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Research article

Mathematical modelling of the dynamics of typhoid fever and two modes of treatment in a Health District in Cameroon

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Abstract: In this paper, we propose a novel mathematical model for indirectly transmitted typhoid fever disease that incorporates the use of modern and traditional medicines as modes of treatment. Theoretically, we provide two Lyapunov functions to prove the global asymptotic stability of the disease-free equilibrium (DFE) and the endemic equilibrium (EE) when the basic reproduction number ($\mathcal{R}_0$) is less than one and greater than one, respectively. The model is calibrated using the number of cumulative cases reported in the Penka-Michel health district in Cameroon. The parameter estimates thus obtained give a value of $\mathcal{R}_0 = 1.2058 > 1$,which indicates that the disease is endemic in the region. The forecast of the outbreak up to November 2026 suggests that the number of cases will be 21,270, which calls for urgent attention on this endemic disease. A sensitivity analysis with respect to the basic reproduction number is conducted, and the main parameters that impact the widespread of the disease are determined. The analysis highlights that the environmental transmission rate β and the decay rate μ_b of the bacteria in the environment are the most influential parameters for $\mathcal{R}_0$. This underscores the urgent need for potable water and adequate sanitation within this area to reduce the spread of the disease. Numerically, we illustrate the usefulness of recourse to any mode of treatment to lessen the number of infected cases and the necessity of switching from modern treatment to the traditional treatment, a useful adjuvant therapy. Conversely, we show that the relapse phenomenon increases the burden of the disease. Hence adopting a synergistic therapy approach will significantly mitigate typhoid disease cases and overcome the cycle of poverty within the afflicted communities.

Keywords: typhoid fever; modern medicine; traditional medicine; stability of equilibria; model calibration; infectious disease; sensitivity analysis

1. Introduction

Typhoid fever (TF) is one of the most common infectious diseases in South Asia and Sub-Saharan Africa, with over 9 million cases per year [1,2]. It is caused by the bacterium *Salmonella typhi*, which is usually spread through contaminated food or water. Persons with typhoid fever carry the bacteria in their bloodstream and intestinal tract. The development of the disease follows three phases: the incubation phase, the invasion phase (acute), and the chronic phase. The incubation period varies between 7 and 21 days [3]. The acute phase is characterized by the gradual onset of fever, headaches, dizziness, insomnia, epistaxis, and sometimes constipation [4]. In the chronic phase, the infected may have encephalitis or inflammation of the brain, dehydration, weakness, abdominal hemorrhage due to severe intestinal perforations, and other serious complications that may lead to death [2].

In Sub-Saharan Africa, it is estimated that more than 80% of the population use medicinal plants as their main source of treatment [5,6]. Antibiotics have been the primary therapy for typhoid fever and also the cornerstone of modern medicine. However, the increased resistance of some bacteria to antibiotics may be one of the reasons why patients seek traditional treatment. One principal reason typhoid fever patients may prefer traditional medicine over modern medicine is the nonexistence of modern healthcare facilities, especially in rural areas. In areas where these facilities exist, the antibiotics are expensive, as the patients are mainly low-income earners. In contrast, traditional medicine is relatively cheap and readily available. The effectiveness of traditional medicine is recognized in several countries and has made important contributions to modern medicine [5,7]. A report in [8] says, WHO has supported clinical trials, leading 14 countries to issue marketing authorization for 89 traditional medicine products that met international and national requirements for registration. It is important to note that since the 1980s, traditional medicine has been benefitting from such authorizations [9,10].

Sometimes, some of the patients taking antibiotics experience a relapse of typhoid fever after an initial recovery. Relapse is the return of a disease or the signs and symptoms of a disease after a period of improvement or treatment. This phenomenon may be due to incomplete treatment or from antibiotics resistance due to the abuse of prescribed antibiotics. The re-emergence of a disease may either be due to relapse or reinfection. Reinfection occurs when a patient after; treatment becomes infected again, meanwhile, relapse is the recurrence of the same infection. Relapse dynamics models account for the possibility that individuals who have been treated for typhoid fever may have a reactivation of the same *Salmonella typhi* bacteria.

Models incorporating treatment relapse are particularly important concerning TF. Many mathematical models have been developed to study the spread of typhoid fever [11–19]. The authors of [13], proposed a human-to-human (direct) and environment-to-human (indirect) transmission model, in which susceptible individuals get infected with *Salmonella typhi* at a rate proportional to the susceptible population and the environmental bacteria concentration at a constant rate. They proved that sanitation, vaccination, and treatment of symptomatic and asymptomatic infected individuals are efficient measures, to reduce the severity of the disease. Considering the latter control measures, [12] presented a model to investigate the

outcome of the disease in Mbandjock, a town in Cameroon. Through calibration, they obtained a control reproduction number of 2.4750, meaning that TF was endemic in that region. Similar to [13], the authors of [18] proposed a model with both direct and indirect transmissions, but also considered in addition the influence of vaccination. Through a sensitivity analysis, they found that the proportion of susceptible unvaccinated immigrants had a high impact on the infected populations. Thus, people entering the town were to be checked, to ensure they were vaccinated against TF. In [11], a non-autonomous model was proposed accounting for temporal variations and it was shown that the human-to-human infection rate had a significant impact on the reproduction number, while the environment-to-human infection rate and the bacteria shedding rate had an effect on long-cycle infections.

Mushayabasa [14], proposed an $S\ E\ I\ I_c\ Q\ R$ compartmental model, with the susceptible individuals (S), exposed individuals (E), symptomatic infected individuals (I), chronic enteric carriers (I_c), quarantined symptomatic persons and chronic enteric carriers (Q), and recovered individuals (R). He assumed that the population reduced due to natural death (μ) and the acquired infection rate (λ) expressed as a function of I and I_c. The disease-free equilibrium was shown to be globally asymptotically stable whenever the reproductive number was less than unity. The transmission of the disease was through human contact only and he concluded that in the event of an outbreak of typhoid in the community the disease can be effectively controlled if optimal intervention strategies are implemented. In [19], a mathematical model that explored the dynamics of typhoid fever transmission with particular focus on the impact of treatment relapse is presented. The study formulated a deterministic mathematical model to analyze both direct and indirect transmission modes of typhoid infection. The findings reveal that limited efficacy of antibiotics and relapse response significantly influence the spread of typhoid infection.

Despite the avalanche of studies on the dynamics of TF, there is little literature on the role of traditional medicine in the treatment of TF. There are some studies on typhoid fever-treating herbs [7], which demonstrated that extracts from these plants have an inhibiting impact on *Salmonella typhi*. Herbal medicine is a feature and at times synonymous with African traditional medicine. The role of traditional medicine in the treatment of COVID-19 has been discussed in [16]. The results prescribed the combination of modern medicine with traditional medicine instead of one medicine as a stand-alone treatment. The mathematical model in the study did not consider possible relapse. However, the COVID-19 virus and *Salmonella typhi* are diseases with different modes of transmission and hence their models are dissimilar.

To the best of our knowledge, no typhoid fever model that incorporates modern treatment and traditional treatment has been proposed in literature so far. This paper contributes to the existing literature by proposing a novel mathematical deterministic model that incorporates these modes of treatment and treatment relapse due to resistance to antibiotics. The structure of the model model described and formulated in Section 2, to an extent, is a modified version of Mushayabasa's in [14]. Essentially, we have replaced the quarantine compartment (Q) with two compartments for treatment modes (modern and traditional). In addition, we assume that the bacterial infection is indirect (environment-to-human). Together with real data, we study and make predictions about the future dynamics of the disease in the locality of Penka-Michel in Cameroon. We theoretically analyze our model and use the fminsearchbnd and ode45 functions in MATLAB for calibration and numerical simulations, respectively.

The rest of the paper is organised as follows. In Section 2, the main assumptions of the model are presented with a detailed description of the model. Section 3 presents the quantitative and qualitative

analysis of the model. In Section 4, we calibrate and validate the model. Section 5 deals with the sensitivity analysis and numerical simulations. The conclusion of the paper is provided in Section 6.

2. Model formulation

2.1. Main assumptions and variables

In this study, the following assumptions are made for our model. These assumptions are crucial in determining the effectiveness and tractability of the model.

Assumption 1. *Infected individuals can choose either modern or traditional treatment. However, individuals under modern treatment can switch to traditional therapy. This assumption is motivated by the resistance of Salmonella to some modern treatment protocols [20].*

Assumption 2. *Although human-to-human transmission of typhoid is possible, it is less probable [21]. Therefore, only indirect means of transmission are considered, i.e., transmission through contaminated food, poor sanitation and unsafe drinking water.*

Assumption 3. *Individuals in the chronic phase of the disease can get serious complications like internal bleeding and encephalitis (brain inflammation) [22]. We assume that this category of patients will choose modern treatment only.*

Assumption 4. *It is known that after recovering from typhoid fever, individuals do develop some level of immunity. Recovery cases develop antibodies and remain immune against the disease for at least three years [23]. Thus, for simplicity, we assume that the recovered individuals enjoy permanent immunity.*

Assumption 5. *We consider a possible relapse of typhoid fever for individuals receiving modern treatment only. In our case, a relapse occurs when patients taking antibiotics fall back to the acute infection stage, after a period of improvement.*

Assumption 6. *The shedding rate of individuals under treatment is negligible. That is, we have well-informed patients who are taking all the precautionary measures to avoid spreading the disease.*

Assumption 7. *Under treatment, the mortality rate due to typhoid is less than 1% [24]. We consider this value negligible and ignore the mortality rate for patients receiving any of the treatments.*

Assumption 8. *The individuals in each group have an equal natural death rate.*

The epidemiological model we develop in this study has eight compartments for the transmission dynamics of the disease. We denote by $N(t)$ the human population at time t, which has been divided into mutually exclusive compartments as follows:

- $S := S(t)$: Susceptible individuals.
- $E := E(t)$: Exposed individuals. This refers to the individuals infected with *Salmonella* but in a latent period.
- $I_a := I_a(t)$: Infected individuals in the acute phase of the disease.
- $I_c := I_c(t)$: Infected individuals in the chronic phase of the infection. The symptoms of these individuals develop very slowly, so the disease persists for a long time in their bodies.
- $M_m := M_m(t)$: Individuals under modern treatment.

- $M_t := M_t(t)$: Individuals under traditional treatment.
- $R := R(t)$: Recovered individuals.
- $B := B(t)$: The concentration of *Salmonella* bacteria in the environment.

$N(t) = S(t) + E(t) + I_a(t) + I_c(t) + M_m(t) + M_t(t) + R(t)$, is the total human population at time t.

2.2. The model equations

In this section, we derive the necessary equations for the construction of our mathematical model while also defining the inherent variables.

The susceptible individuals are recruited at a constant number π, through birth or immigration. The susceptible population diminishes either due to natural death at the rate μ, or due to *Salmonella* bacteria infection. We assume that the infection pressure λ, the rate at which susceptible individuals acquire the infection after their exposure to the disease, is given by the Holling Type II functional response (see [21]). That is

$$\lambda = \frac{\beta B}{(B + k_b)},$$

where β is the ingestion rate (that is, the product of the contact rate between individuals and the environment, and the percentage of *Salmonella* successfully ingested). The quantity k_b is the concentration of bacteria in what is being consumed which gives 50% chance of getting infected. The fraction $B/(B+k_b)$, measures the probability of individuals getting infected through contaminated food or water. It is clear that λ is an increasing function of the concentration of *Salmonella (B)* and when B is large enough ($B \gg k_b$), λ saturates at the constant value β. If $B \ll k_b$, λ will grow linearly with B. Thus, the dynamic equation of the susceptible compartment is depicted by:

$$\frac{dS}{dt} = \pi - (\lambda + \mu)S \tag{2.1}$$

Individuals in the exposed compartment exit this class either through death due to natural causes at the rate μ, or enter the acute infection compartment at the rate α. This leads to the dynamic equation of compartment E as:

$$\frac{dE}{dt} = \lambda S - (\mu + \alpha)E. \tag{2.2}$$

The acute infected compartment (I_a) is increased by movements of individuals from the exposed group at the rate α, or from the modern treatment class as a result of treatment failure (antibiotics resistance), at the rate θ_m. Individuals leaving compartment (I_a) enters either compartment (M_m) at the rate γ_{am}, the chronic infection stage (I_c) at the rate κ, the traditional medicine treatment class (M_t) at the rate γ_{at}, or these infected individuals die due to the disease at the rate δ_a or die due to natural causes at the rate μ. The dynamic equation of I_a is given by:

$$\frac{dI_a}{dt} = \alpha E + \theta_m M_m - (\mu + \gamma_{am} + \gamma_{at} + \kappa + \delta_a)I_a. \tag{2.3}$$

The infected individuals in the chronic stage compartment are replenished by the κI_a individuals who left compartment I_a. The number of individuals in I_c is reduced by choosing the modern treatment, at

the rate ω_{cm}, by natural mortality or by disease-induced mortality, at the rate δ_c. In compartment I_c, the dynamic equation is:

$$\frac{dI_c}{dt} = \kappa I_a - (\mu + \delta_c + \omega_{cm})I_c. \tag{2.4}$$

Table 1. Model parameters and their epidemiological interpretations.

Parameter	Epidemiological interpretation	Unit
π	Constant recruitment of susceptible individuals	ind.week^{-1}
β	Ingestion rate of *Salmonella*	week^{-1}
μ	Natural death rate of individuals	week^{-1}
$1/\alpha$	Incubation period of infected individuals	week^{-1}
γ_{am}	Treatment rate for individuals in I_a who choose modern medicine	week^{-1}
ω_{cm}	Treatment rate for individuals in I_c who choose modern medicine	week^{-1}
γ_{at}	Treatment rate for individuals in I_a who choose traditional medicine	week^{-1}
κ	Exit rate from the acute to chronic infection stage	week^{-1}
δ_a	Disease-induced mortality rate in compartment I_a	week^{-1}
δ_c	Disease-induced mortality rate in compartment I_c	week^{-1}
θ_m	Relapse rate of infected individuals treated by modern medicine to acute infection stage	week^{-1}
σ_m	Recovery rate of the infected individuals in compartment M_m	week^{-1}
σ_t	Recovery rate of the infected individuals in compartment M_t	week^{-1}
ψ_{mt}	Switching rate of individuals from modern to traditional medicine	week^{-1}
η_a	Shedding rate of *Salmonella* in the environment by individuals in I_a	sal.ind.$^{-1}$.week^{-1}
η_c	Shedding rate of *Salmonella* in the environment by individuals in I_c	sal.ind.$^{-1}$.week^{-1}
k_b	Concentration of *Salmonella* bacteria in food or water which gives a 50% of chance of getting infection	cell/ml
r	Environmental growth rate of *Salmonella*	week^{-1}
μ_b	Decay rate of *Salmonella* in the environment	week^{-1}

The acute infected individuals move into the traditional treatment compartment at the rate γ_{at} , while those receiving modern treatment switch to this compartment at the rate ψ_{mt} . The population of M_t decreases either by recovery at a rate σ_t, or by natural mortality at a rate μ. The dynamic equation of M_t is thus given as:

$$\frac{dM_t}{dt} = \gamma_{at}I_a + \psi_{mt}M_m - (\mu + \sigma_t)M_t. \tag{2.5}$$

Compartment M_m is supplied by compartment I_a and I_c at the rates γ_{am} and ω_{cm}, respectively. This population M_m decreases in four different ways: Switching to traditional treatment at a rate ψ_{mt}, having a relapse at the rate θ_m, recovering at a rate σ_m, and death due to natural mortality at the rate μ. This leads to the following dynamic equation of M_m:

$$\frac{dM_m}{dt} = \gamma_{am}I_a + \omega_{cm}I_c - (\mu + \theta_m + \sigma_m + \psi_{mt})M_m.$$

Patients in compartments M_m and M_t die due natural causes at the rate μ and recover at the rates σ_m and σ_t, respectively. This population decreases by natural mortality. The dynamic equation of R is:

$$\frac{dR}{dt} = \sigma_t M_t + \sigma_m M_m - \mu R,$$

We assume that *Salmonella* bacteria have a natural growth rate r in the environment. Infected individuals in the compartments I_a and I_c shed bacteria in the environment at the rates η_a and η_c, respectively. The bacterial decay rate in the environment is μ_b. Thus, the dynamic equation of the concentration of bacteria is given as:

$$\frac{dB}{dt} = rB + \eta_a I_a + \eta_c I_c - \mu_b B.$$

Table 1 presents the descriptions of all the parameters of interest in our model. The Flow diagram of the model is given in Figure 1. Putting all the equations together give System (2.6) of non-linear differential equations, which is the main model of this paper.

$$\begin{cases} \frac{dS}{dt} &= \pi - (\lambda + \mu)S, \\ \frac{dE}{dt} &= \lambda S - (\mu + \alpha)E, \\ \frac{dI_a}{dt} &= \alpha E + \theta_m M_m - (\mu + \gamma_{am} + \gamma_{at} + \kappa + \delta_a)I_a, \\ \frac{dI_c}{dt} &= \kappa I_a - (\mu + \delta_c + \omega_{cm})I_c, \\ \frac{dM_m}{dt} &= \gamma_{am} I_a + \omega_{cm} I_c - (\mu + \theta_m + \sigma_m + \psi_{mt})M_m, \\ \frac{dM_t}{dt} &= \gamma_{at} I_a + \psi_{mt} M_m - (\mu + \sigma_t)M_t, \\ \frac{dR}{dt} &= \sigma_t M_t + \sigma_m M_m - \mu R, \\ \frac{dB}{dt} &= rB + \eta_a I_a + \eta_c I_c - \mu_b B, \end{cases} \tag{2.6}$$

subject to the initial conditions

$$S(0) = S_0,\ E(0) = E_0,\ I_a(0) = I_{a_0},\ I_c = I_{c_0},\ M_t(0) = M_{t_0},\ M_t(0) = M_{t_0},\ R(0) = R_0,\ B(0) = B_0.$$

For mathematical convenience, we set

$$\begin{aligned} k_1 &= \mu + \alpha, \quad k_2 = \mu + \gamma_{am} + \gamma_{at} + \kappa + \delta_a, \quad k_3 = \mu + \delta_c + \omega_{cm}, \quad k_4 = \mu + \theta_m + \sigma_m + \psi_{mt}, \\ k_5 &= \mu + \sigma_t, \quad k_6 = \mu_b - r, \quad k_7 = \mu + \gamma_{at} + \delta_a, \quad k_8 = \mu + \delta_c, \quad k_9 = \mu + \sigma_m + \psi_{mt}. \\ k_{10} &= (k_3 k_4 k_2 - k_3 \gamma_{am}\theta_m - \omega_{cm}\kappa\,\theta_m) \\ &= k_8\theta_m\kappa + k_8\theta_m k_7 + k_8 k_9\gamma_{am} + k_8 k_9\kappa + k_8 k_9 k_7 + \omega_{cm}\theta_m k_7 + \omega_{cm}k_9\gamma_{am} + \omega_{cm}k_9\kappa + \omega_{cm}k_9 k_7. \end{aligned}$$

Throughout this paper, we assume $\mu_b > r$ in order for k_6 to be positive. The biological significance of this assumption is that without shedding of *Salmonella typhi* in the environment, the concentration of the bacteria will decrease exponentially [25].

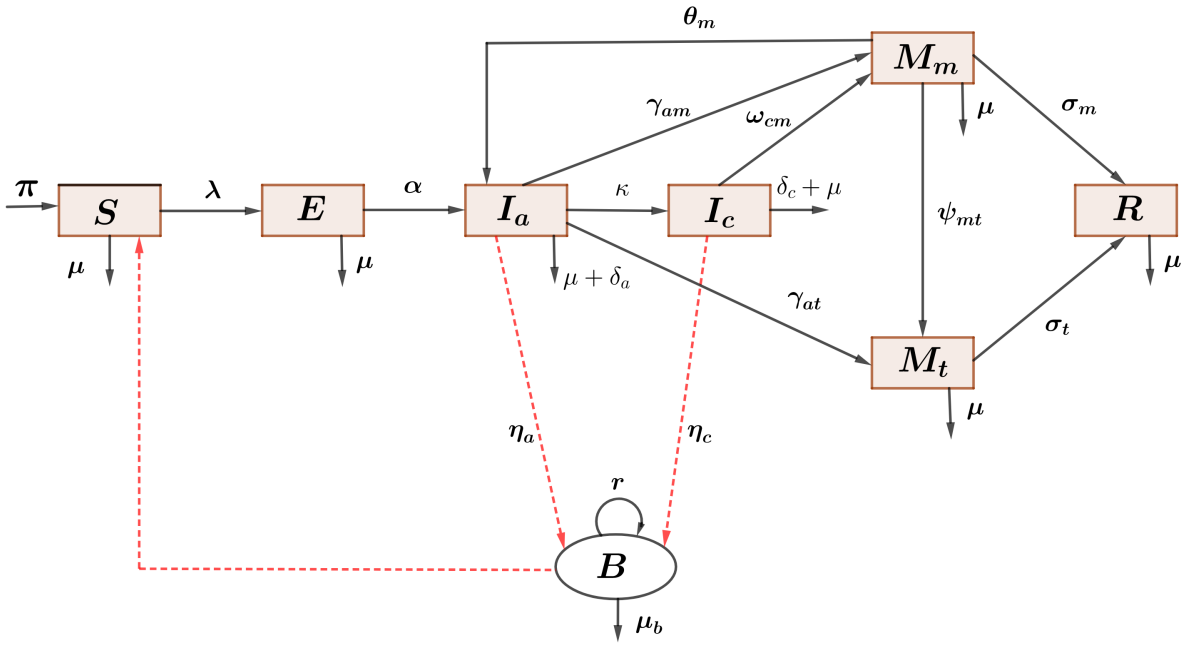


Figure 1. Flow diagram of model.

3. Theoretical analysis of the model

3.1. Well-posedness of the model

Model (2.6) is about a human population and a bacterial population. It is important to check if this model has a solution and if the variables remain positive for a positive initial condition. This is ensured by the following result.

Theorem 3.1. *Model (2.6) is a dynamic system on the biologically feasible compact domain:*

$$\Omega = \left\{ (S, E, I_a, I_c, M_m, M_t, R, B) \in \mathbb{R}_+^8, \quad N(t) \leq \frac{\pi}{\mu}, \quad B(t) \leq \frac{\pi(\eta_a + \eta_c)}{k_6 \mu} \right\}. \tag{3.1}$$

Proof. According to Cauchy-Lipschitz theorem, Model (2.6) has a unique local solution as its right-hand side is locally Lipschitz.

To show that $S(t) \geq 0$ for all $t \geq 0$, we rewrite the first equation of (2.6) as follows:

$$\frac{dS}{dt}\left[S(t)\exp\left(\int_0^t \lambda(s)ds + \mu t\right)\right] = \pi \exp\left(\int_0^t \lambda(s)ds + \mu t\right).$$

Integrating the above equation from 0 to t gives

$$S(t)\exp\left(\int_0^t \lambda(s)ds + \mu t\right) - S(0) = \int_0^t \left\{\pi \exp\left(\int_0^p \lambda(s)ds + \mu p\right)\right\} dp.$$

This leads to

$$S(t) = \left[S(0) + \int_0^t \left\{\pi \exp\left(\int_0^p \lambda(s)ds + \mu p\right)\right\} dp\right] \exp\left(-\mu t - \int_0^t \lambda(s)ds\right) \geq 0.$$

Thus, if $S(0) > 0$, then $S(t) > 0$, for all $t \geq 0$.

To show that $E(t)$, $I_a(t)$, $I_c(t)$, $M_m(t)$, $M_t(t)$, $B(t)$ and $R(t)$ are positive when $E(0) \geq 0$, $I_a(0) \geq 0$, $I_c(0) \geq 0$, $M_m(0) \geq 0$, $M_t(0) \geq 0$, $R(0) \geq 0$, $B(0) \geq 0$, we consider the following sub-system

$$\begin{cases} \dfrac{dE}{dt} = \lambda S - k_1 E, \\ \dfrac{dI_a}{dt} = \alpha E + \theta_m M_m - k_2 I_a, \\ \dfrac{dI_c}{dt} = \kappa I_a - k_3 I_c, \\ \dfrac{dM_m}{dt} = \gamma_{am} I_a + \omega_{cm} I_c - k_4 M_m, \\ \dfrac{dM_t}{dt} = \gamma_{at} I_a + \psi_{mt} M_m - k_5 M_t, \\ \dfrac{dR}{dt} = \sigma_t M_t + \sigma_m M_m - \mu R, \\ \dfrac{dB}{dt} = \eta_a I_a + \eta_c I_c - k_6 B. \end{cases} \tag{3.2}$$

This can be rewritten as

$$\frac{dX}{dt} = AX(t), \tag{3.3}$$

where

$$X = \begin{pmatrix} E \\ I_a \\ I_c \\ M_m \\ M_t \\ R \\ B \end{pmatrix} \quad \text{and} \quad A = \begin{pmatrix} -k_1 & 0 & 0 & 0 & 0 & 0 & \dfrac{\beta S}{B + k_b} \\ 0 & -k_2 & 0 & \theta_m & 0 & 0 & 0 \\ 0 & \kappa & -k_3 & 0 & 0 & 0 & 0 \\ 0 & \gamma_{am} & \omega_{cm} & -k_4 & 0 & 0 & 0 \\ 0 & \gamma_{at} & 0 & \psi_{mt} & -k_5 & 0 & 0 \\ 0 & 0 & 0 & \sigma_m & \sigma_t & -\mu & 0 \\ 0 & \eta_a & \eta_c & 0 & 0 & 0 & -k_6 \end{pmatrix}$$

Clearly, A is a Metzler matrix. Hence System (3.2) is positively invariant in $\mathbb{R}^7_+$.

Furthermore, by adding the first seven equations of System (2.6), we have:

$$\frac{dN(t)}{dt} = \pi - \mu N - \delta_a I_a - \delta_c I_c \leq \pi - \mu N. \tag{3.4}$$

The application of Gronwall's inequality gives

$$N(t) \leq \frac{\pi}{\mu} + \left(N(0) - \frac{\pi}{\mu}\right) \exp(-\mu t), \quad \forall t \geq 0.$$

Thus,

$$\text{if } N(0) \leq \frac{\pi}{\mu}, \text{ then for all } t \geq 0, \ N(t) \leq \frac{\pi}{\mu}.$$

Finally, under the hypothesis that $N(0) \leq \pi/\mu$ and knowing that $I_a \leq N,\ I_c \leq N,\ M_m \leq N$, and $M_t \leq N$, the application of Gronwall's inequality once more leads to

$$B(t) \leq \frac{\pi(\eta_a + \eta_c)}{k_6\mu} \quad \forall t \geq 0, \quad \text{whenever} \quad B(0) \leq \frac{\pi(\eta_a + \eta_c)}{k_6\mu} \quad \forall t \geq 0.$$

Using the fact that the solutions of (2.6) are bounded on $\mathbb{R}^+_8$, we then conclude that with a non-negative initial condition, the solution of System (2.6) remains non-negative and exists globally over time.

3.2. Disease-free equilibrium and its stability

The unique DFE of System (2.6) is given by:

$$P_0 = (S_0, 0, 0, 0, 0, 0, 0, 0), \quad \text{with} \quad S_0 = \frac{\pi}{\mu}. \tag{3.5}$$

We use the next-generation matrix approach [26, 27], to compute $\mathcal{R}_0$. According to [27], the vector of the new infections $\mathcal{F}$ and that of the remaining transfer terms $\mathcal{V}$ are respectively given by:

$$\mathcal{F} = \begin{pmatrix} \lambda S \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad \text{and} \quad \mathcal{V} = \begin{pmatrix} k_1 E \\ -\alpha E - \theta_m M_m + k_2 I_a \\ -\kappa I_a + k_3 I_c \\ -\gamma_{am} I_a - \omega_{cm} I_c + k_4 M_m \\ -\gamma_{at} I_a - \psi_{mt} M_m + k_5 M_t \\ -\eta_a I_a - \eta_c I_c + k_6 B \end{pmatrix}$$

The next-generation matrix FV^{-1}, where F and V are the Jacobian matrices of $\mathcal{F}$ and $\mathcal{V}$ at the DFE, respectively, is given by:

$$FV^{-1} = \begin{pmatrix} \frac{\beta\,\pi\,\alpha\,k_4\,(\eta_a k_3 + \eta_c \kappa)}{\mu\,k_b k_{10} k_1 k_6} & A_{12} & A_{13} & A_{14} & 0 & A_{16} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

where the expressions for $A_{12},\ A_{13},\ A_{14}$ and A_{16} are given in Appendix A.

Hence

$$\mathcal{R}_0 := \rho(FV^{-1}) = \frac{\beta\,\pi\,\alpha\,k_4\,(\eta_a k_3 + \eta_c \kappa)}{\mu\,k_b k_{10} k_1 k_6}. \tag{3.6}$$

The relevance of the reproduction number $\mathcal{R}_0$ is established in the following result [27].

Lemma 3.1. *The DFE P_0 of System (2.6) is locally asymptotically stable (LAS) if $\mathcal{R}_0 < 1$ and it is unstable if $\mathcal{R}_0 > 1$.*

According to Lemma 3.1, the disease dies out when if $\mathcal{R}_0 < 1$ provided that the initial population sizes are in the basin of attraction of the DFE. For the global control of the disease, the global asymptotic stability needs to be proven.

Theorem 3.2. *Assume $\mathcal{R}_0 < 1$, then the DFE point P_0 of Model (2.6) is globally asymptotically stable (GAS) in Ω.*

Proof. Let us consider the candidate Lyapunov function

$$V = \frac{\alpha\, k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_1 k_6} E + \frac{k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_6} I_a + \frac{k_{12}}{k_{10} k_6} I_c + \frac{\theta_m(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_6} M_m + \frac{1}{k_6} B\,, \tag{3.7}$$

where

$$k_{12} = \eta_c \gamma_{am}(\mu + \sigma_m + \psi_{mt}) + \eta_c \theta_m(\mu + \gamma_{at} + \kappa + \delta_a) + \omega_{cm}\theta_m \eta_a.$$

Differentiating V on both sides gives

$$\frac{dV}{dt} = \frac{\alpha\, k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_1 k_6} \frac{dE}{dt} + \frac{k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_6} \frac{dI_a}{dt} + \frac{k_{12}}{k_{10} k_6} \frac{dI_c}{dt} + \frac{\theta_m(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_6} \frac{dM_m}{dt} + \frac{1}{k_6} \frac{dB}{dt} \tag{3.8}$$

That is,

$$\begin{aligned}
\frac{dV}{dt} &= \frac{\alpha\, k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_1 k_6}(\lambda S - k_1 E) + \frac{k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_6}(\alpha E + \theta_m M_m - k_2 I_a) \qquad (3.9)\\
&\quad + \frac{k_{12}}{k_{10} k_6}(\kappa I_a - k_3 I_c) + \frac{\theta_m\, k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_1 k_6}(\gamma_{am} I_a + \omega_{cm} I_c - k_4 M_m) + \frac{1}{k_6}(\eta_a I_a + \eta_c - k_6 B)\\
&= \frac{k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_6}\left(\frac{-\alpha(\mu + \alpha)}{k_1} + \alpha\right) E + \frac{(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_6}(k_4 \theta_m - k_4 \theta_m) M_m\\
&\quad + \frac{1}{k_6 k_{10}}\{-k_2 k_4(\eta_a k_3 + \eta_c \kappa) + k_{12}\kappa + (\eta_a k_3 + \eta_c \kappa)\theta_m \gamma_{am} + k_{10}\eta_a\} I_a\\
&\quad + \frac{1}{k_6 k_{10}}\{-k_{12} k_3 + (\eta_a k_3 + \eta_c \kappa)\omega_{cm}\theta_m + k_{10}\eta_c\} I_c + \frac{\alpha k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_1 k_6}\lambda S - B\\
&= \frac{\alpha k_4(\eta_a k_3 + \eta_c \kappa)}{k_{10} k_1 k_6}\lambda S - B. \qquad (3.10)
\end{aligned}$$

The resulting equation is due to the fact that

$$\frac{1}{k_6 k_{10}}\{-k_2 k_4(\eta_a k_3 + \eta_c \kappa) + k_{12}\kappa + (\eta_a k_3 + \eta_c \kappa)\theta_m \gamma_{am} + k_{10}\eta_a\} = 0,$$

and

$$\frac{1}{k_6 k_{10}}\{-k_{12} k_3 + (\eta_a k_3 + \eta_c \kappa)\omega_{cm}\theta_m + k_{10}\eta_c\} = 0.$$

Following (3.6), Equation (3.9) becomes

$$\frac{dV}{dt} = \left(\mathcal{R}_0 k_b \frac{\mu}{\beta\pi}\right)\lambda S - B = \left(\mathcal{R}_0 k_b \frac{\mu}{\beta\pi}\right)\frac{\beta B}{B + k_b} S - B \tag{3.11}$$

Since $S \leq N \leq \dfrac{\pi}{\mu} = S_0$, and $\dfrac{1}{B + k_b} \leq \dfrac{1}{k_b}$, we have:

$$\frac{dV}{dt} \leq -B(1 - \mathcal{R}_0)$$

Thus, whenever $\mathcal{R}_0 < 1$, we have $dV/dt \leq 0$, and V is a strict Lyapunov function in Ω. Hence, the disease-free equilibrium P_0 is globally asymptotically stable.

Figure 2 illustrates the GAS of the DFE for Model (2.6) when $\mathcal{R}_0 < 1$.

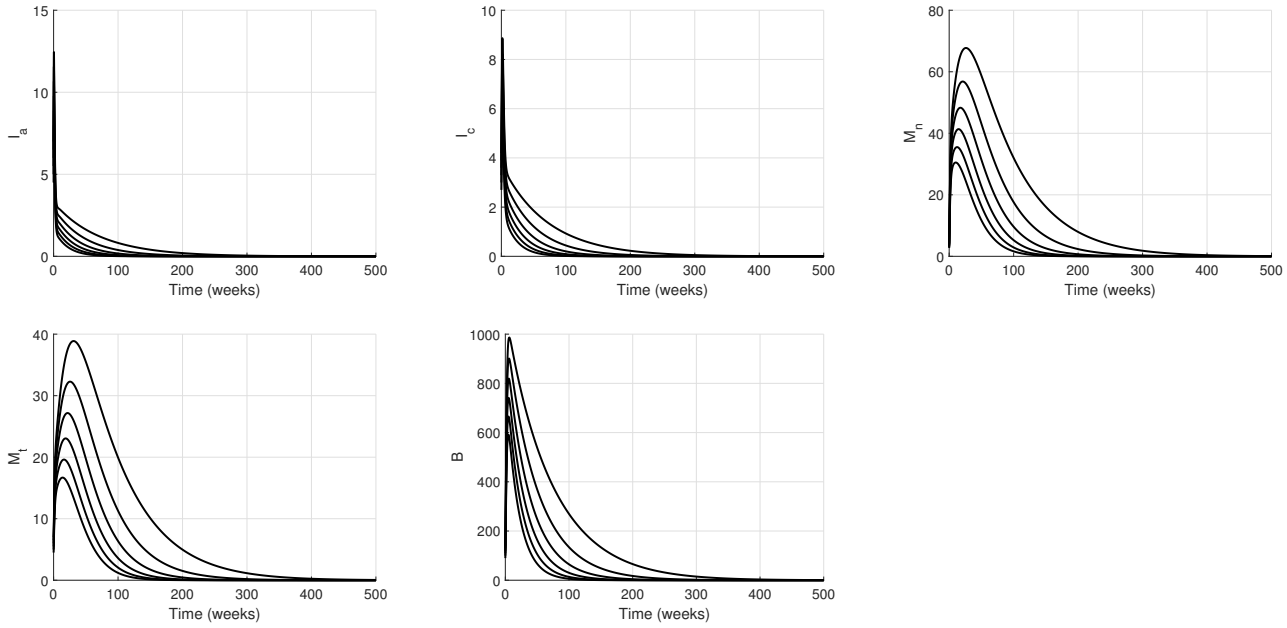


Figure 2. GAS of the DFE. This figure is plotted with $\theta_m = 0.00067$ and $\beta = 0.0025$. The other parameters are as shown in Table 2. The value of $\mathcal{R}_0 = 0.6318$.

3.3. Interior equilibrium of the model and its stability

Theorem 3.3. *Model (2.6) has a unique positive equilibrium if and only if* $\mathcal{R}_0 > 1$.

Proof. Let us denote by $\varepsilon^* = (S^*, E^*, I_a^*, I_c^*, M_m^*, M_t^*, R^*, B^*)$ a nontrivial equilibrium for Model (2.6). Setting the right-hand side of Model (2.6) to zero gives:

$$\begin{cases} S^* = \dfrac{\pi}{\lambda^* + \mu}, \quad E^* = \dfrac{\lambda^* \pi}{k_1 (\lambda^* + \mu)}, \quad I_a^* = \dfrac{k_3 k_4 \alpha \lambda^* \pi}{k_{10} k_1 (\lambda^* + \mu)}, \quad I_c^* = \dfrac{k_4 \kappa \alpha \lambda^* \pi}{k_{10} k_1 (\lambda^* + \mu)}, \\ M_m^* = \dfrac{\alpha \lambda^* \pi (\gamma_{am} k_3 + \omega_{cm} \kappa)}{k_{10} k_1 (\lambda^* + \mu)}, \quad M_t^* = \dfrac{(\gamma_{at} k_3 k_4 + \psi_{mt} \gamma_{am} k_3 + \psi_{mt} \omega_{cm} \kappa) \alpha \lambda^* \pi}{k_5 k_{10} k_1 (\lambda^* + \mu)}, \\ R^* = \dfrac{\alpha \lambda^* \pi (\gamma_{at} k_3 k_4 \sigma_t + \psi_{mt} \sigma_t \gamma_{am} k_3 + \psi_{mt} \sigma_t \omega_{cm} \kappa + k_5 \sigma_m \gamma_{am} k_3 + k_5 \sigma_m \omega_{cm} \kappa)}{\mu k_5 k_{10} k_1 (\lambda^* + \mu)}, \\ B^* = \dfrac{(\eta_a k_3 + \eta_c \kappa) k_4 \alpha \lambda^* \pi}{k_6 k_{10} k_1 (\lambda^* + \mu)}, \end{cases} \tag{3.12}$$

with

$$\lambda^* = \frac{\beta B^*}{B^* + k_b} \tag{3.13}$$

Substituting the expressions in (3.12) in Eq (3.13) gives

$$\lambda^* \left[(k_4\alpha\,\pi\,\eta_a k_3 + k_4\alpha\,\pi\,\eta_c\kappa + k_b k_6 k_{10} k_1)\lambda^* - k_b k_6 k_{10} k_1 \mu\ (\mathcal{R}_0 - 1) \right] = 0. \tag{3.14}$$

That is

$$\lambda^* = \frac{k_b k_6 k_{10} k_1 \mu\ (\mathcal{R}_0 - 1)}{k_4\alpha\,\pi\,\eta_a k_3 + k_4\alpha\,\pi\,\eta_c\kappa + k_b k_6 k_{10} k_1}. \tag{3.15}$$

Hence, when $\mathcal{R}_0 \leq 1$, the unique equilibrium is the DFE, while when $\mathcal{R}_0 > 1$, the DFE P_0 coexists with the unique endemic equilibrium ε^*.

We study the local stability of ε^* in Theorem 3.4.

Theorem 3.4. *System (2.6) has a trans-critical bifurcation at $\mathcal{R}_0 = 1$, which is the bifurcation parameter. Moreover, the unique endemic equilibrium ε^* is LAS when $\mathcal{R}_0 > 1$.*

Proof. Let us consider the case where $\mathcal{R}_0 = 1$, and choose $\beta = \beta^*$ as a bifurcation parameter.

$$\mathcal{R}_0 = 1 \Leftrightarrow \beta^* = \frac{k_1 k_b k_6 k_{10}}{\alpha\pi k_4 (\kappa\eta_c + k_3\eta_a)}.$$

The Jacobian matrix of System (2.6) at the DFE is given as,

$$J_{\beta^*} = \begin{pmatrix} -\mu & 0 & 0 & 0 & 0 & 0 & 0 & -g_1 \\ 0 & -k_1 & 0 & 0 & 0 & 0 & 0 & g_1 \\ 0 & \alpha & -k_2 & 0 & \theta_m & 0 & 0 & 0 \\ 0 & 0 & k & -k_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_{am} & \omega_{cm} & -k_4 & 0 & 0 & 0 \\ 0 & 0 & \gamma_{at} & 0 & \psi_{mt} & -k_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma_m & \sigma_t & -\mu & 0 \\ 0 & 0 & \eta_a & \eta_c & 0 & 0 & 0 & -k_6 \end{pmatrix}$$

System (2.6), with $\beta = \beta^*$ has a nonhyperbolic equilibrium point. The other eigenvalues have negative real parts. Therefore, the center manifold theory [28] can be applied to analyze the dynamics of System (2.6) near the bifurcation parameter β^*. The components of a right eigenvector $w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7, w_8)^T$ of J_{β^*} and a non-negative left-eigenvector $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7, v_8)^T$ of J_{β^*} associated with the zero eigenvalue are, respectively, given as

$$\begin{cases} w_1 = -\dfrac{g_1}{\mu} w_8 < 0, \quad w_2 = \dfrac{g_1 g_5}{k_1} > 0, \quad w_3 = \dfrac{k_3}{k} w_4 > 0, \quad w_4 > 0 \\ w_5 = g_2 w_4 > 0, \quad w_6 = g_3 w_4 > 0, \quad w_7 = g_4 w_4 > 0, \quad w_8 = g_5 w_4 > 0, \\ \text{with} \quad g_2 = \dfrac{\gamma_{am} k_3}{\kappa k_4} + \dfrac{\omega_{cm}}{k_4} \qquad g_3 = \dfrac{\gamma_{at} k_3}{k_5 \kappa} + \dfrac{\psi_{mt}\gamma_{am} k_3}{k_5 k_4 \kappa} + \dfrac{\psi_{mt}\omega_{cm}}{k_5 k_4} \\ \qquad g_1 = \dfrac{\pi\beta^*}{\mu k_b} \qquad g_4 = \dfrac{(\sigma_m g_2 + \sigma_t g_3)}{\mu}, \qquad g_5 = \dfrac{\eta_a k_3}{\kappa k_6} + \dfrac{\eta_c}{k_6} \end{cases}$$

and

$$\begin{cases} v_1 = v_6 = v_7 = 0, \quad v_2 = \dfrac{\alpha}{k_1} v_3 > 0, \quad v_3 > 0, \\ v_4 = \left(\dfrac{\omega_{cm}\theta_m}{k_3 k_4} + \dfrac{\eta_c g_1 \alpha}{k_1 k_3 k_6} \right) v_3 > 0, \quad v_5 = \dfrac{\theta_m v_3}{k_4} > 0, \quad v_8 = \dfrac{g_1 \alpha}{k_1 k_6} v_3 > 0. \end{cases}$$

The coefficients a and b as defined in [28] are:

$$b = v_2 \sum_{i=1}^{8} w_i \frac{\partial^2 f_2}{\partial x_i \partial \beta^*}(p_0) = \frac{v_2 \omega_8 \pi}{\mu k_b} = \frac{v_2 \left(\dfrac{\eta_a k_3}{\kappa k_6} + \dfrac{\eta_c}{k_6} \right) \omega_4 \pi}{\mu k_b} > 0,$$

and

$$\begin{aligned} a &= \sum_{k,i,j=1}^{8} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(P_0) \\ &= -2 v_2 \frac{\omega_8^2 \beta^* \pi}{k_b^2 \mu^2}(1 + 2\mu) = -2 v_2 \frac{\left(\dfrac{\eta_a k_3}{\kappa k_6} + \dfrac{\eta_c}{k_6} \right)^2 \beta^* \pi}{k_b^2 \mu^2}(1 + 2\mu)\omega_4 < 0 \end{aligned} \tag{3.16}$$

Since $a < 0$ and $b > 0$, the model has a trans-critical bifurcation at $\mathcal{R}_0 = 1$ and the endemic equilibrium is LAS for $\mathcal{R}_0 > 1$, but close to 1 [28].

Figure 3 illustrates the forward bifurcation for Model (2.6).

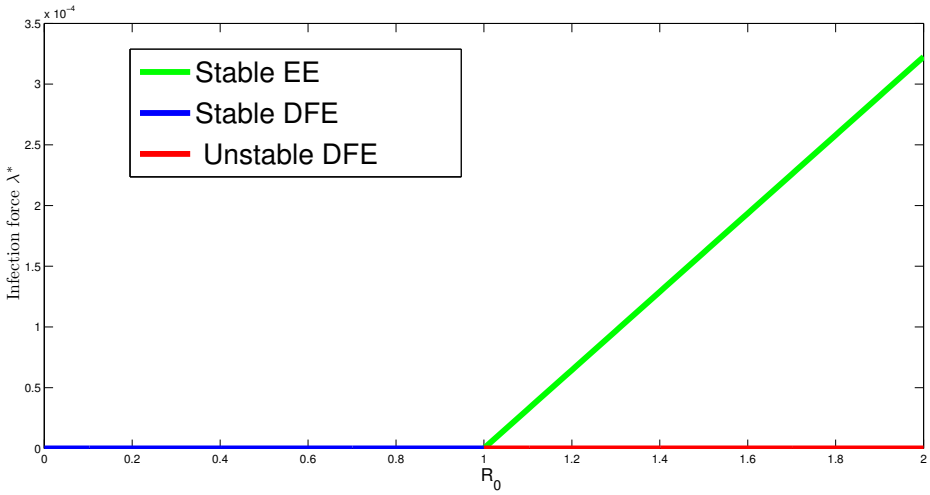


Figure 3. The forward bifurcation curve for the model system in (2.6) in the $(\mathcal{R}_0, \lambda^*)$ plane.

Theorem 3.4 proves the persistence of the disease when $\mathcal{R}_0 > 1$, for values close to 1. To determine the asymptotic behavior of the model for higher values of $\mathcal{R}_0$, the global asymptotic stability of ε^* has to be proven. This is stated in Theorem 3.5.

Theorem 3.5. *The endemic equilibrium ε^* for Model* 2.6 *is GAS provided that $\mathcal{R}_0 > 1$.*

Proof. See Appendix B.

Figure 4 illustrates the persistence of typhoid and the global asymptotic stability of ε^* when $\mathcal{R}_0 > 1$ for trajectory plot when using the values of Table 2 and $\mathcal{R}_0 > 1$. From this figure, we can observe that the infected individuals and bacteria are always present in the population. This means that the trajectories converge to the endemic equilibrium point. Thus, whenever $\mathcal{R}_0 > 1$, the disease persists in the host population as established in Theorem 3.3.

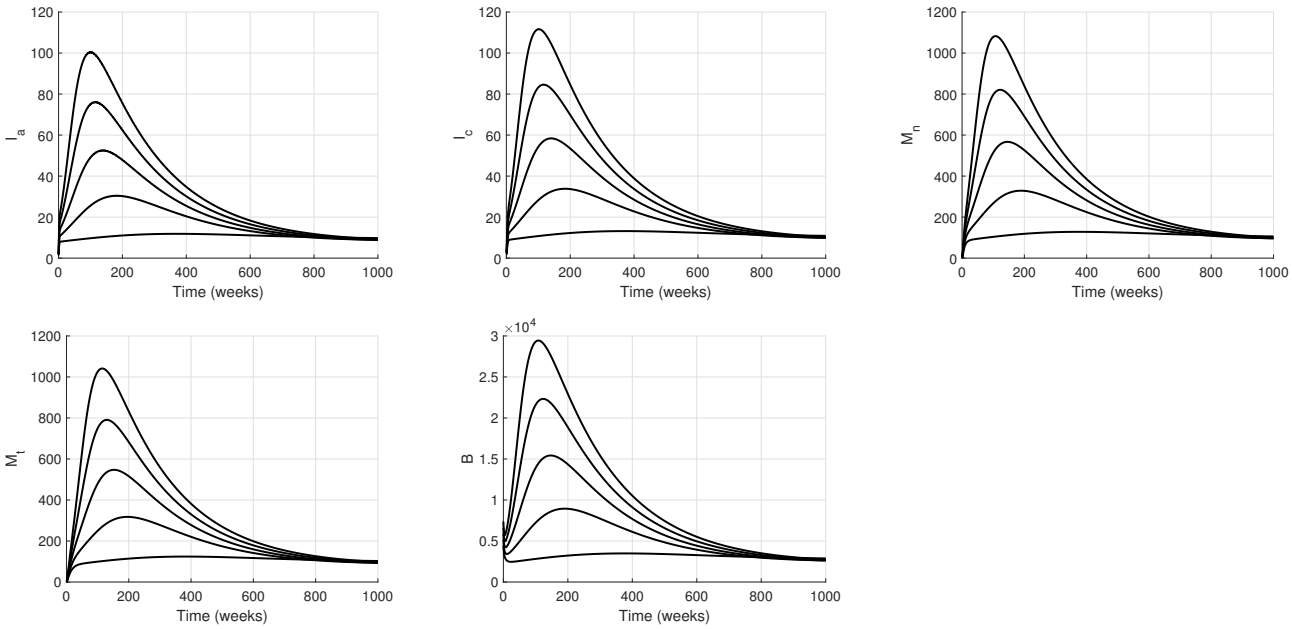
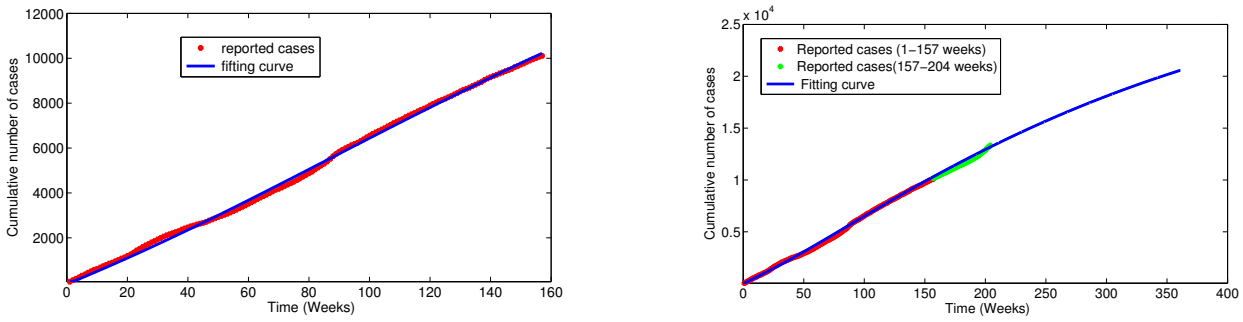


Figure 4. GAS of the EE. This figure is plotted with $\theta_m = 0.097$. The other parameter values are as in Table 2. The value of $\mathcal{R}_0 = 1.8$.

4. Model calibration and sensitivity analysis

4.1. Model calibration



(a) Model fit on the cumulative number of cases per week between 30 December 2019 and 1 January 2023

(b) Model validation and prediction on the dynamics of typhoid disease for the period up to November 2026

Figure 5. Model fit and calibration on the dynamics of typhoid fever disease in Penka-Michel.

In this section, we fitted our model to the weekly cumulative reported cases of TF in the Penka-Michel health district in Cameroon from 30 December 2019 to 1 January 2023 (157 weeks). The number of infected cases during the first week was 48. We used the following initial conditions for the human population: $S(0) = 120{,}000$, $E(0) = 0$, $I_a(0) = 10$, and $I_c(0) = 20$, $M_m(0) = 10$, $M_t(0) = 8$, $R(0) = 0$. The value $B(0) = 7371$ was obtained by calibration as a parameter.

According to [29], the life expectancy in Cameroon is 54.4 years. Therefore, the estimated value for μ is 0.000353 per week. For simplicity, an estimate for π is $\pi = S_0 \times \mu = 42.36$. The data were fitted using the nonlinear least squares algorithm implemented by the fminsearcbnd function in MATLAB. Plots of the model's fit and calibration are shown in Figure 5.

Table 2. Parameter value estimates.

Parameter	Range	Values	Source
κ	[0.1 , 1]	0.7	[14]
δ_c	[0.1 , 0.7]	0.462	[14]
δ_a	[0.01 , 0.04]	0.028	[14]
r	[0.07 , 0.126]	0.098	[30]
k_b	[49,900 , 55,000]	50.000	[21]
μ_b	[0.1 , 0.7]	0.2415	[30]
σ_m	[0.01 , 0.03]	0.0174	[31]
α	[0 , 1]	0.7	[14]
η_a	[10 , 25]	20	Assumed
η_c	[10 , 25]	20	Assumed
μ	[0.0001 , 0.0005]	0.000353	Calculated
π	[20 , 50]	42.36	Calculated
β	[0.001 , 0.005]	0.004	Fitted
θ_m	[0.001 , 0.008]	0.0067	Fitted
γ_{at}	[0 , 3]	0.630	Fitted
γ_{am}	[0.1 , 4]	1.456	Fitted
ω_{cm}	[0 , 3]	0.167	Fitted
ψ_{mt}	[0.01 , 0.05]	0.037	Fitted
σ_t	[0 , 1]	0.098	Fitted
$B(0)$	–	7371.15787	Fitted
$\mathcal{R}_0$	–	1.2058	Estimated

Figure 5a presents model fit to the cumulative cases of diagnosed typhoid fever, while Figure 5b shows the model's validation and prediction on future cases based on our model. The fitted parameters as well as those obtained from literature are presented in Table 2. The results in Figure 5a, show that our model is a very good fit for the typhoid disease dynamics in Penka-Michel. To validate our model, in Figure 5a, we plot the curve from 2 January 2023 to 5 November 2023 (from Week 158 to Week 201). The model gives an estimate of 12,950 cases of typhoid at the end of Week 201. We observe that this number is quite close to the 12,873 reported cases at that same period. Hence, the model can be used for predictions on the disease trend in the district. Extrapolation of the trend curve up to 6 November 2026 (Week 358), predicts a total number of 21,270 cases of typhoid before the end of 2026. This knowledge,

together with a basic reproduction number $\mathcal{R}_0 = 1.2058 > 1$, calls for the urgent need to put control measures in place to overcome the present trend of the disease. However, a knowledge on the most influential parameters in the model is crucial for an effective control strategy.

4.2. Sensitivity analysis

Sensitivity analysis has almost becoming an integral part of mathematical modeling. In infectious disease modeling, it is the technique commonly used to determine which parameters have a significant effect on the spread of an infectious disease. We have shown that $\mathcal{R}_0$ verifies the sharp threshold property, and hence, the control of the disease lies in the control of $\mathcal{R}_0$. We performed global sensitivity analysis on $\mathcal{R}_0$ to identify its most influential parameters. The sensitivity analysis actually assesses the weight and type of change on the basic reproduction number when the model parameters vary across the entire range of values as shown in Table 2. We used the Latin hypercube sampling (LHS) technique to run 2500 simulations and we compute thr partial rank correlation coefficients (PRCC) between $\mathcal{R}_0$ and each parameter of Model (2.6). Usually, parameters with high PRCC absolute values (> 0.5 or < -0.5) and with small p-values (< 0.05) are considered most influential on $\mathcal{R}_0$ [32].

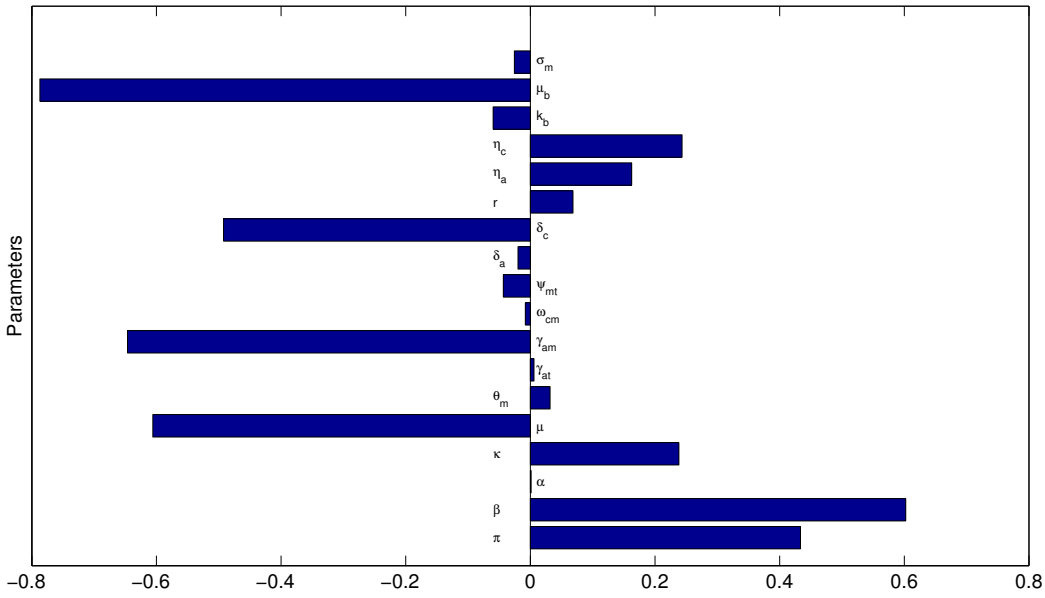


Figure 6. Partial correlation coefficients showing the effects of parameter variation on $\mathcal{R}_0$ using the parameter values in Table 2.

The PRCC computed values are displayed in Figure 6. This figure shows that μ_b, γ_{am} and β are the most influential parameters in either decreasing or increasing the value of $\mathcal{R}_0$. The analysis shows that shedding rate of *Salmonella typhi* in the environment increases the burden of the disease. The modern medicine parameter is seen to be crucial in decreasing the value of $\mathcal{R}_0$. Other parameters that significantly reduce $\mathcal{R}_0$ whenever they increase are μ and δ_c. Finally, though γ_{at} and ψ_{mt} are not among the most influential parameters, the results point out that taking either of the treatments or switching

from modern treatment to traditional therapy will decrease the disease burden. This highlights the important role traditional medicine should play in the control of typhoid fever.

Using PRCC and scatterplots together provides a robust way to understand and visualize the relationships (monotonicity) between the model's parameters and outputs. A monotonic relationship means that the output consistently increases or decreases as the parameter changes. PRCC measures the strength and direction of the monotonic relationship between a model parameter and the model output while controlling for other parameters. Figure 7 depicts scatterplots for each parameter against the model output $\mathcal{R}_0$. The plots show the monotonicity between each parameter of our model and $\mathcal{R}_0$.

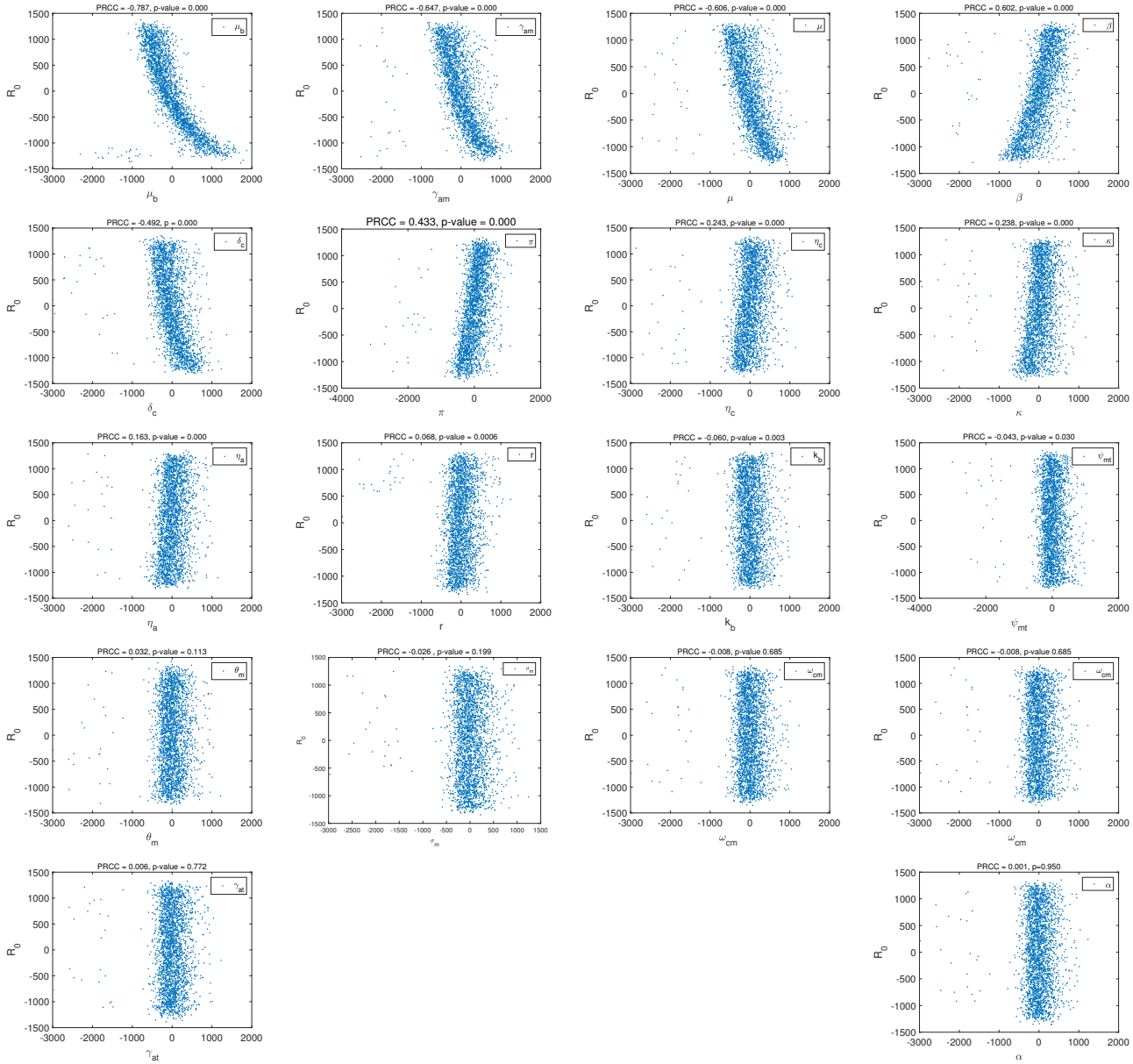
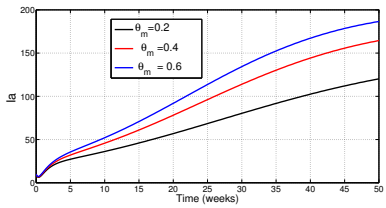


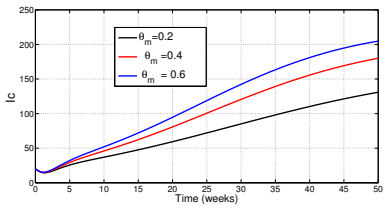
Figure 7. Scatterplots of PRCC values for each model parameter versus $\mathcal{R}_0$.

5. Numerical simulations

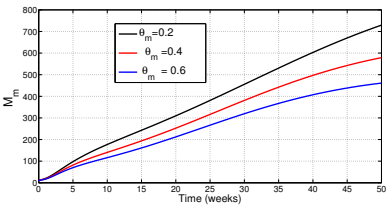
In this section, we provide some simulations to illustrate how a change in the parameters influences the model's dynamics. Most of the parameters used are presented in Table 2. In Figure 8, we explore the impact of relapse over time by considering varying values of θ_m: $\theta_m = 0.2$; $\theta_m = 0.4$, and $\theta_m = 0.6$. It is seen that as the value of θ_m increases, typhoid cases also increase. This is an indication that resistance to modern treatment leads to a relapse into the disease stage.



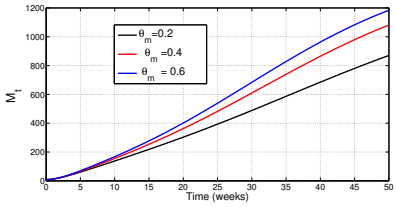
(a) Evolution over time of acute infected patients for varying relapse rates



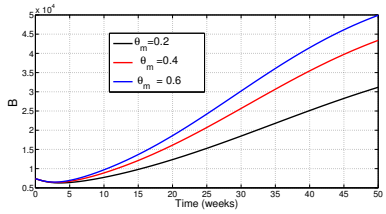
(b) Evolution over time of chronic infected patients for varying relapse rates



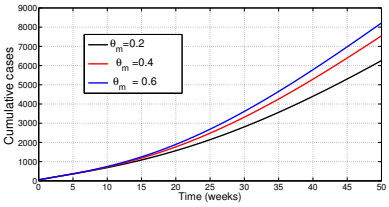
(c) Evolution over time of patients undergoing modern medicine for varying relapse rates



(d) Evolution over time of patients undergoing traditional medicine for varying relapse rates

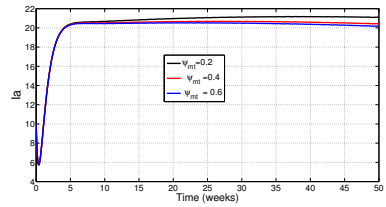


(e) Evolution over time of bacterial concentration for varying relapse rates

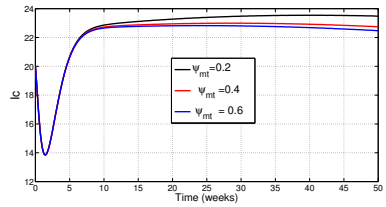


(f) Evolution over time of cumulative infected cases for varying relapse rates

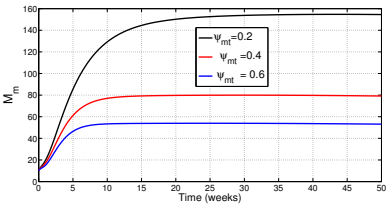
Figure 8. Influence of relapse on the model variables.



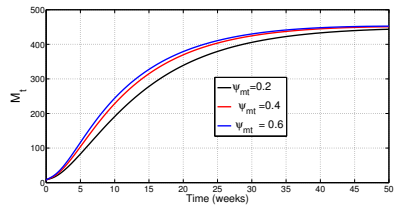
(a) Evolution over time acute infected patients for varying switching rates



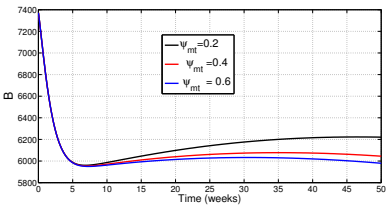
(b) Evolution over time of chronic infected patients for varying switching rates



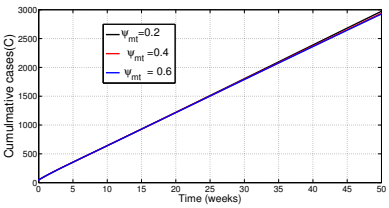
(c) Evolution over time of patients switching from modern to traditional for varying switching rates



(d) Evolution over time of patients receiving traditional medicine for varying switching rates



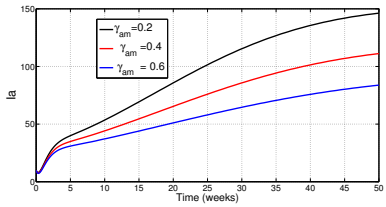
(e) Evolution over time of bacterial concentration for varying switching rates



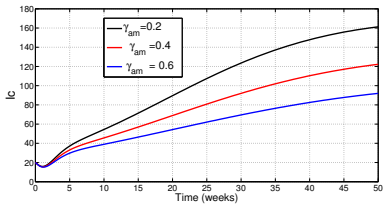
(f) Evolution over time of cumulative infected cases for varying switching rates

Figure 9. Importance of switching from modern to traditional treatment.

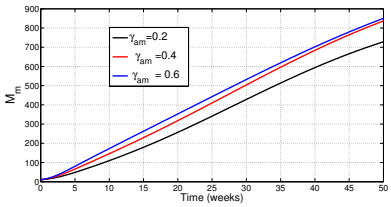
One way of avoiding the relapse of TF is to switch from modern treatment to traditional therapy. Figure 9, gives a picture of the dynamics as infected individuals receiving modern treatment switch to traditional treatment at the rates $\psi_{mt} = 0.2$; $\psi_{mt} = 0.4$, and $\psi_{mt} = 0.6$. The output shows that over time, there is a decrease in the number of cases as the rate of movement from the modern treatment class to the traditional medicine compartment increases. This is a pointer to the positive impact traditional medicine has on lessening the burden of the typhoid fever disease.



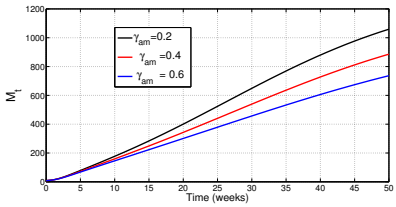
(a) Evolution over time of acute infected patients for the varying treatment rates (γ_{am})



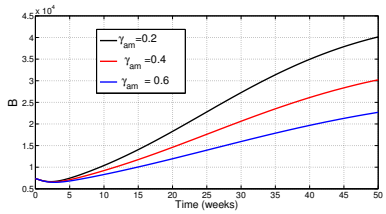
(b) Evolution over time of hronic infected patients for the varying treatment rates (γ_{am})



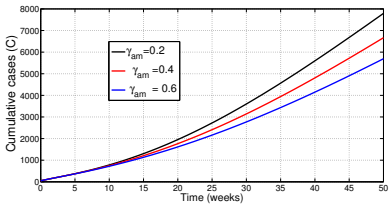
(c) Evolution over time of patients receiving modern medicine for the varying treatment rates (γ_{am})



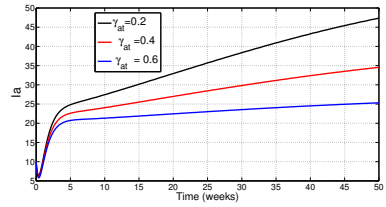
(d) Evolution over time of patients receiving traditional medicine for the varying treatment rates (γ_{am})



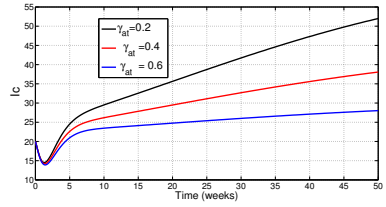
(e) Evolution over time of bacterial concentration for the varying treatment rates (γ_{am})



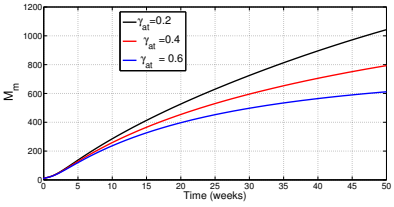
(f) Evolution over time of cumulative infected cases for the varying treatment rates (γ_{am})



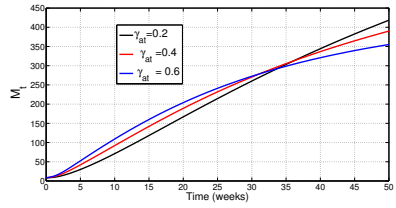
(g) Evolution over time of acute infected patients evolution over time for the varying treatment rates (γ_{at})



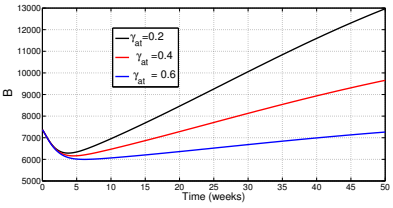
(h) Evolution over time of chronic infected patients for the varying treatment rates (γ_{at})



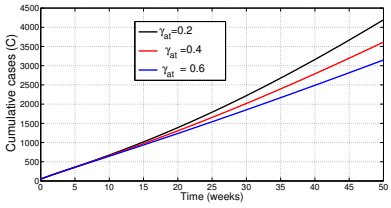
(i) Evolution over time patients receiving modern medicine for the varying treatment rates (γ_{at})



(j) Evolution over time patients receiving traditional medicine for the varying treatment rates (γ_{at})



(k) Evolution over time of bacterial concentration for the varying treatment rates (γ_{at})



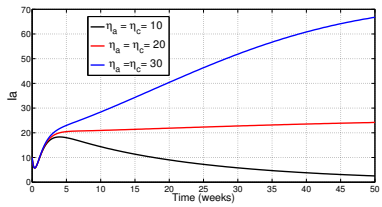
(l) Evolution over time of cumulative cases for the varying treatment rates (γ_{at})

Figure 10. Importance of taking treatment against typhoid fever.

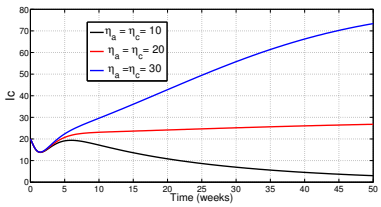
Though it is recommended to switch from modern treatment to traditional treatment, it is imperative to at least receive some treatment, be it modern or traditional. Figure 10 presents different scenarios that emphasize the importance of taking treatment against typhoid fever. The different subfigures (10a–10f) affirm that receiving any of the two modes of treatment will cause a decrease in the number of cases.

In Figure 11, we investigate the impact of *Salmonella* bacteria shedding in the environment. It is seen that when the concentration of the bacteria increases in the environment, the number of cases increases as well. This calls for the necessity of adopting measures to prevent the spread of the disease, such as good sanitation habits, eating safe food and drinking potable water.

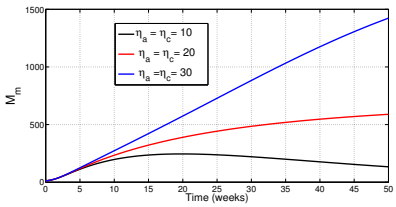
The key parameters in our model by virtue of their influence and importance are: γ_{am}, γ_{at}, μ_b and ω_{cm}. Studying the effect of these parameters on the basic reproduction number ($\mathcal{R}_0$) is crucial in order to understand the disease dynamics. In our context, this will help in either choosing a particular mode of treatment or adopting a synergistic therapy approach in the treatment of typhoid fever. Figure 12 presents the effect of each of these parameters on $\mathcal{R}_0$, when all other parameter values are as shown in Table 2 . The parameters γ_{am} and γ_{at} measure the rate at which individuals in the acute stage of disease choose the modern medicine and traditional medicine, respectively. Meanwhile ω_{cm} measures the rate at which patients in the chronic stage of typhoid choose modern treatment, and μ_b is the decay rate of the bacteria in the environment. Figure 12a shows that $\gamma_{am} = 2.07$ (30% relative error) is the minimum value for $\mathcal{R}_0 < 1$. With this value, $\mathcal{R}_0 = 0.9967 < 1$, which means the disease will be under control. Figure 12b gives a minimum value of $\gamma_{at} = 2.49$ (36.38% relative error). The corresponding value of the basic reproduction number is $\mathcal{R}_0 = 0.9904 < 1$. Figure 12c focuses on the effect of concentration of bacterium *Salmonella typhi* in the environment. The value of μ_b should be $\mu_b = 0.44$ (45.5% relative error), and this gives $\mathcal{R}_0 = 0.9914 < 1$. Interestingly, unlike the other three, the output in Figure 12d, indicates that there is no value of ω_{cm} for which $\mathcal{R}_0 < 1$. This tells us that with the choice of modern medicine alone, the disease will prevail. It is therefore obvious that symptoms of the disease will not disappear for chronically sick patients receiving modern treatment only. There is a need to explore other means through which the disease can be controlled.



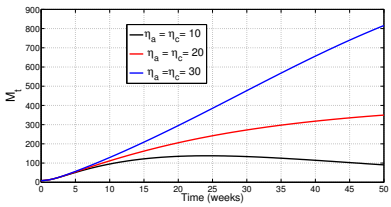
(a) Evolution over time of acute infected patients for varying shedding rates



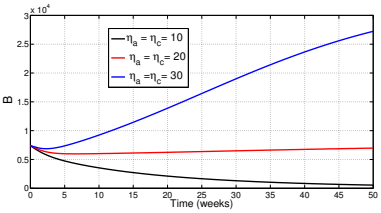
(b) Evolution over time of chronic infected patients for varying shedding rate



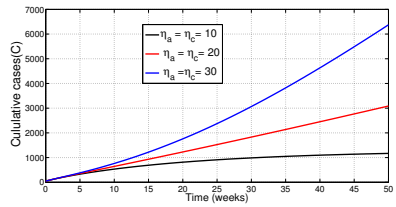
(c) Evolution over time of patients receiving modern treatment for varying shedding rate



(d) Evolution over time of patients receiving traditional treatment for varying shedding rate



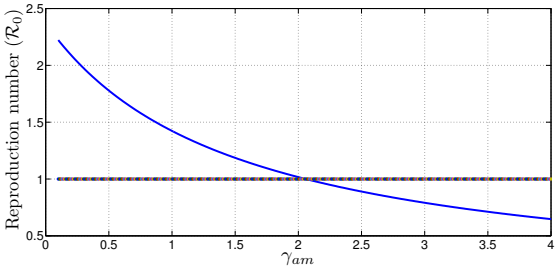
(e) Evolution over time of bacterial concentration for varying shedding rate



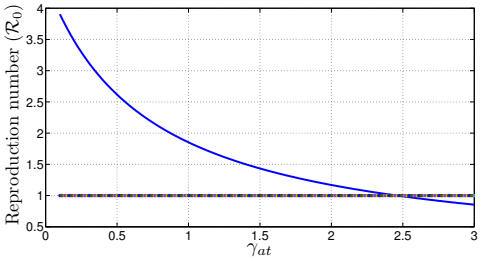
(f) Evolution over time of cumulative cases for varying shedding rate

Figure 11. Influence of *Salmonella typhi* shedding.

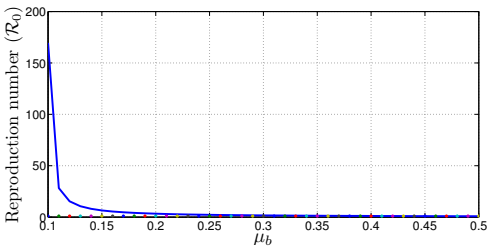
Contour plots make it easy for us to simultaneously compare how different conditions on the influential and important parameters affect $\mathcal{R}_0$. We use contour plots to display the change of $\mathcal{R}_0$ in the 2-dimensional space parameter (ω_{cm}, γ_{at}), (ω_{cm}, μ_b), (γ_{am}, and γ_{at}), respectively. These plots help to in determining joint parameters values that produce a value of $\mathcal{R}_0 < 1$. The contour plots are given in Figure 13. Figure 13a depicts the correlation between the rate at which patients in the chronic stage of typhoid choose modern treatment and the rate at which infected persons in the acute phase choose traditional medicine and their effect on the reproduction number. It is seen that $\mathcal{R}_0 < 1$, if ($\omega_{cm} \geq 1.0, \gamma_{at} \geq 1.1$). This is an indication that neither modern medicine alone nor traditional medicine alone can eradicate the disease. Figure 13b shows the correlation between the rate at which patients in the chronic stage of typhoid choose modern treatment and the decay rate of the bacteria in the environment and their effect on $\mathcal{R}_0$. The output demonstrates that to maintain $\mathcal{R}_0 < 1$, it is important to maintain the shedding rate of *Salmonella typhi* bacteria within the interval $[0.17, 0.32]$ and ensure that the rate at which patients choose modern treatment should be above 1.3767. Similarly, Figure 13c reveals that, it is important that the rate at which infected individuals choose modern medicine is above 2.8371, while the rate at which infected persons opt for traditional medicine must be at least 2.1786, in order for $\mathcal{R}_0$ to be less than unity. In summary, the plots emphasize the necessity to associate traditional medicine with modern medicine in the treatment of typhoid fever.



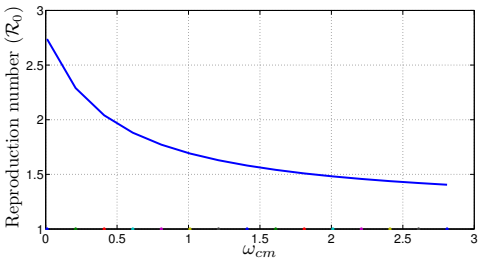
(a) Graph of $\mathcal{R}_0$ versus γ_{am}



(b) Graph of $\mathcal{R}_0$ versus γ_{at}

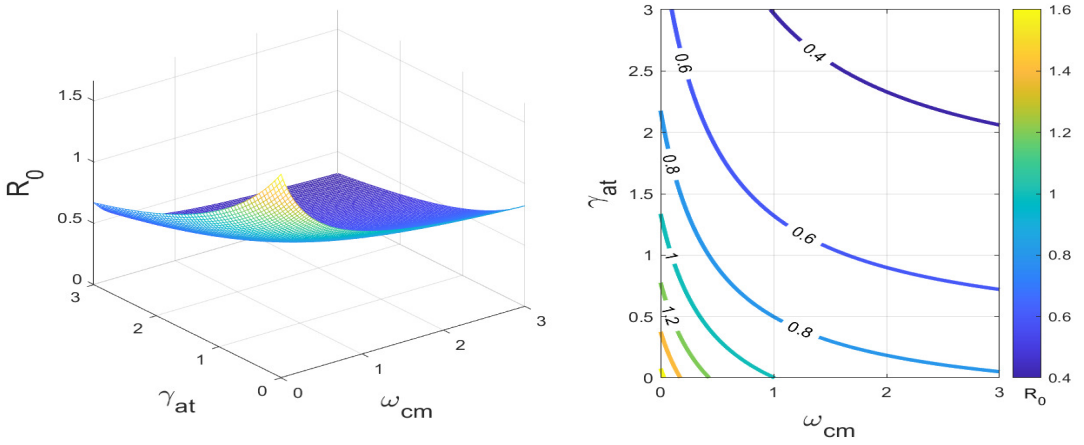


(c) Graph of $\mathcal{R}_0$ versus μ_b

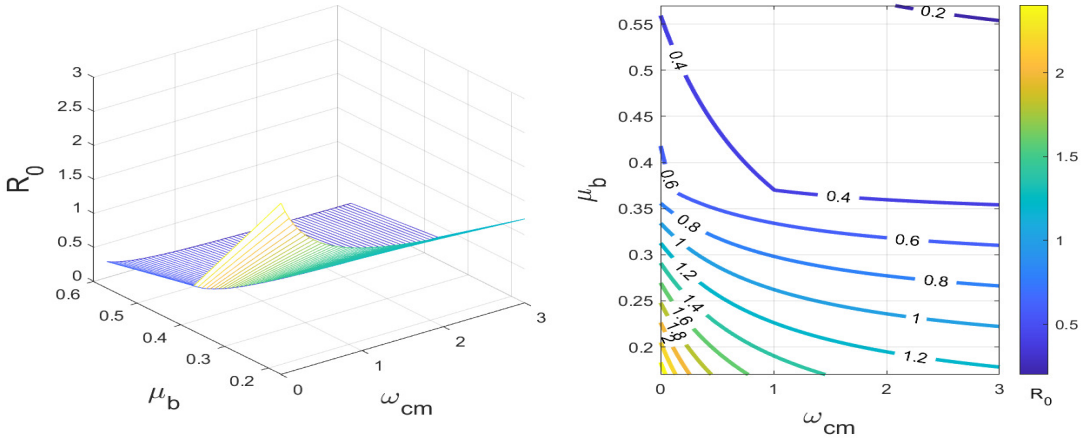


(d) Graph of $\mathcal{R}_0$ versus ω_{cm}

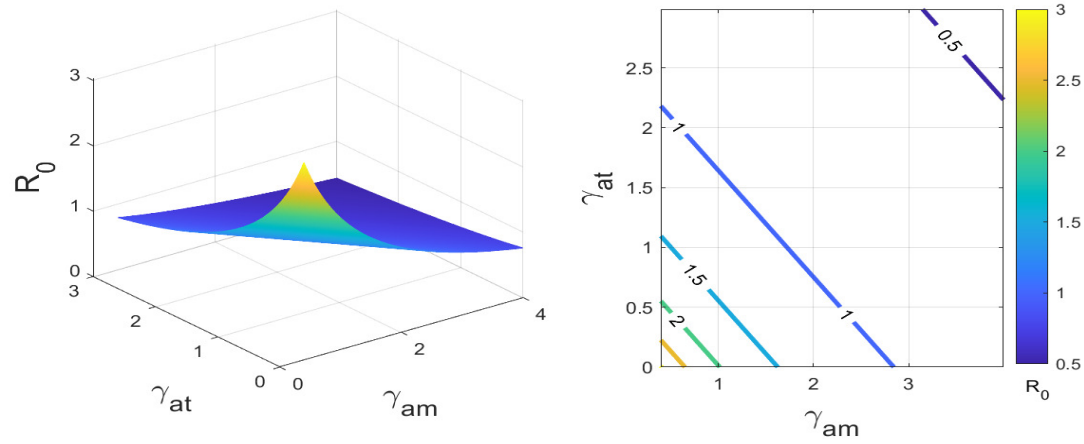
Figure 12. Plots of $\mathcal{R}_0$ versus some influential and important parameters when all other parameter values are as given in Table 2.



(a) Contour plot showing how $\mathcal{R}_0$ depends on γ_{at} and ω_{cm}



(b) Contour plot showing how $\mathcal{R}_0$ depends on μ_b and ω_{cm}



(c) Contour plot showing how $\mathcal{R}_0$ depends on γ_{at} and γ_{am}

Figure 13. Effects of two selected influential and important parameters on $\mathcal{R}_0$ with all other parameter values given as in Table 2.

6. Conclusions

Typhoid fever has remained a major public health concern in Cameroon, especially in communities where there are inadequate preventive measures against the spread of the disease such as, good sanitation habits, eating safe food, and drinking potable water. Resistance of the disease to antibiotics is worrisome. Mathematical models that will improve our understanding suggest that new combination therapies and good practices that culminate in tackling and reducing the disease burden are important. In this paper, we have proposed a typhoid fever mathematical model that takes into account the evolution of the disease from the incubation phase to the invasion (acute) and chronic phases. The key novelty of the proposed model is the inclusion of modern and traditional treatment components. This is done to assess the impacts of both modes of treatment on the *Salmonella typhi* bacteria. Theoretical analysis of the model was performed. We have proved that the basic reproduction number $\mathcal{R}_0$ is a sharp threshold that ensures the global asymptotic stability of the DFE when its value is less than one and endemicity of the disease otherwise. Thus, for efficient control of the disease, one has to reduce $\mathcal{R}_0$ to below one.

We calibrated the model using weekly reported cumulative cases of typhoid fever in the Penka-Michel health district in Cameroon from 30 November 2019 to 1 January 2023. The model provides a good fit for data, and this means the predictions will be more reliable and accurate over time. The model was validated using weekly cumulative cases from 2 January 2023 to 5 November 2023. It is common knowledge that a well-calibrated model will have an $\mathcal{R}_0$ value that closely matches the observed transmission dynamics of a disease. We obtained $\mathcal{R}_0 = 1.2058$, which is an indication that the disease would persist if the necessary control measures are not put in place. In addition, the model predicts that by the end of 2026, more than 21,270 reported cases will be registered. Numerical results suggest that a reduction in the number of cases will be achieved if patients are advised to at least receive some treatment (modern or traditional) and eventually to switch from modern to traditional treatment if symptoms persist. Conversely, we have found that relapses due to antibiotics resistance will increase the level of the disease.

The results from the proposed model imply that integrating traditional medicine into conventional medicine will be effective in the treatment of typhoid fever and prevent antibiotics resistance. Traditional medicine is a useful adjuvant therapy for patients who choose modern medicine. Moreover, it is common practice in Cameroon that many typhoid patients, after receiving antibiotics, continue their treatment at home with traditional medicine. Hence, adopting a synergistic therapy approach in the treatment of typhoid fever will significantly mitigate typhoid disease cases.

In future research, the proposed model can be extended to include the optimal control of vaccination with relapse and reinfection.

Use of AI tools declaration

The authors declare they have not used artificial intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare no conflict of interest.

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Appendix

Appendix A Next–generation matrix coefficients

The coefficients of the next-generation matrix are given as follows:

$$\begin{cases} A_{11} = \dfrac{\beta\,\pi\,\alpha\,k_4\,(\eta_a k_3 + \eta_c \kappa)}{\mu\,k_b k_{10} k_1 k_6}, \quad A_{12} = \dfrac{\beta\,\pi\,k_4\,(\eta_a k_3 + \eta_c \kappa)}{\mu\,k_b k_{10} k_1 k_6}, \\ A_{13} = \dfrac{\beta\,\pi\,(k_2 k_4 \eta_c - \gamma_{at}\theta_m \gamma_{am} + \theta_m \omega_{cm} \eta_a)}{\mu\,k_b k_{10} k_1 k_6}, \quad A_{14} = \dfrac{\beta\,\pi\,\theta_m\,k_4\,(\eta_a k_3 + \eta_c \kappa)}{\mu\,k_b k_{10} k_6}, \quad A_{16} = \dfrac{\beta\pi}{\mu k_b k_6} \end{cases}$$

Appendix B Proof of Theorem 3.5

Let us consider the Volterra candidate Lyapunov function,

$$\begin{aligned} Z &= \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + \left(E - E^* - E^* \ln \frac{E}{E^*}\right) + a_1 \left(I_a - I_a^* - I_a^* \ln \frac{I_a}{I_a^*}\right) + a_2 \left(I_c - I_c^* - I_c^* \ln \frac{I_c}{I_c^*}\right) \\ &+ a_3 \left(M_m - M_m^* - M_m^* \ln \frac{M_m}{M_m^*}\right) + a_4 \left(M_t - M_t^* - M_t^* \ln \frac{M_t}{M_t^*}\right) + a_5 \left(B - B^* - B^* \ln \frac{B}{B^*}\right) \end{aligned} \tag{B.1}$$

where $a_i,\ i = 1, \cdots, 5$ are positive numbers to be determined. We use the following function $H(c) = 1 - c + \ln(c)$, which is negative when $c > 0$, and is equal to zero for $c = 1$. The time derivative of Z along the trajectories of System (2.6) yields

$$\begin{aligned} \frac{dZ}{dt} &= \left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + \left(1 - \frac{E^*}{E}\right)\frac{dE}{dt} + a_1 \left(1 - \frac{I_a^*}{I_a}\right)\frac{dI_a}{dt} + a_2 \left(1 - \frac{I_c^*}{I_c}\right)\frac{dI_c}{dt} \\ &+ a_3 \left(1 - \frac{M_m^*}{M_m}\right)\frac{dM_m}{dt} + a_4 \left(1 - \frac{M_t^*}{M_t}\right)\frac{dM_t}{dt} + a_5 \left(1 - \frac{B^*}{B}\right)\frac{dB}{dt} \end{aligned} \tag{B.2}$$

The following relations can be shown from (2.6):

$$\begin{cases} \pi = \lambda^* S^* + \mu S^*; \quad k_1 = \dfrac{\lambda^* S^*}{E^*}; \quad k_2 = \dfrac{\alpha}{I_a^*} E^* + \dfrac{\theta_m}{I_a^*} M_m^*; \quad k_3 = \dfrac{\kappa I_a^*}{I_c^*}; \\ k_4 = \dfrac{\gamma_{am}}{M_m^*} I_a^* + \dfrac{\omega_{cm}}{M_m^*} I_c^*; \quad k_5 = \dfrac{\gamma_{at}}{M_t^*} I_a^* + \dfrac{\psi_{mt}}{M_t^*} M_m^*; \quad k_6 = \dfrac{\eta_a}{B^*} I_a^* + \dfrac{\eta_c}{B^*} I_c^*. \end{cases} \tag{B.3}$$

Let us denote $\lambda S = f(B, S)$, i.e., $\lambda^* S^* = f(B^*, S^*)$. To prove the global asymptotic stability of the endemic equilibrium, we use the following inequality.

$$\begin{aligned} \text{Let } F &= 2 - \frac{E}{E^*} - \frac{S}{S^*} - \frac{E^*}{E}\frac{f(B,S)}{f(B^*,S^*)} + \frac{S^*}{S}\frac{f(B,S)}{f(B^*,S^*)}. \text{ Then} \\ F &= H\left(\frac{S}{S^*}\right) - \ln\left(\frac{S}{S^*}\right) + H\left(\frac{E^*}{E}\frac{f(B,S)}{f(B^*,S^*)}\right) - \ln\left(\frac{E^*}{E}\frac{f(B,S)}{f(B^*,S^*)}\right) \\ &\quad - \frac{E}{E^*} + \frac{B}{B^*} + H\left(\frac{B}{B^*}\frac{S}{S^*}\frac{f(B^*,S^*)}{f(B,S)}\right) - \ln\frac{B}{B^*}\frac{S}{S^*}\frac{f(B^*,S^*)}{f(B,S)} \\ &\quad + \left(1 - \frac{BS}{B^*S^*}\frac{f(B^*,S^*)}{f(B,S)}\right)\left(\frac{S^* f(B,S)}{S f(B^*S^*)} - 1\right) \\ &\leq \frac{B}{B^*} - \frac{E}{E^*} - \ln\left(\frac{E^*}{E}\frac{f(B,S)}{f(B^*,S^*)}\right) - \ln\left(\frac{B}{B^*}\frac{S}{S^*}\frac{f(B^*,S^*)}{f(B,S)}\right) \end{aligned} \tag{B.4}$$

As

$$\begin{aligned} \left(1 - \frac{BS}{B^*S^*}\frac{f(B^*,S^*)}{f(B,S)}\right)\left(\frac{S^* f(B,S)}{S f(B^*S^*)} - 1\right) &= \frac{1 - \dfrac{B + k_b}{B^* + k_b}}{\dfrac{B(B^* + k_b)}{B^*(B + k_b)} - 1} = \frac{\dfrac{B^* - B}{B^* + k_b}}{\dfrac{k_b(B - B^*)}{B^*(B + kb)}} \\ &= \frac{-k_b (B - B^*)^2}{B^*(B^* + k_b)(B + k_b)} \leq 0. \end{aligned} \tag{B.5}$$

one has,

$$\begin{aligned} 2 - \frac{E}{E^*} - \frac{S}{S^*} - \frac{E^*}{E}\frac{f(B,S)}{f(B^*,S^*)} + \frac{S^*}{S}\frac{f(B,S)}{f(B^*,S^*)} &\leqslant \frac{B}{B^*} - \frac{E}{E^*} - \ln\left(\frac{E^*}{E}\frac{f(B,S)}{f(B^*,S^*)}\right) - \ln\left(\frac{B}{B^*}\frac{S}{S^*}\frac{f(B^*,S^*)}{f(B,S)}\right) \\ &\leq \frac{B}{B^*} - \frac{E}{E^*} - \ln\frac{E^*}{E} - \ln\frac{f(B,S)}{f(B^*,S^*)} - \ln\frac{B}{B^*} \\ &\quad - \ln\frac{S}{S^*} + \ln\frac{f(B,S)}{f(B^*S^*)} \\ &\leq \frac{B}{B^*} - \ln\frac{B}{B^*} - \frac{E}{E^*} + \ln\frac{E}{E^*} \end{aligned} \tag{B.6}$$

$$\begin{aligned} 1 + \frac{M_m}{M_m^*} - \frac{I_a}{I_a^*} - \frac{M_m I_a^*}{I_a^* M_m} &= \frac{M_m}{M_m^*} - 1 - \frac{M_m}{M_m^*} + 2 + \frac{M_m}{M_m^*} - \frac{I_a}{I_a^*} - \frac{M_m^* M_m}{M_m M_m^*} - \frac{I_a^* M_m}{I_a M_m^*} \\ &= \left(\frac{M_m}{M_m^*} - 1\right)\left(1 - \frac{M_m M_m^*}{M_m^* M_m}\right) + \frac{M_m}{M_m^*} - \frac{I_a}{I_a^*} \end{aligned}$$

$$
\begin{aligned}
&+ \quad H\left(\frac{M_m^* M_m}{M_m M_m^*}\right) - \ln \frac{M_m^* M_m}{M_m M_m^*} + H\left(\frac{I_a^* M_m}{I_a M_m^*}\right) - \ln \frac{I_a^* M_m}{I_a M_m^*} \\
&\leq \quad \frac{M_m}{M_m^*} - 1 + 1 - \frac{I_a}{I_a^*} - \ln\left(\frac{I_a^*}{I_a}\frac{M_m}{M_m^*}\right) = \frac{M_m}{M_m^*} - \ln \frac{M_m}{M_m^*} - \frac{I_a}{I_a^*} + \ln \frac{I_a}{I_a^*} \qquad \text{(B.7)}
\end{aligned}
$$

$$
\begin{aligned}
1 + \frac{E}{E^*} - \frac{I_a}{I_a^*} - \frac{E I_a^*}{I_a^* E} &= \frac{E}{E^*} - 1 - \frac{E}{E^*} + 2 + \frac{E}{E^*} - \frac{I_a}{I_a^*} - \frac{E^* E}{E E^*} - \frac{I_a^* E}{I_a E^*} \\
&= \left(\frac{E}{E^*} - 1\right)\left(1 - \frac{E E^*}{E^* E}\right) + \frac{E}{E^*} - \frac{I_a}{I_a^*} + H\left(\frac{E^* E}{E E^*}\right) \\
&- \ln \frac{E^* E}{E E^*} + H\left(\frac{I_a^* E}{I_a E^*}\right) - \ln \frac{I_a^* E}{I_a E^*} \\
&\leq \frac{E}{E^*} - 1 + 1 - \frac{I_a}{I_a^*} - \ln\left(\frac{I_a^*}{I_a}\frac{E}{E^*}\right) = \frac{E}{E^*} - \ln \frac{E}{E^*} - \frac{I_a}{I_a^*} + \ln \frac{I_a}{I_a^*} \qquad \text{(B.8)}
\end{aligned}
$$

$$
\begin{aligned}
1 + \frac{I_a}{I_a^*} - \frac{I_c}{I_c^*} - \frac{I_a I_c^*}{I_a^* I_c} &= \frac{I_a}{I_a^*} - 1 - \frac{I_a}{I_a^*} + 2 + \frac{I_a}{I_a^*} - \frac{I_c}{I_c^*} - \frac{I_a^* I_a}{I_a I_a^*} - \frac{I_c^* I_a}{I_c I_a^*} \\
&= \left(\frac{I_a}{I_a^*} - 1\right)\left(1 - \frac{I_a I_a^*}{I_a^* I_a}\right) + \frac{I_a}{I_a^*} - \frac{I_c}{I_c^*} + H\left(\frac{I_a^* I_a}{I_a I_a^*}\right) \\
&- \ln \frac{I_a^* I_a}{I_a I_a^*} + H\left(\frac{I_c^* I_a}{I_c I_a^*}\right) - \ln \frac{I_c^* I_a}{I_c I_a^*} \\
&\leq \frac{I_a}{I_a^*} - 1 + 1 - \frac{I_c}{I_c^*} - \ln\left(\frac{I_c^*}{I_c}\frac{I_a}{I_a^*}\right) = \frac{I_a}{I_a^*} - \ln \frac{I_a}{I_a^*} - \frac{I_c}{I_c^*} + \ln \frac{I_c}{I_c^*} \qquad \text{(B.9)}
\end{aligned}
$$

$$
\begin{aligned}
1 + \frac{I_a}{I_a^*} - \frac{M_m}{M_m^*} - \frac{I_a M_m^*}{I_a^* M_m} &= \frac{I_a}{I_a^*} - 1 - \frac{I_a}{I_a^*} + 2 + \frac{I_a}{I_a^*} - \frac{M_m}{M_m^*} - \frac{I_a^* I_a}{I_a I_a^*} - \frac{M_m^* I_a}{M_m I_a^*} \\
&= \left(\frac{I_a}{I_a^*} - 1\right)\left(1 - \frac{I_a I_a^*}{I_a^* I_a}\right) + \frac{I_a}{I_a^*} - \frac{M_m}{M_m^*} + H\left(\frac{I_a^* I_a}{I_a I_a^*}\right) \\
&- \ln \frac{I_a^* I_a}{I_a I_a^*} + H\left(\frac{M_m^* I_a}{M_m I_a^*}\right) - \ln \frac{M_m^* I_a}{M_m I_a^*} \\
&\leq \frac{I_a}{I_a^*} - 1 + 1 - \frac{M_m}{M_m^*} - \ln\left(\frac{M_m^*}{M_m}\frac{I_a}{I_a^*}\right) \\
&= \frac{I_a}{I_a^*} - \ln \frac{I_a}{I_a^*} - \frac{M_m}{M_m^*} + \ln \frac{M_m}{M_m^*} \qquad \text{(B.10)}
\end{aligned}
$$

$$
\begin{aligned}
1 + \frac{I_c}{I_c^*} - \frac{M_m}{M_m^*} - \frac{I_c M_m^*}{I_c^* M_m} &= \frac{I_c}{I_c^*} - 1 - \frac{I_c}{I_c^*} + 2 + \frac{I_c}{I_c^*} - \frac{M_m}{M_m^*} - \frac{I_c^* I_c}{I_c I_c^*} - \frac{M_m^* I_c}{M_m I_c^*} \\
&= \left(\frac{I_c}{I_c^*} - 1\right)\left(1 - \frac{I_c I_c^*}{I_c^* I_c}\right) + \frac{I_c}{I_c^*} - \frac{M_m}{M_m^*} + H\left(\frac{I_c^* I_c}{I_c I_c^*}\right)
\end{aligned}
$$

$$
\begin{aligned}
&- \ln\frac{I_c^* I_c}{I_c I_c^*} + H\left(\frac{M_m^* I_c}{M_m I_c^*}\right) - \ln\frac{M_m^* I_c}{M_m I_c^*} \\
&\leq \frac{I_c}{I_c^*} - 1 + 1 - \frac{M_m}{M_m^*} - \ln\left(\frac{M_m^*}{M_m}\frac{I_c}{I_c^*}\right) = \frac{I_c}{I_c^*} - \ln\frac{I_c}{I_c^*} - \frac{M_m}{M_m^*} + \ln\frac{M_m}{M_m^*} \quad \text{(B.11)}
\end{aligned}
$$

$$
\begin{aligned}
1 + \frac{M_m}{M_m^*} - \frac{M_t}{M_t^*} - \frac{M_m M_t^*}{M_t^* M_m} &= \frac{M_m}{M_m^*} - 1 - \frac{M_m}{M_m^*} + 2 + \frac{M_m}{M_m^*} - \frac{M_t}{M_t^*} - \frac{M_m^* M_m}{M_m M_m^*} - \frac{M_t^* M_m}{M_t M_m^*} \\
&= \left(\frac{M_m}{M_m^*} - 1\right)\left(1 - \frac{M_m M_m^*}{M_m^* M_m}\right) + \frac{M_m}{M_m^*} - \frac{M_t}{M_t^*} + H\left(\frac{M_m^* M_m}{M_m M_m^*}\right) \\
&- \ln\frac{M_m^* M_m}{M_m M_m^*} + H\left(\frac{M_t^* M_m}{M_t M_m^*}\right) - \ln\frac{M_t^* M_m}{M_t M_m^*} \\
&\leq \frac{M_m}{M_m^*} - 1 + 1 - \frac{M_t}{M_t^*} - \ln\left(\frac{M_t^*}{M_t}\frac{M_m}{M_m^*}\right) \\
&= \frac{M_m}{M_m^*} - \ln\frac{M_m}{M_m^*} - \frac{M_t}{M_t^*} + \ln\frac{M_t}{M_t^*} \quad \text{(B.12)}
\end{aligned}
$$

$$
\begin{aligned}
1 + \frac{I_a}{I_a^*} - \frac{B}{B^*} - \frac{I_a B^*}{I_a^* B} &= \frac{I_a}{I_a^*} - 1 - \frac{I_a}{I_a^*} + 2 + \frac{I_a}{I_a^*} - \frac{B}{B^*} - \frac{I_a^* I_a}{I_a I_a^*} - \frac{B^* I_a}{B I_a^*} \\
&= \left(\frac{I_a}{I_a^*} - 1\right)\left(1 - \frac{I_a I_a^*}{I_a^* I_a}\right) + \frac{I_a}{I_a^*} - \frac{B}{B^*} + H\left(\frac{I_a^* I_a}{I_a I_a^*}\right) - \ln\frac{I_a^* I_a}{I_a I_a^*} + H\left(\frac{B^* I_a}{B I_a^*}\right) - \ln\frac{B^* I_a}{B I_a^*} \\
&\leq \frac{I_a}{I_a^*} - 1 + 1 - \frac{B}{B^*} - \ln\left(\frac{B^*}{B}\frac{I_a}{I_a^*}\right) = \frac{I_a}{I_a^*} - \ln\frac{I_a}{I_a^*} - \frac{B}{B^*} + \ln\frac{B}{B^*}
\end{aligned}
$$

$$
\begin{aligned}
1 + \frac{I_c}{I_c^*} - \frac{B}{B^*} - \frac{I_c B^*}{I_c^* B} &= \frac{I_c}{I_c^*} - 1 - \frac{I_c}{I_c^*} + 2 + \frac{I_c}{I_c^*} - \frac{B}{B^*} - \frac{I_c^* I_c}{I_c I_c^*} - \frac{B^* I_c}{B I_c^*} \\
&= \left(\frac{I_c}{I_c^*} - 1\right)\left(1 - \frac{I_c I_c^*}{I_c^* I_c}\right) + \frac{I_c}{I_c^*} - \frac{B}{B^*} + H\left(\frac{I_c^* I_c}{I_c I_c^*}\right) \\
&- \ln\frac{I_c^* I_c}{I_c I_c^*} + H\left(\frac{B^* I_c}{B I_c^*}\right) - \ln\frac{B^* I_c}{B I_c^*} \\
&\leq \frac{I_c}{I_c^*} - 1 + 1 - \frac{B}{B^*} - \ln\left(\frac{B^*}{B}\frac{I_c}{I_c^*}\right) = \frac{I_c}{I_c^*} - \ln\frac{I_c}{I_c^*} - \frac{B}{B^*} + \ln\frac{B}{B^*} \quad \text{(B.13)}
\end{aligned}
$$

Substituting Eq (B.3) into Eq (B.2) leads to (B.14).

$$
\begin{aligned}
\frac{dZ}{dt} &= \left(1 - \frac{S^*}{S}\right)(f(B^*, S^*) + \mu S^* - f(B, S) - \mu S) + \left(1 - \frac{E^*}{E}\right)\left(f(B, S) - \frac{E}{E^*} f(B^*, S^*)\right) \\
&+ a_1\left(1 - \frac{I_a^*}{I_a}\right)\left(\alpha E + \theta_m M_m - (\frac{\alpha}{I_a^*} E^* + \frac{\theta_m}{I_a^*} M_m^*) I_a\right) + a_2\left(1 - \frac{I_c^*}{I_c}\right)\left(\kappa I_a - \frac{\kappa I_a^*}{I_c^*} I_c\right) \\
&+ a_3\left(1 - \frac{M_m^*}{M_m}\right)\left(\gamma_{am} I_a + \omega_{cm} I_c - \frac{\gamma_{am} I_a^* M_m}{M_n^*} - \omega_{cm} I_c^* \frac{M_m}{M_m^*}\right)
\end{aligned}
$$

$$
\begin{aligned}
&+a_4\left(1-\frac{M_t^*}{M_t}\right)\left(\gamma_{at}I_a+\psi_{mt}M_m-\gamma_{at}\frac{I_a^*M_t}{M_t^*}-\frac{\psi_{mt}M_m^*M_t}{M_t^*}\right)\\
&+a_5\left(1-\frac{B^*}{B}\right)\left(\eta_aI_a+\eta_cI_c-\frac{\eta_a}{B^*}I_a^*B-\frac{\eta_c}{B^*}I_c^*B\right),\\
=\;&-\mu\frac{(s-s^*)^2}{S}+f(B^*,S^*)-f(B,S)-f(B^*,S^*)\frac{S^*}{S}+f(B,S)\frac{S^*}{S}+f(B^*,S^*)\\
&-f(B,S)\frac{E^*}{E}-f(B^*,S^*)\frac{E}{E^*}+f(B,S)+a_1\left\{\alpha E-\alpha E^*\frac{I_a^*}{I_a}-\alpha E\frac{I_a^*}{I_a^*}+\alpha E^*\right\}\\
&+a_1\left\{\theta_mM_m-\theta_mM_m^*\frac{I_a}{I_a^*}-\theta_mM_m\frac{I_a^*}{I_a}+\theta_mM_m^*\right\}+a_2\left\{\kappa I_a-\kappa I_a\frac{I_c^*}{I_c}-a_2\kappa I_a^*-\kappa I_a^*\frac{I_c}{I_c^*}+kI_a^*\right\}\\
&+a_3\left\{\gamma_{am}I_a^*-\gamma_{am}I_a\frac{M_m^*}{M_m}+\gamma_{am}I_a-\gamma_{am}I_a\frac{M_m^*}{M_m}\right\}+a_3\left\{\omega_{cm}I_c^*-\omega_{cm}I_c\frac{M_m^*}{M_m}-\omega_{cm}I_c^*\frac{M_m}{M_m^*}+\omega_{cm}I_c\right\}\\
&+a_4\left\{\gamma_{at}I_a^*-\gamma_{at}I_a\frac{M_t^*}{M_t}-\gamma_{at}I_a^*\frac{M_t}{M_t^*}+\gamma_{at}I_a\right\}+a_4\left\{\psi_{mt}M_m-\psi_{mt}M_m\frac{M_t}{M_t^*}-\psi_{mt}M_m\frac{M_t^*}{M_t}+\psi_{mt}M_m^*\right\}\\
&+a_5\left\{\eta_aI_a-\eta_aI_a^*\frac{B}{B^*}-\eta_aI_a\frac{B}{B^*}+\eta_aI_a^*\right\}+a_5\left\{\eta_cI_c-\eta_cI_c^*\frac{B}{B^*}-\eta_cI_c\frac{B^*}{B}+\eta_cI_c^*\right\}\\
\le\;&f(B^*,S^*)\left\{2-\frac{E}{E^*}-\frac{S^*}{S}-\frac{f(B,S)}{f(B^*,S^*)}\frac{E^*}{E}+\frac{f(B,S)}{f(B^*,S^*)}\frac{S^*}{S}\right\}+a_1\alpha E^*\left(\frac{E}{E^*}-\frac{I_a}{I_a^*}-\frac{EI_a^*}{E^*I_a}+1\right)\\
&+a_1\theta_mM_m^*\left(\frac{M_m}{M_m^*}-\frac{I_a}{I_a^*}-\frac{M_mI_a^*}{I_a^*M_m}+1\right)+a_2\kappa I_a^*\left(\frac{I_a}{I_a^*}-\frac{I_c}{I_c^*}-\frac{I_aI_c^*}{I_a^*I_c}+1\right)\\
&+a_3\gamma_{am}I_a^*\left(\frac{I_a}{I_a^*}-\frac{M_m}{M_m^*}-\frac{I_aM_m^*}{I_a^*M_m}+1\right)\\
&+a_3\omega_{cm}I_c^*\left(\frac{I_c}{I_c^*}-\frac{M_m}{M_m^*}-\frac{I_cM_m^*}{I_c^*M_m}+1\right)+a_4\gamma_{at}I_a^*\left(\frac{I_a}{I_a^*}-\frac{M_t}{M_t^*}-\frac{I_aM_t^*}{I_a^*M_t}+1\right)\\
&+a_4\psi_{mt}M_m^*\left(\frac{M_m}{M_m^*}-\frac{M_t}{M_t^*}-\frac{M_mM_t^*}{M_m^*M_t}+1\right)a_5\eta_aI_a^*\left\{\frac{I_a}{I_a^*}-\frac{B}{B^*}-\frac{I_aB^*}{I_a^*B}+1\right\}\\
&+a_5\eta_cI_c^*\left\{\frac{I_c}{I_c^*}-\frac{B}{B^*}-\frac{I_cB^*}{I_c^*B}+1\right\}
\end{aligned}
\tag{B.14}
$$

According to (B.6), we have

$$
\begin{aligned}
\frac{dZ}{dt}\;\le\;&f(B^*,S^*)\left\{\frac{B}{B^*}-\ln\frac{B}{B^*}-\frac{E}{E^*}+\ln\frac{E^*}{E}\right\}\\
&+a_1\alpha E^*\left\{\frac{E}{E^*}-\ln\frac{E}{E^*}-1-\frac{I_a}{I_a^*}+\ln\frac{I_a}{I_a^*}+1-\frac{EI_a^*}{E^*I_a}+\ln\frac{EI_a^*}{E^*I_a}+1\right\}\\
&+a_1\theta_mM_m^*\left\{\frac{M_m}{M_m^*}-\ln\frac{M_m}{M_m^*}-1-\frac{I_a}{I_a^*}+\ln\frac{I_a}{I_a^*}+1-\frac{M_mI_a^*}{M_m^*I_a}+\ln\frac{M_mI_a^*}{M_m^*I_a}+1\right\}\\
&+a_2\kappa I_a^*\left\{\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-1-\frac{I_c}{I_c^*}+\ln\frac{I_c}{I_c^*}+1-\frac{I_aI_c^*}{I_a^*I_c}+\ln\frac{I_aI_c^*}{I_a^*I_c}+1\right\}\\
&+a_3\gamma_{am}I_a^*\left\{\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-1-\frac{M_m}{M_m^*}+\ln\frac{M_m}{M_m^*}+1-\frac{I_aM_m^*}{I_a^*M_m}+\ln\frac{I_aM_m^*}{I_a^*M_m}+1\right\}
\end{aligned}
$$

$$
\begin{aligned}
&+a_3\omega_{cm}I_c^*\left\{\frac{I_c}{I_c^*}-\ln\frac{I_c}{I_c^*}-1-\frac{M_m}{M_m^*}+\ln\frac{M_m}{M_m^*}+1-\frac{I_cM_m^*}{I_c^*M_m}+\ln\frac{I_cM_m^*}{I_c^*M_m}+1\right\}\\
&+a_4\gamma_{at}I_a^*\left\{\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-1-\frac{M_t}{M_t^*}+\ln\frac{M_t}{M_t^*}+1-\frac{I_aM_t^*}{I_a^*M_t}+\ln\frac{I_aM_t^*}{I_a^*M_t}+1\right\}\\
&+a_4\psi_{mt}M_m^*\left\{\frac{M_m}{M_m^*}-\ln\frac{M_m}{M_m^*}-1-\frac{M_t}{M_t^*}+\ln\frac{M_t}{M_t^*}+1-\frac{M_mM_t^*}{M_m^*M_t}+\ln\frac{M_mM_t^*}{M_m^*M_t}+1\right\}\\
&+a_5\eta_aI_a^*\left\{\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-1-\frac{B}{B^*}+\ln\frac{B}{B^*}+1-\frac{I_aB^*}{I_a^*B}+\ln\frac{I_aB^*}{I_a^*B}+1\right\}\\
&+a_5\eta_cI_c^*\left\{\frac{I_c}{I_c^*}-\ln\frac{I_c}{I_c^*}-1-\frac{B}{B^*}+\ln\frac{B}{B^*}+1-\frac{I_cB^*}{I_c^*B}+\ln\frac{I_cB^*}{I_c^*B}+1\right\}
\end{aligned}
$$

Now using Eqs (B.7) to (B.13), we have

$$
\begin{aligned}
\frac{dZ}{dt} \leq\ & f(B^*S^*)\left\{\frac{B}{B^*}-\ln\frac{B}{B^*}-\frac{E}{E^*}+\ln\frac{E}{E^*}\right\}+a_1\alpha E^*\left(\frac{E}{E^*}-\ln\frac{E}{E^*}-\frac{I_a}{I_a^*}+\ln\frac{I_a}{I_a^*}\right)\\
&+a_1\theta_mM_m^*\left(\frac{M_m}{M_m^*}-\ln\frac{M_m}{M_m^*}-\frac{I_a}{I_a^*}+\ln\frac{I_a}{I_a^*}\right)+a_2\kappa I_a^*\left(\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-\frac{I_c}{I_c^*}+\ln\frac{I_c}{I_c^*}\right)\\
&+a_3\gamma_{am}I_a^*\left(\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-\frac{M_m}{M_m^*}+\ln\frac{M_m}{M_m^*}\right)+a_3\omega_{cm}I_c^*\left(\frac{I_c}{I_c^*}-\ln\frac{I_c}{I_c^*}-\frac{M_m}{M_m^*}+\ln\frac{M_m}{M_m^*}\right)\\
&+a_4\gamma_{at}I_a^*\left\{\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-\frac{M_t}{M_t^*}+\ln\frac{M_t}{M_t^*}\right\}+a_4\psi_{mt}M_m^*\left\{\frac{M_m}{M_m^*}-\ln\frac{M_m}{M_m^*}-\frac{M_t}{M_t^*}+\ln\frac{M_t}{M_t^*}\right\}\\
&+a_5\eta_aI_a^*\left\{\frac{I_a}{I_a^*}-\ln\frac{I_a}{I_a^*}-\frac{B}{B^*}+\ln\frac{B}{B^*}\right\}+a_5\eta_cI_c^*\left\{\frac{I_c}{I_c^*}-\ln\frac{I_c}{I_c^*}-\frac{B}{B^*}+\ln\frac{B}{B^*}\right\} \qquad \text{(B.15)}
\end{aligned}
$$

Let $l(x,x^*):=\dfrac{x}{x^*}-\ln\dfrac{x}{x^*}\geq 1>0$ for $x>0$, and $x^*>0$. Therefore,

$$
\begin{aligned}
\frac{dZ}{dt} =\ & f(B^*,S^*)\left\{l(B,B^*)-l(E,E^*)\right\}+a_1\alpha E^*\left\{l(E,E^*)-l(I_a,I_a^*)\right\}+a_1\theta_mM_m^*\left\{l(M_m,M_m^*)-l(I_a,I_a^*)\right\}\\
&+a_2\kappa I_a^*\left\{l(I_a,I_a^*)-l(I_c,I_c^*)\right\}+a_3\gamma_{am}I_a^*\left\{l(I_a,I_a^*)-l(M_m,M_m^*)\right\}\\
&+a_3\omega_{cm}I_c^*\left\{l(I_c,I_c^*)-l(M_m,M_m^*)\right\}+a_4\gamma_{at}I_a^*\left\{l(I_a,I_a^*)-l(M_t,M_t^*)\right\}\\
&+a_4\psi_{mt}M_m^*\left\{l(M_m,M_m^*)-l(M_t,M_t^*)\right\}+a_5\eta_aI_a^*\left\{l(I_a,I_a^*)-l(B,B^*)\right\}+a_5\eta_cI_c^*\left\{l(I_c,I_c^*)-l(B,B^*)\right\}\\
=\ & \left\{f(B^*,S^*)-a_5\eta_aI_a^*-a_5\eta_cI_c^*\right\}l(B,B^*)+\left\{-f(B^*,S^*)+a_1\alpha E^*\right\}l(E,E^*)\\
&+\left\{a_2\kappa I_a^*+a_3\gamma_{am}I_a^*+a_4\gamma_{at}I_a^*+a_5\eta_aI_a^*-a_1\alpha E^*-a_1\theta_mM_m^*\right\}l(I_a,I_a^*) \qquad \text{(B.16)}\\
&+\left\{a_3\omega_{cm}I_c^*+a_5\eta_cI_c^*-a_2\kappa I_a^*\right\}l(I_c,I_c^*)\\
&+\left\{a_1\theta_mM_m^*-a_3\left(\gamma_{am}I_a^*+\omega_{cm}I_c^*\right)+a_4\psi_{mt}M_m^*\right\}l(M_m,M_m^*)-\left\{a_4\gamma_{at}I_a^*+a_4\psi_{mt}M_m^*\right\}l(M_t,M_t^*)
\end{aligned}
$$

Using the fact that $-\left\{a_4\gamma_{at}I_a^*+a_4\psi_{mt}M_m^*\right\}l(M_t,M_t^*)=-k_5M_t^*l(M_t,M_t^*)<0$, we get

$$
\begin{aligned}
\frac{dZ}{dt} \leq\ & \left\{f(B^*,S^*)-a_5\eta_aI_a^*-a_5\eta_cI_c^*\right\}l(B,B^*)+\left\{-f(B^*,S^*)+a_1\alpha E^*\right\}l(E,E^*)\\
&+\left\{a_2\kappa I_a^*+a_3\gamma_{am}I_a^*+a_4\gamma_{at}I_a^*+a_5\eta_aI_a^*-a_1\alpha E^*-a_1\theta_mM_m^*\right\}l(I_a,I_a^*)
\end{aligned}
$$

$$
\begin{aligned}
&+\{a_3\omega_{cm}I_c^* + a_5\eta_c I_c^* - a_2\kappa I_a^*\}\, l(I_c, I_c^*)\\
&+\{a_1\theta_m M_m^* - a_3\left(\gamma_{am}I_a^* + \omega_{cm}I_c^*\right) + a_4\psi_{mt}M_m^*\}\, l(M_m, M_m^*)\\
=\ &\left[f(B^*, S^*) - a_5\eta_a I_a^* - a_5\eta_c I_c^*\right] l(B, B^*) + \left[-f(B^*, S^*) + a_1\alpha E^*\right] l(E, E^*)\\
&+\left[a_2\kappa I_a^* + a_3\gamma_{am}I_a^* + a_4\gamma_{at}I_a^* + a_5\eta_a I_a^* - a_1\alpha E^* - a_1\theta_m M_m^*\right] l(I_a, I_a^*)\\
&+\left[a_3\omega_{cm}I_c^* + a_5\eta_c I_c^* - a_2\kappa I_a^*\right] l(I_c, I_c^*)\\
&+\left[a_1\theta_m M_m^* - a_3\left(\gamma_{am}I_a^* + \omega_{cm}I_c^*\right) + a_4\psi_{mt}M_m^*\right] l(M_m, M_m^*)
\end{aligned}
\tag{B.17}
$$

We choose a_i such that the expressions in the square brackets vanish. That is, a_i are solutions of the system

$$
\begin{aligned}
f(B^*, S^*) - a_5\eta_a I_a^* - a_5\eta_c I_c^* &= 0 && \text{(B.18)}\\
-f(B^*, S^*) + a_1\alpha E^* &= 0 && \text{(B.19)}\\
a_2\kappa I_a^* + a_3\gamma_{am}I_a^* + a_4\gamma_{at}I_a^* + a_5\eta_a I_a^* - a_1\alpha E^* - a_1\theta_m M_m^* &= 0 && \text{(B.20)}\\
a_3\omega_{cm}I_c^* + a_5\eta_c I_c^* - a_2\kappa I_a^* &= 0 && \text{(B.21)}\\
a_1\theta_m M_m^* - a_3\left(\gamma_{am}I_a^* + \omega_{cm}I_c^*\right) + a_4\psi_{mt}M_m^* &= 0 && \text{(B.22)}
\end{aligned}
$$

Then by (B.18) and (B.19), we have:

$$
\begin{cases}
a_5 = \dfrac{f(B^*, S^*)}{\eta_a I_a^* + \eta_c I_c^*} = \dfrac{f(B^*, S^*)}{k_6 B^*} = \dfrac{k_1 E^*}{k_6 B^*}\\
a_1 = \dfrac{f(B^*, S^*)}{\alpha E^*} = \dfrac{k_1}{\alpha}
\end{cases}
$$

Equation (B.22) leads to

$$
\frac{f(B^*, S^*)}{\alpha E^*}\theta_m + a_4\psi_{mt}M_m^* = a_3\left(\gamma_{am}I_a^* + \omega_{cm}I_c^*\right).
$$

Consequently,

$$
a_3 = \frac{f(B^*, S^*)\theta_m M_m^* + a_4\alpha E^*\psi_{mt}M_m^*}{\alpha E^*\left(\gamma_{am}I_a^* + \omega_{cm}I_c^*\right)} = \frac{k_1\theta_m + \alpha a_4\psi_{mt}}{\alpha k_4} \tag{B.23}
$$

Let us consider (B.20) and (B.21). Here a_2 and a_5 verify the system

$$
\begin{aligned}
a_2\kappa I_a^* + a_5\eta_a I_a^* &= a_1\left(\alpha E^* + \theta_m M_m^*\right) - a_3\gamma_{am}I_a^* - a_4\gamma_{at}I_a^* && \text{(B.24)}\\
-a_2\kappa I_a^* + a_5\eta_c I_c^* &= -a_3\omega_{cm}I_c^*, && \text{(B.25)}
\end{aligned}
$$

Using Eq (B.25), we have

$$
\begin{aligned}
a_2 &= \frac{\eta_c I_c^*\{(f(B^*, S^*))\}}{\kappa I_a^*\left(\eta_a I_a^* + \eta_c I_c^*\right)} + \frac{\omega_{cm}I_c^*\left(f(B^*, S^*)\theta_m M_m^* + a_4\alpha E^*\psi_{mt}M_m^*\right)}{\alpha E^*\kappa I_a^*\left(\gamma_{am}I_a^* + \omega_{cm}I_c^*\right)},\\
&= \eta_c I_c^*\frac{k_1 E^*}{k_6 B^*} + \omega_{cm}I_c^*\frac{k_1\theta_m + \alpha\psi_{mt}a_4}{\alpha k_4} && \text{(B.26)}
\end{aligned}
$$

For $a_4 = 1$, we get:

$$\begin{cases} a_1 = \dfrac{k_1}{\alpha}; \quad a_2 = \eta_c I_c^* \dfrac{k_1 E^*}{k_6 B^*} + \omega_{cm} I_c^* \dfrac{k_1\theta_m + \alpha\psi_{mt}}{\alpha k_4}; \\ a_3 = \dfrac{k_1\theta_m + \alpha\psi_{mt}}{\alpha k_4}; \quad a_5 = \dfrac{k_1 E^*}{k_6 B^*}. \end{cases} \tag{B.27}$$

These values of $a_i,\ i = 1, \cdots, 5$ imply that $\dfrac{dZ}{dt} \leq 0$.

Furthermore, the equality $\dfrac{dZ}{dt} = 0$ holds only for

$$S = S^*, E = E^*, I_a = I_a^*, I_c = I_c^*, M_m = M_m^*, M_t = M_t^*, R = R^*, B = B^*.$$

Thus, $\{\varepsilon^*\}$ is the largest positive invariant set which is contained in the set

$$\{(S, E, I_a, I_c, M_m, M_t, R, B) \in \Omega : S = S^*, E = E^*, I_a = I_a^*, I_c = I_c^*, M_m = M_m^*, M_t = M_t^*, R = R^*, B = B^*\}.$$

Hence, it follows from LaSalle's invariance principle [33] that any solution of Eq (2.6) with an initial condition in Ω converges to the endemic equilibrium point ε^*, as $t \longrightarrow \infty$. Therefore, the positive equilibrium ε^* is globally asymptotically stable if $\mathcal{R}_0 > 1$.



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