Before treatment, the death rate from TF infection cases ranged between 10% to 20%; however, with early treatment, the rate dropped below 1% [8].

Numerous researchers have developed mathematical models to analyze infectious disease dynamics while incorporating different control techniques. For instance, Idisi et al. [21] formulated a new mathematical model for Monkeypox, a viral disease affecting animals, which can occasionally be transmitted to humans. The model reveals the impact of intense awareness on controlling and mitigating the disease. The model concludes that consistency and continuous awareness programs are needed to increase public health measures and reduce new cases. Similarly, Abidemi and Peter [22] present a nonlinear mathematical model of dengue dynamics incorporating asymptomatic, isolation, and vigilant compartments. According to the study, the burden of dengue disease can be considerably decreased by lowering vigilant persons and raising isolation rates for symptomatic and asymptomatic infected people. Likewise, Peter et al. [23] presents an epidemic model of COVID-19 based on an eight-dimensional system of ordinary differential equations. It analyzes the control reproduction number and its equilibrium stability. They found that the most influential parameters are effective transmission rate, first vaccine dose rate, second dose vaccination rate, and recovery rate due to the second dose. The study concludes that adhering to preventive measures significantly reduces the spread of the disease, with increased first and second-dose vaccination rates reducing the disease burden.

Sangotola et al. [24] developed a five-compartment model to comprehend the dynamics of tuberculosis in communities. When the basic reproduction number is less than one, it shows a locally asymptotic disease-free equilibrium point; when it is more significant than one, it reveals an endemic equilibrium. Control measures were evaluated using numerical simulations and sensitivity analysis. Their research determines the optimal ways to control tuberculosis infection, emphasizing early treatment and prevention strategies, and shows that both were effective. Equally, a mathematical model was presented by Ajao et al. [25] to study transmission dynamics and control of HIV infection. The study shows a disease-free equilibrium is globally asymptotically stable when the basic reproduction number is less than unity, and a unique endemic equilibrium exists when the basic reproduction number exceeds unity. Numerical simulations validate the results. Treatment fraction significantly influences latently-infected individuals and AIDS class. Similarly, Duru et al. [26] formulated a new model for the coinfection of malaria and Zika virus diseases, incorporating vaccination, treatment, and vector control using sterile-insect technology. The study reveals that reducing reproduction numbers is not enough to eradicate co-infection, and the two diseases positively impact each other's spread. Effective treatment, vaccination rates, and vector control using sterile-insect techniques significantly help control individual diseases and co-infection. The study concludes that effectively controlling malaria and Zika virus requires measures to prevent their spread in both human and mosquito populations. While Yunus and Olayiwola [27] used fractional-order mathematical modelling to assess COVID-19 vaccination efficacy in Nigeria. Results show that an integer order strategy is most effective in controlling the spread of the virus. The findings highlight the importance of fractional calculus in vaccine implementation and call for global efforts to maximize vaccination for public health. A deterministic vaccine model for studying the effects of vaccination and treatment on human Monkeypox in sub-Saharan Africa was developed by Bolaji *et al.* [28]. The study revealed two equilibria: locally asymptotically stable disease-free equilibrium (DFE) and locally asymptotically stable endemic equilibrium (endemic equilibrium). Numerical simulations show that increased vaccination rates reduce the prevalence of the deadly disease, while missed vaccinations cause severe disease. More extraordinary efforts towards vaccination can significantly reduce the loss of more people to the virus.

In the same way, several mathematical models have been developed to explain the dynamics of the typhoid disease epidemic. For example, Nyaberi and Musaili [7] developed a mathematical model of typhoid transmission and examined how treatment affects the dynamics of the disease. Findings from the model numerical simulations demonstrate that effective treatment is sufficient to eradicate typhoid disease. Also Irena and Gakkhar [29] developed a mathematical model that predicts the best control measures for two different strains of typhoid. It considers carriers, symptomatic persons, and bacteria in the environment. The study suggests that the most effective control strategy in reducing asymptomatic carriers to near zero, is sanitation/proper hygiene along with optimal treatment. Kailan and Seidu [6] developed a mathematical model to study the transmission dynamics of TF. The model reproduction number R_0 was derived using the next-generation matrix approach, while the model equilibria and stability were established based on Routh-Hurwitz criteria. Treatment and booster vaccination was employed as a control intervention. The findings reveal that booster vaccination might not be beneficial in endemic areas. In addition, Tijani et al. [2] examines the impact of limited antibiotic efficacy on typhoid fever transmission. It uses a deterministic model to analyze the transmission mode and sensitivity analysis. The study identifies sanitation and hygiene practices as the most influential single control, followed by strategy 6 (a combination of sanitation and hygiene practices, an awareness campaign, and the potency of antibiotics administered to typhoid patients) for double control and strategy 6 and screening control for triple controls. The overall cost-effectiveness analysis suggests that sanitation and hygiene practices and awareness campaigns are the most cost-effective strategies for eradicating typhoid infection and preventing susceptible populations from contracting the bacteria.

No model for optimal control of TF has been suggested that incorporates treatment and medically hygienic compartments at the population level, as well as the use of environmental sanitation with personal hygiene practices and treatment efforts, as control methods. Consequently, this study aims to examine how people becoming medically vigilant and hygienic can help curtail TF spread and the impacts of deplored environmental sanitation and treatment efforts.

The remaining portions of the article are structured as follows: Section 2 presents the formulation and description of the relevant optimal control model. In Section 3, the model optimal control analysis is presented. Numerical simulation was done in Section 4 to demonstrate the analytical results and examine the effect of model parameters on model output behaviour. Ultimately, Section 5 presents the primary findings derived from the research.

2. Formulation of optimal control problem

Considering the non-optimal control deterministic model of the TF model studied by Lawal *et al.* [5], we propose an optimal control TF model which captures treatment and medically hygienic compartments at the population level. Specifically, susceptible humans S(t), exposed humans E(t), infected humans with symptoms I(t), T(t) denotes individuals undergoing treatment for TF infection, R(t) for recovered persons, and M(t) for medically vigilant and hygienic humans. The variable $B_c(t)$ describes the population of bacteria in the environment. Consequently, the total human population is given by

$$N(t) = S(t) + E(t) + I(t) + T(t) + R(t) + M(t).$$
 (1)

To develop the optimal possible control model for TF dynamics, we further consider the following two time-dependent control variables:

(i) $0 \le u_1(t) \le 1$ is a control variable for environmental sanitation and personal hygiene practices, which accounts for the efforts deplored to ensure environmental sanitation and personal hygiene practices which will guarantee clean area devoid of bacteria that could contaminate the water and food supply. Hence, the incidence function becomes

$$\beta S \left(B_c + \eta I \right) = (1 - u_1(t))\beta S \left(B_c + \eta I \right).$$

This control increases the likely bacterial decay rate. So, the bacterial decay rate is modified as

$$\mu_1 = \mu_1 + a_1 u_1(t),$$

where a_1 represents the increased bacterial mortality rate resulting from chemical intervention.

(ii) The second control variable $0 \le u_2(t) \le 1$ indicates the treatment efforts, which include all ancillary actions like the patient's care (transporting patients in ambulances and isolating infected patients in hospitals) and the delivery of appropriate treatment. We expect each patient's treatment to be effective and last a different amount of time (based on their immune system's response). Thus, we consider the constant treatment rate of symptomatic infectious individuals, denoted as γ , as $u_2(t)$. Also, the recovery rates of symptomatic infectious and treated individuals are modified based on the treatment such that

$$\sigma_1 = \sigma_1 + a_2 u_2(t), \ \sigma_2 = \sigma_2 + a_2 u_2(t),$$

where a_2 is the proportion of patients in class who receive effective treatment, *I*. Following the ideas in Abboubakar

Table 1: Description of the model's variables.

Variable	Description
S	Population of susceptible person
Ε	Population of exposed person
Ι	Population of symptomatic infected person
Т	Population of treated (including drug complaint and non-drug complaint) person
R	Population of recovered person
М	Population of medically vigilant and hygienic person
B_c	Concentration of bacteria in the environment
Ν	Total population of person

and Racke [30], we consider that treatment enables a reduction in the death caused by the disease in those with clinical symptoms. Thus,

$$\delta_1 = (1 - a_2 u_2(t))\delta_1, \ \delta_2 = (1 - a_2 u_2(t))\delta_2.$$

It also allows for reducing the excretion of bacteria in symptomatic infectious individuals. So,

$$\rho = (1 - a_2 u_2(t))\rho.$$

With the above description and assumptions, the optimal control model for TF dynamics is obtained as:

$$\begin{aligned} \frac{dS}{dt} &= (1 - \phi)\Lambda + \varepsilon R - (1 - u_1(t))\beta S (B_c + \eta I) - \mu S, \\ \frac{dE}{dt} &= (1 - u_1(t))\beta S (B_c + \eta I) - (\alpha + \mu)E, \\ \frac{dI}{dt} &= \alpha E + \xi T - (u_2(t) + \sigma_1 + a_2u_2(t) + \mu \\ &+ (1 - a_2u_2(t))\delta_1)I, \\ \frac{dT}{dt} &= u_2(t)I - (\xi + \sigma_2 + a_2u_2(t) + \mu + (1 - a_2u_2(t))\delta_2)T, \\ \frac{dR}{dt} &= (\sigma_1 + a_2u_2(t))I + (1 - \varphi)(\sigma_2 + a_2u_2(t))T \\ &- (\theta + \varepsilon + \mu)R, \\ \frac{dM}{dt} &= \phi \Lambda + \varphi(\sigma_2 + a_2u_2(t))T + \theta R - \mu M, \\ \frac{dB_c}{dt} &= (1 - a_2u_2(t))\rho I - (\mu_1 + a_1u_1(t))B_c, \end{aligned}$$
(2)

with initial conditions:

$$S(0) = S_0, E(0) = E_0, I(0) = I_0, T(0) = T_0,$$

$$R(0) = R_0, M(0) = M_0, B_c(0) = B_{0c}.$$
(3)

Our primary objective is to minimize the number of symptomatic infectious human sub-populations and the size of bacteria in the community as well as the costs associated with the implementation of environmental sanitation and personal hygiene control $(u_1(t))$, and treatment control $(u_2(t))$. The potential impact of this research on public health is significant. We aim to maximize the size of medically vigilant and hygienic human sub-population. Thus, we consider the objective (or cost) functional defined as

$$\mathcal{J}(u_1, u_2) = \int_0^{t_f} \left(A_1 I - A_2 M + A_3 B_c + \frac{1}{2} B_1 u_1^2 + \frac{1}{2} B_2 u_2^2 \right) dt,$$
(4)

subject to the state system in equation (2), where A_1 , A_2 , and A_3 represent the positive weight constraints for symptomatic infectious human, medically hygienic individuals and bacteria population and B_1 , B_2 stands for the positive weight constants for the optimal control variables, u_1 and u_2 . the optimal control intervention is implemented over the interval $[0, t_f]$ where the final time interval is denoted by t_f . The double control functions characterize the non-linearity of the control intervention. As a result, the nonlinear terms $\frac{1}{2}B_1u_1^2$ and $\frac{1}{2}B_2u_2^2$ are used to represent the cost function associated with environmental sanitation and personal hygiene, and treatment control strategies. Determining a control pair $u^* = (u_1^*, u_2^*)$ which satisfies

$$\mathcal{J}(u^*) = \min\{J(u_1, u_2) : (u_1, u_2) \in U\},\tag{5}$$

is subject to the model dynamics, where U is a non-empty Lesbesgue's measurable set for the controls $0 \le u_1(t) \le 1$ and $0 \le u_2(t) \le 1$ with $t \in [0, t_f]$.

Tables 1 and 2 provide the details of the state variables and parameters employed in model in equation (2), respectively.

3. Analysis of the optimal control model

To find the optimal TF control measures (environmental sanitation with personal hygiene and treatments), the optimal control problem for model (equation (2)) is formulated by taking into account the two time-dependent control variables $u_1(t)$ and $u_2(t)$. With respect to the state variables S, E, I, T, R, M and B_c , we take into consideration the control variables $u(t) = [u_1(t), u_2(t)]$ for the optimal control problem of the given system which is derived from Pontryagin's maximum principle [31]. The Hamiltonian is given as:

$$H = A_1 I - A_2 M + A_3 B_c + \frac{1}{2} B_1 u_1^2(t) + \frac{1}{2} B_2 u_2^2 + \lambda_1 \Big\{ (1 - \phi) \Lambda + \epsilon R - (1 - u_1) \beta S(B_c + \eta I) - \mu S \Big\} + \lambda_2 \Big\{ (1 - u_1) \beta S(B_c + \eta I) - (\alpha + \mu) E \Big\}$$

Table 2: Description of the model's parameters.

Parameter	Description
α	Growth rate from exposed state to infectious state
η	Relative transmissibility of symptomatic humans
Λ	Recruitment rate for human population
μ	Natural death rate in humans
$1 - \phi$	Proportion of susceptible humans recruitment rate
μ_1	Decay rate of bacteria from the environment
ε	Per capita rate of immunity loss
arphi	Progression rate of drug-compliant humans to vigilant class
σ_1	Recovery rate of symptomatic humans
ξ	Relapse rate for non-drug compliant humans
σ_2	Recovery rate of drug compliant humans
ho	Bacteria shedding rate from symptomatic humans
a_1	Additional mortality rate of bacteria induced by the chemical intervention
δ_2	Disease-induced death in non-drug compliant individuals
a_2	Proportion of effective treatment for symptomatic infectious individuals
ϕ	Proportion of the medically vigilant humans recruitment rate
δ_1	Disease-induced death in symptomatic infectious individuals
β	Effective transmission rate in human

$$+ \lambda_{3} \Big\{ \alpha E + \xi T - (u_{2} + \sigma_{1} + a_{2}u_{2} + \mu + (1 - a_{2}u_{2})\delta_{1})I \Big\}$$

$$+ \lambda_{4} \Big\{ u_{2}I - (\xi + \sigma_{2} + a_{2}u_{2} + \mu + (1 - a_{2}u_{2})\delta_{2})T \Big\}$$

$$+ \lambda_{5} \Big\{ (\sigma_{1} + a_{2}u_{2})I + (1 - \varphi)(\sigma_{2} + a_{2}u_{2})T$$

$$- (\theta + \epsilon + \mu)R \Big\}$$

$$+ \lambda_{6} \Big\{ \phi \Lambda + \varphi(\sigma_{2} + a_{2}u_{2})T + \theta R - \mu M \Big\}$$

$$+ \lambda_{7} \Big\{ (1 - a_{2}u_{2})\rho I - (\mu_{1} + a_{1}u_{1})B_{c} \Big\},$$
(6)

where λ_1 , λ_2 , λ_3 , λ_4 , λ_5 , λ_6 , λ_7 are the co-state variables. A pointwise Hamiltonian *H* must be minimized with respect to $u_1(t)$ and $u_2(t)$ for equation (2) to become a problem satisfying the necessary conditions that an optimal control must satisfy based on Pontryagin's Maximum Principle [32].

Theorem 3.1. The optimal controls u_1^* and u_2^* and solutions S(t), E(t), I(t), T(t), R(t), M(t) and $B_c(t)$ of the corresponding state system in equation (2), then there exists adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6$, and λ_7 satisfying

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S}, \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial E}, \frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial I}, \frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial T}, \\ \frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial R}, \frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial M}, \frac{d\lambda_7}{dt} = -\frac{\partial H}{\partial B_c}.$$

Then,

$$\begin{split} \frac{d\lambda_1}{dt} &= \lambda_1 \mu + (\lambda_1 - \lambda_2)(1 - \mu_1)\beta(B_c + \eta I), \\ \frac{d\lambda_2}{dt} &= \lambda_2(\alpha + \mu) - \lambda_3 \alpha, \\ \frac{d\lambda_3}{dt} &= -A_1 + (\lambda_1 - \lambda_2)(1 - u_1)\beta\eta S + \lambda_3[u_2 + \sigma_1 \\ &+ a_2u_2 + \mu + (1 - a_2u_2)\delta_1] - \lambda_4 u_2 \\ &- \lambda_5(\sigma_1 + a_2u_2) - \lambda_7(1 - a_2u_2)\rho \\ \frac{d\lambda_4}{dt} &= -\left\{\lambda_3 \xi + \lambda_4[\xi + \sigma_2 + a_2u_2 + \mu \\ &+ (1 - a_2u_2)\delta_2] - \lambda_5(1 - \varphi)(\sigma_2 + a_2u_2) \\ &- \lambda_6 \varphi(\sigma_2 + a_2u_2)\right\}, \end{split}$$
(7)
$$\begin{aligned} \frac{d\lambda_5}{dt} &= -\lambda_1 \epsilon + \lambda_5(\theta + \epsilon + \mu) - \lambda_6 \theta, \\ \frac{d\lambda_6}{dt} &= A_2 + \lambda_6 \mu, \\ \frac{d\lambda_7}{dt} &= -A_3 + (\lambda_1 - \lambda_2)(1 - u_1)\beta S + \lambda_7(\mu_1 + a_1u_1), \end{split}$$

together with transversality conditions

$$\lambda_1(t_f) = 0, \ \lambda_2(t_f) = 0, \ \lambda_3(t_f) = 0, \ \lambda_4(t_f) = 0, \lambda_5(t_f) = 0, \ \lambda_6(t_f) = 0, \ \lambda_7(t_f) = 0.$$
(8)

Applying the optimality conditions and imposing bounds on the controls yield

$$u_1^* = \max\left\{0, \min\left\{1, \frac{(\lambda_2 - \lambda_1)\beta S(B_c + \eta I) + \lambda_7 a_1 B_c}{B_1}\right\}\right\},$$

$$u_2^* = \max\left\{0, \min\left\{1, \frac{\mathcal{G}}{B_2}\right\}\right\},$$
(9)

where
$$\mathcal{G} = \lambda_3(1 + a_2 - a_2\delta_1)I + \lambda_4(a_2 - a_2\delta_2)T + \lambda_7a_2\rho I - \lambda_4I - \lambda_5a_2I - \lambda_5(1 - \varphi)a_2T - \lambda_6\varphi a_2T$$
.

Proof. To find the control variables u_1 and u_2 , there is a need to solve the given optimality conditions by taking the partial derivative of the Hamiltonian in equation (6) with respect to each of the state variables, S, V, E, I, T, R, M, B_c , the adjoint system of equations (7) is obtained, such that.

 $\frac{d\lambda_1}{dt} = \frac{-\partial H}{\partial S}, \frac{d\lambda_2}{dt} = \frac{-\partial H}{\partial V}, \frac{d\lambda_3}{dt} = \frac{-\partial H}{\partial E}, \frac{d\lambda_4}{dt} = \frac{-\partial H}{\partial I}, \frac{d\lambda_5}{dt} = \frac{-\partial H}{\partial T}, \frac{d\lambda_5}{dt} = \frac{-\partial H}{\partial T}, \frac{d\lambda_6}{dt} = \frac{-\partial H}{\partial R}, \frac{d\lambda_7}{dt} = \frac{-\partial H}{\partial M}, \frac{d\lambda_8}{dt} = \frac{-\partial H}{\partial B_c}.$ Additionally, with transversality conditions in equation (8) and solving the partial differential equation $\frac{\partial H}{\partial u_i} = 0, i = 1, 2$ to determine the optimal control characterization in equation (9) of the two control variables as

$$\frac{\partial H}{\partial u_1} = 0$$
, for u_1^*

and

$$\frac{\partial H}{\partial u_2} = 0$$
, for u_2^* .

Differentiating system in equation (6) with respect to u_i , $0 < u_i \le 1$, where i = 1, 2, to obtain

$$\frac{\partial H}{\partial u_1} = -B_1 u_1 + (\lambda_2 - \lambda_1)\beta S (B_c + \eta I) + \lambda_7 a_1 B_c = 0,$$

implying that

$$B_1 u_1 = (\lambda_2 - \lambda_1) \beta S (B_c + \eta I) + \lambda_7 a_1 B_c.$$

Therefore,

$$u_{1}^{*} = \frac{(\lambda_{2} - \lambda_{1})\beta S (B_{c} + \eta I) + \lambda_{7} a_{1} B_{c}}{B_{1}},$$

$$\lambda_{3}(1 + a_{2} - a_{2}\delta_{1})I + \lambda_{4}(a_{2} - a_{2}\delta_{2})T + \lambda_{7}a_{2}\rho I$$

$$u_{2}^{*} = \frac{-\lambda_{4}I - \lambda_{5}a_{2}I - \lambda_{5}(1 - \varphi)a_{2}T - \lambda_{6}\varphi a_{2}T}{B_{2}}.$$
 (10)

Therefore, by standard control arguments imposing the bounds on the controls yields

$$u_1^* = \min\left\{0, \max\left(1, \frac{(\lambda_2 - \lambda_1)\beta S(B_c + \eta I) + \lambda_7 a_1 B_c}{B_1}\right)\right\},\$$
$$u_2^* = \min\left\{0, \max\left(1, \frac{\mathcal{G}}{B_2}\right)\right\}.$$
(11)

This ends the proof.

4. Numerical simulation, results and efficiency analysis

4.1. Numerical simulation

Numerical methods are employed to investigate the impact of control strategies on the number of TF cases within a community. We solve the optimality system using a fourth-order forward-backwards Runge-Kutta iterative strategy. Using the initial conditions at t = 0, the transversality conditions in equation (8), the characterization of the optimal control in equation (9), together with the state system in equation (2) and adjoint system in equation (6) that make up the optimality system, the

Table 3: Model parameter values.

Parameter	Baseline value	Source
a_2	0.7	[30]
γ	0.002	[34]
ϕ	0.15	Assumed
ε	0.000904	[30]
μ	$\frac{1}{20348.75}$	Estimated from [35]
η	0.00001	Assumed
α	0.03	[30]
β	0.00000001	Assumed
δ_1	0.2	[36]
ξ	0.000009	Assumed
δ_2	0.001	[34]
μ_1	0.4	[34]
σ_2	0.1	[34]
arphi	0.005	Assumed
σ_1	0.75	[36]
ho	0.50	[36]
a_1	0.3	[30]
Λ	10726.44506419313	Estimated from [35]

optimal control solution is obtained. Optimality system details numerical procedure can be found in Lenhart and Workman [33]. This section uses numerical simulations to examine the dynamical behaviour of the TF model in equation (2) using the same parameter values as Lawal *et al.* [5]. We assume N(0) = S(0) + E(0) + I(0) + T(0) + R(0) + M(0) such that S(0) = N(0) - (E(0) + I(0) + T(0) + R(0) + M(0)). Thus, S(0) = 87,307,900. In addition, the numeric values of the weight constants that appear in the objective functional in equation (4) are taken as $A_1 = 0.1$, $A_2 = 0.3$, $A_3 = 0.5$, $B_1 = 15$ and $B_2 = 25$. It is important to mention that these weight values are basically theoretical (as they are not related to any real data) for the implementation of the optimal control strategies examined in this paper.

The optimality system is implemented under three different control combination strategies involving the use of at least any of the two time-dependent control functions considered in this paper. These strategies are defined as follows: Strategy 1 (S1) is the use of environmental sanitation and personal hygiene practices only (u_1) , strategy 2 (S2) is the treatment control only (u_2) , while strategy 3 (S3), combines environmental sanitation and proper personal hygiene practices with treatment (u_1, u_2) .

5. Results

5.1. Implementing environmental sanitation and personal hygiene (u₁) as control (strategy 1)

Figure 1 illustrates using environmental sanitation as a control measure to stop the spread of typhoid infection within the human population. Setting $u_2 = 0$ to demonstrate how well environmental sanitation with personal hygiene as a control reduces the spread of the disease i.e applying $u_1 \neq 0$ to limit the transmission by optimizing the objective functional (*J*). Figure

1a depicts how the susceptible human population peaks initially and then declines throughout the 69 days, rising from the 70day to the 100-day mark due to control measures being put in place, which raises the susceptible population.

Figure 1b demonstrates that the exposed population increased until day 7, peaked on day 10, and then significantly decreased over the 100 days. However, when compared to the scenario without control, Figures 1c show a substantial decline in the infected population, which is a promising sign of the effectiveness of control measures. Figure 1d reveals that when no control is used, the incidence of new infections rises. However, when environmental sanitation with personal hygiene was implemented as control, the number of new TF cases decreased starting at day 65 and continuing for up to 100 days. This underscores the significant role of environmental sanitation as a control technique in lowering the spread of disease in the environment, as seen in Figure 1e. As a result, environmental sanitation plays a pivotal role in preventing the spread of disease within the population, empowering us with an effective tool for disease control. Figure 1f depicts the control profile, which indicates that u_1 should remain at zero for 69 days before rapidly increasing to one (1) and maintained for the remainder of the simulation period before declining to zero at the 100-day mark. This finding provides epidemiological insight into how to reduce the prevalence of TF in the general population. This can be achieved by supporting susceptible persons in adhering to strict environmental sanitation with personal hygiene regulations. One practical example of a control tactic is the government's periodic enforcement of environmental sanitation laws on the populace.

5.2. Implementing treatment (u_2) as control (strategy 2)

Our research, as depicted in Figure 2, is a significant step in disease control. By applying the treatment u_2 to infected individuals and minimizing the objective functional J, we effectively eliminate the other control, u_1 , setting it to zero, i.e., $u_1 = 0, u_2 \neq 0$. Figures 2a show a significant increase in the susceptible population, while Figures 2b -2c depict a steady decrease in the number of exposed and infected individuals. This is a clear indication of the drug's efficacy in treating the infected, a stark contrast to the scenario without control.

Comparably, a population with a steadily dropping disease incidence is shown in Figure 2d, which shows a dramatic decline that starts on day 20 of the simulation and lasts 100 days. Similarly, Figure 2e shows the decline in the bacterial population, illustrating how treating infectious people lowers the risk of the diseases spreading into the environment.

Conversely, in Figure 2f, the control profile shows how treatment control started at the lowest possible level and gradually rose to the upper bound of 1 between days 3 and 5, after which it dropped to the lower bound and remained there for the remaining 22 days of the simulation. After that, there was a rapid increase to the maximum bound, which was sustained, and at t = 100 days, the infection rapidly decreased from the upper to the lower bound.

These findings underscore the crucial role of the audience in implementing effective disease control measures. The implication is clear: employing the treatment rate as a control measure is a powerful tool in preventing the spread of TF in the population.

5.3. Combination of environmental sanitation with personal hygiene and treatment (u1) and (u2) as control (strategy 3)

To maximize the objective functional J, the environmental sanitation control (u_1) and the infected individual's treatment (u_2) demonstrate the efficacy of the two controls at the same time, as shown in Figure 3. Figures 3a through 3e show the results of applying the two (2) controls simultaneously. At the same time, Figure 3a illustrates how the number of susceptible people is rising rapidly due to improved environmental sanitation, personal hygiene, and treatment, leading to an increase in the population of susceptible individuals. Figure 3b demonstrates a significant decrease in the exposed human population, which peaked at the start of the simulation and continued to diminish throughout the rest of the period. Similarly, Figure 3c shows a progressive decrease in the number of symptomatic infectious humans compared to the absence of control. The most striking result, however, is the impact of the two controls on the number of new cases of infection. When no control was applied, the number of new cases peaked initially and increased rapidly. However, with the concurrent application of the two controls, this number drastically decreased, starting to decline on the seventh day of the control intervention. Between days 20 and 100, there was a notable decrease in the number of new cases of TF, as shown in Figure 3d. Comparably, as Figure 3e illustrates, the simultaneous application of the two controls also reduces environmental bacterial transmission. Between the 30 and 100 days after the control interventions were put into place, the bacterial population saw a significant decline from its peak and was almost nonexistent. In contrast, the control profile depicted in Figure 3f demonstrates the incidence of TF infection rises on the fifth day, necessitating the application of control; it then falls on the seventh day and remains stable until the twenty-first day at which point it peaks and requires the application of control intervention, leading to a sharp decline in the infection rate.

5.4. Efficiency analysis

In this subsection, efficiency indices of the three different control combination strategies are calculated to identify the most efficient intervention that can be implemented to avert the highest infections in the population. Thus, according to Olaniyi *et al.* [37] and Yusuf and Abidemi [38], the efficiency index (EI) is defined mathematically as

$$EI = \frac{\text{Total infection averted by the control intervention}}{\text{Total infection without any control intervention}} \times 100.$$

According to Table 4, Strategy 1 has the lowest Efficiency Index of 0.745333, Strategy 2 has the highest Efficiency Index of 40.60931, and Strategy 3 is next with the Efficiency Index of 40.46399. It's crucial to act on these findings, as the most effective method to stop typhoid disease from spreading throughout the community is by using strategy 2.





Figure 1: Simulation depicting the dynamics of TF model in equation (2) with profile for optimal environmental sanitation only.

6. Discussion

Based on the proposed compartmental optimal control model for the transmission dynamics of TF with the inclusion of a medically hygienic class, our study estimated the cases of TF infection averted in Nigeria following the introduction of environmental sanitation with personal hygiene and treatment through efficiency analysis. Considering three scenarios for optimal control implemented: environmental sanitation with personal hygiene only, treatment only and a combination of





Figure 2: Dynamics of the states variables of model in equation (2) for TF with profile for optimal treatment only.

environmental sanitation with personal hygiene and treatment strategies, this study demonstrates a significant drop in the population that is infectious and exposed, as well as a drop in the number of new cases of TF. These findings are encouraging indicators of the efficacy of environmental sanitation with personal hygiene used as a control.

Furthermore, this study predicts that treating infected individuals will considerably reduce TF cases and deaths in the





Figure 3: Simulation showing the dynamics of TF the states variables of model in equation (2) with profile for optimal combination of environmental sanitation with personal hygiene and treatment only.

human population. However, introducing the optimal combination of environmental sanitation with personal hygiene and treatment substantially reduced TF incidence in the human population. Our results are consistent with those reported in a modelling study examining control strategies impact on TF transmission (see Refs. [2, 6, 7, 29]). Our analysis reveals that

Table 4: Efficiency indices of S1, S2 and S3.

Strategy	Total infection averted	EI
S 1	1.284769×10^{7}	0.745333
S 3	6.974983×10^{8}	40.46399
S2	7.000033×10^{8}	40.60931

over 12 million cases of TF were averted with the optimal implementation of environmental sanitation and personal hygiene only. However, this strategy was found to be the least effective of all the three strategies under consideration. This result aligns with the work of Irena and Gakkhar [29], which also suggests that sanitation (proper hygiene) was the least effective strategy in reducing the TF burden in the community. In another study, Tijani *et al.* [2] examined the impact of sanitation and hygiene practices and awareness as a single control and identified sanitation with hygiene practices combined with awareness campaigns as the most influential single control and cost-effective strategy.

Additionally, optimal treatment only reduces the TF considerably by averting over 700 million cases of TF (see Table 4). This aligns with the works of previous researchers on mathematical analysis of optimal control strategies of TF, such as Nyaberi1 and Musaili [7] and Kailan and Seidu [6], which revealed that treatment was the most effective in reducing the disease incidence and the number of infectious individuals in the population.

7. Conclusion

This study formulated the transmission dynamics of TF disease as an optimal control problem by incorporating two control strategies that will help curtail the transmission of the disease in the population. Analysis of the optimal control strategy was done using Pontryagin's maximum principle to determine the effectiveness of the two (2) controls: environmental sanitation with personal hygiene u_1 and treatment of infected individuals u_2 as well as the impact of a potential combination of these two controls. The optimal environmental sanitation with personal hygiene was combined with additional control variables to create three distinct strategies that significantly decreased TF cases. It was observed that implementing the control(s), individually or concurrently, will remarkably reduce disease transmission in the population after some time compared to the case without optimal control strategies. Similarly, the optimal control problem was also analyzed, and the Pontryagin maximum principle was used to derive the optimal control characterization. In addition, numerical simulation and efficiency analysis were carried out to determine the strategies that prevent the most significant number of TF cases. Consequently, the findings indicated that strategy 3 (combination of environmental sanitation with personal hygiene and treatment) is the most efficient in controlling the spread of TF in the community. In contrast, strategy 1 (control with environmental sanitation and personal hygiene) is the least efficient control. As a result, it is recommended that any control approach must consider a combination of environmental sanitation and personal hygiene with timely treatment of the individuals who exhibit typhoid disease symptoms be used to avert the continuous spread of the disease if resources like decent toilets, portable water, a clean environment, medical facilities, and money for medications are easily accessible.

References

- C. S. Marchello, M Birkhold & J. A. Crump, "Complications and mortality of typhoid fever: a global systematic review and meta-analysis", Journal of Infection 6 (2020) 902. https://doi.org/10.1016/j.jinf.2020.10.030
- [2] K. A. Tijani, C. E. Madubueze & R. I. Gweryina, "Typhoid fever dynamical model with cost-effective optimalcontrol", Journal of the Nigerian Society of Physical Sciences 5 (2023) 1579. https://doi.org/10.46481/jnsps. 2023.1579.
- [3] A. A. Momoh, Y. Afiniki, D. Dethie & A. Abubakar, "Curtailing the spread of typhoid fever: An optimal control approach", Results in Control and Optimization 13 (2023) 100326. https://doi.org/10.1016/j.rico. 2023.100326.
- [4] J. E. Meiring & P. I. Johnston, "Typhoid fever: A reduction and a resurgence", The American Journal of Tropical Medicine and Hygiene 109 (2023) 219. https://doi.org/10.4269/ajtmh.23-0286.
- [5] F. O. Lawal, T. T. Yusuf & A. Abidemi, "Modelling the impact of vaccination on transmission dynamics of typhoid fever", Results in Control and Optimization 13 (2023) 100310. https://doi.org/10.1016/j.rico.2023. 100310.
- [6] A. Kailan Suhuyini & B. Seidu, "A mathematical model on the transmission dynamics of typhoid fever with treatment and booster vaccination" Frontiers in Applied Mathematics and Statistics 9 (2023) 1151270. https://doi.org/10.3389/fams.2023.1151270.
- [7] H. O. Nyaberi & J. S. Musaili, "Mathematical modeling of the impact of treatment on the dynamics of typhoid", Journal of the Egyptian Mathematical Society 29 (2021) 15. https://doi.org/10.1186/ s42787-021-00125-8.
- [8] L. Matsebula, F. Nyabadza & J. Mushanyu. "Mathematical analysis of typhoid fever transmission dynamics with seasonality and fear", Commun. Math. Biol. Neurosci 2021 (2021) 36. https://doi.org/10.28919/ cmbn/5590.
- [9] O. O. Odikamnoro, I. M. Ikeh, F. N. Okoh, S. C. Ebiriekwe, I. A. Nnadozie, J. O. Nkwuda & G. C. Asobie, "Incidence of malaria/typhoid co-infection among adult population in unwana community, afikpo north local government area, ebonyi state, southeastern nigeria", African journal of infectious diseases 12 (2018) 33. https://doi.org/10.21010/ajid. v12i1.6.
- [10] J. Kim, V. Mogasale, J. Im, E. Ramani & F. Marks, "Updated estimates of typhoid fever burden in sub-saharan africa", The Lancet Global Health 5 (2017) e969. DOI:https://doi.org/10.1016/S2214-109X(17)30328-5.
- [11] B. B. Mirembe, S. Mazeri, R. Callaby, L. Nyakarahuka, C. Kankya & A. Muwonge, "Temporal, spatial and household dynamics of typhoid fever in kasese district, uganda", Plos one 14 (2019) e0214650. https://doi.org/10.1371/journal.pone.0214650.
- [12] O. A. Adesegun, O. O. Adeyemi, O. Ehioghae, D. F. Rabor, T. O. Binuyo, B. A. Alafin, O. B. Nnagha, A. O. Idowu & A. Osonuga, "Current trends in the epidemiology and management of enteric fever in africa: a literature review", Asian Pacific Journal of Tropical Medicine 13 (2020) 204. https: //doi.org/10.4103/1995-7645.283515.
- [13] M. Antill'on, J. L. Warren, F. W. Crawford, D. M. Weinberger, E. K"ur"um, G. D. Pak, F. Marks & V. E. Pitzer, "The burden of typhoid fever in low-and middle-income countries: a metaregression approach", PLoS neglected tropical diseases 11 (2017) e0005376. https://doi.org/10. 1371/journal.pntd.0005376.
- [14] A. Jemilohun, A. Adeyanju & M. Bello, "How useful is the widal test in modern clinical practice in developing countries: a review", International Journal of Tropical Disease and Health 26 (2017) 1. https://doi.org/10. 9734/IJTDH/2017/36691.

- [15] A. Mawazo, G. M. Bwire & M. I. Matee, "Performance of widal test and stool culture in the diagnosis of typhoid fever among suspected patients in dar es salaam, tanzania", BMC research notes **12** (2019) 316. https: //doi.org/10.1186/s13104-019-4340-y.
- [16] B. Veeraraghavan, A. K. Pragasam, Y. D. Bakthavatchalam & R. Ralph, "Typhoid fever: issues in laboratory detection, treatment options and concerns in management in developing countries", Future science OA 4 (2018) FSO312. https://doi.org/10.4155%2Ffsoa-2018-0003.
- [17] D. Amicizia, L. Arata, F. Z. Angrillo, D. Panatto & R. Gasparini "Overview of the impact of typhoid and paratyphoid fever. utility of ty21a vaccine (vivotif®)", Journal of preventive medicine and hygiene 58 (2017) E1. http://www.ncbi.nlm.nih.gov/pmc/articles/pmc5432773/.
- [18] R. Milligan, M. Paul, M. Richardson & A. Neuberger," Vaccines for preventing typhoid fever", Cochrane Database of Systematic Reviews 5 (2018) 5. https://doi.org/10.1002/14651858.CD001261.pub4.
- [19] Z. A. Bhutta, M. I. Khan, M. I. Soofi & R. L. Ochiai, "New advances in typhoid fever vaccination strategies", in *Hot Topics in Infection and Immunity in Children VII*, Advances in Experimental Medicine and Biology, vol. 697, Springer, New York, NY, 2011, pp. 17-39. https://doi.org/ 10.1007/978-1-4419-7185-2_3.
- [20] C. B Acosta-Alonzo, I. V. Erovenko, A. Lancaster, H. Oh, J. Rychtar & D. Taylor, "High endemic levels of typhoid fever in rural areas of Ghana may stem from optimal voluntary vaccination behaviour", Proceedings of the Royal Society A 476 (2020) 20200354. https://doi.org/10.1098/rspa. 2020.0354.
- [21] O. I. Idisi, T. T. Yusuf, E. Adeniyi, A. A. Onifade, Y. T. Oyebo, A. T. Samuel & L. A. Kareem, "A new compartmentalized epidemic model to analytically study the impact of awareness on the control and mitigation of the monkeypox disease", Healthcare Analytics 4 (2023) 100267. https://doi.org/10.1016/j.health.2023.100267.
- [22] A. Abidemi & O. J. Peter, "Host-vector dynamics of dengue with asymptomatic, isolation and vigilant compartments: insights from modelling", The European Physical Journal Plus, **138** (2023) 199. https://doi.org/10. 1140/epjp/s13360-023-03823-7.
- [23] O. J. Peter, S. Panigoro, A. Abidemi, M. Ojo & F. A. Oguntolu, "Mathematical model of covid-19 pandemic with double dose vaccination", Acta biotheoretica 71 (2023) 9. https://doi.org/10.1007/s10441-023-09460-y.
- [24] A. O. Sangotola, S. B. Adeyemo, O. A. Nuga, A. E. Adeniji & A. J. Adigun, "A tuberculosis model with three infected classes", Journal of the Nigerian Society of Physical Sciences 6 (2024) 1881. https://doi.org/ 10.46481/jnsps.2024.1881.
- [25] S. Ajao, I. Olopade, T. Akinwumi, S. Adewale & A. Adesanya, "Understanding the transmission dynamics and control of hiv infection: A mathematical model approach", Journal of the Nigerian Society of Physical Sciences, pages 5 (2023) 1389. https://doi.org/10.46481/jnsps.2023.1389.

- [26] E. C. Duru, G. C. E. Mbah, M. C. Anyanwu & N. T. Nnamani, "Modelling the co-infection of malaria and zika virus disease", Journal of the Nigerian Society of Physical Sciences 6 (2024) 1938. https://doi.org/10. 46481/jnsps.2024.1938.
- [27] A. O. Yunus and M. O. Olayiwola, "The analysis of a novel covid-19 model with the fractional-order incorporating the impact of the vaccination campaign in nigeria via the laplace-adomian decomposition method', Journal of the Nigerian Society of Physical Sciences 6 (2024) 1830. https://doi.org/0.46481/jnsps.2024.1830.
- [28] B. Bolaji, A. Ibrahim, F. Ani, B. Omede & G. Acheneje, "A model for the control of transmission dynamics of human monkeypox disease in subsaharan africa", Journal of the Nigerian Society of Physical Sciences 6 (2024) 1800. https://doi.org/10.46481/jnsps.2024.1800.
- [29] T. K. Irena & S. Gakkhar, "Optimal control of two-strain typhoid transmission using treatment and proper hygiene/sanitation practices", Journal of Computational Analysis and Applications **30** (2022) 355. http: //www.eudoxuspress.com/index.php/pub/article/view/121.
- [30] H. Abboubakar & R. Racke, "Mathematical modeling, forecasting & optimal control of typhoid fever transmission dynamics", Chaos, Solitons and Fractals 149 (2021) 111074. https://doi.org/10.1016/j.chaos.2021. 111074.
- [31] L. S Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze & E. F. Mishchenko, *The mathematical theory of optimal processes*, John Wiley & Sons, New York, 1962. https://doi.org/10.1002/zamm.19630431023.
- [32] L. S. Pontryagin, "Mathematical theory of optimal processes", Routledge, London, 2018. https://doi.org/10.1201/9780203749319.
- [33] S. Lenhart and J. T. Workman, Optimal control applied to biological models, CRC press, New York, 2007. https://doi.org/10.1201/ 9781420011418.
- [34] A. Alhassan, A. A. Momoh, S. A. Abdullahi & A. Audu, "Mathematical model for the transmission dynamics of typhoid fever infection with treatment", International Journal of Science for Global Sustainability 7 (2021) 13. https://fugus-ijsgs.com.ng/index.php/ijsgs/article/view/25.
- [35] National Population Comission worldometer, "Current population of Nigeria". [Online]. http://nationalpopulation.gov.ng. Retrieved November 18th 2022.
- [36] Ibrahim M. O. Edogbanya H. O. Oguntolu F. A. Oshinubi K. Ibrahim A. A Peter, O. J., T. A, Ayoola & J. O Lawal, "Direct and indirect transmission of typhoid fever model with optimal control", Results in Physics 27 (2021) 104463. https://doi.org/10.1016/j.rinp.2021.104463.
- [37] S. Olaniyi, O. D. Falowo, K. O. Okosun, M. Mukamuri, O. S. Obabiyi & O. A. Adepoju, "Effect of saturated treatment on malaria spread with optimal intervention", Alexandria Engineering Journal 65 (2023) 443. https://doi.org/10.1016/j.aej.2022.09.024.
- [38] T. T. Yusuf and A. Abidemi, "Effective strategies towards eradicating the tuberculosis epidemic: An optimal control theory alternative", Healthcare Analytics 3 (2023) 100131. https://doi.org/10.1016/j.health.2022.100131.