J. Math. Biol. (2018) 77:647–670
https://doi.org/10.1007/s00285-018-1219-9

Mathematical Biology

Assessing the potential impact of limited public health resources on the spread and control of typhoid

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Received: 9 December 2016 / Revised: 5 February 2018 / Published online: 27 February 2018

Abstract Typhoid fever is a systemic infection caused by *Salmonella* Typhi and occurs predominantly in association with poor sanitation and lack of clean drinking water. Despite recent progress in water and sanitation coverage, the disease remains a substantial public health problem in many developing countries. A mathematical model for the spread of typhoid has been formulated using non linear ordinary differential equations. The model includes a special treatment function to assess the effects of limited treatment resources on the spread of typhoid. It is shown that the model has multiple equilibria and using the center manifold theory, the model exhibits the phenomenon of backward bifurcation whose implications are discussed. The results suggest the need for comprehensive and accessible treatment facilities to curtail typhoid infection.

Keywords Typhoid · Treatment · Treatment function · Reproduction number

Mathematics Subject Classification 92B05 · 92D25 · 92D30 · 34C23 · 34D20 · 34G20

1 Introduction

Typhoid fever is a bacterial infection caused by *Salmonella* Typhi. It is usually spread by ingestion of contaminated food or water. Symptoms include lasting high fevers,

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weakness, stomach pains, headache and loss of appetite. Those infected may also have constipation or a rash. However, it is possible to be a carrier of typhoid without exhibiting symptoms, such as the infamous case of "Typhoid Mary," a cook in New York City in the early 1900s believed to have infected dozens of people as an asymptomatic carrier of the disease. In rare cases, typhoid can lead to internal bleeding and even death (Center for Disease Control and Prevention). Factors such as poor sanitation and lack of clean drinking water are predominantly associated with typhoid (World Health Organization (WHO) 2016).

Despite recent progress in the provision of clean water and good sewage systems especially in developed nations, typhoid is still endemic in many developing countries and remains a substantial public health problem with approximately 21 million cases and 222,000 typhoid-related deaths annually worldwide (World Health Organization (WHO) 2016). The progressive deterioration of public health infrastructure especially in developing countries have seen such rare diseases like typhoid becoming more commonly encountered within the population. For instance, a deadly typhoid outbreak was confirmed in Zimbabwe's capital Harare starting in early November 2011. More recently in 2016, Zimbabwe has been hit with several cases of typhoid fever where some confirmed typhoid cases were reported in most urban areas and other parts of the country such as Hopley, Glen Norah and Hatfield suburbs in Harare, and Redcliffe Kwekwe. The rise and return of typhoid fever in Zimbabwe especially in Harare is believed to have been triggered by the water problems in the city and, as a result, many residents lack access to clean water. Impoverished residents often rely on water from open, shallow wells that are likely to be contaminated. Some have been without access to filtered, piped water for months as a result of Zimbabwe's economic turmoil. The lack of water, combined with record high temperatures, has created a perfect environment for infectious diseases such as typhoid. The same poor water and sanitation conditions in Harare prevail in most of Zimbabwe's urban areas and other parts of the country. The government in response sent teams to assess the situation in affected areas, particularly in Hopley, where there is strong suspicion that people could be sick from their homes. The teams were responsible for interviewing and treating all suspected cases. However, as noted in the 2011 typhoid outbreak in Zimbabwe where the number of cases surpassed 1500 within weeks, the local hospitals were congested and incapacitated to cater for all typhoid patients. This negatively impacted the control efforts aimed at eradicating typhoid as was observed then that patients who were not timely treated contributed in spreading the disease to uninfected individuals. In recent years, mathematical models describing the spread of typhoid fever in a community have been proposed, see for example, González-Guzmán (1989), Adetunde (2008), Mushayabasa et al. (2013), Mushayabasa et al. (2014), Mushayabasa (2014), Pitzer et al. (2014), Bakach et al. (2015), Omame et al. (2015), Mutua et al. (2015), Nthiiri et al. (2016), Kgosimore and Kelatlhegile (2016). In all these models, it is assumed that the rate of entering treatment is proportional to the number of infected individuals present. This is reasonable approximation to the truth when the number of infected individuals in need of treatment is not too large and below the capacity of health care services. However, in reality, every community or country has an appropriate or limited capacity for treatment. In fact, the resources for treatment maybe limited, for example, medicines are not sufficient, hospital beds are limited and so on.

So this approximation cannot reflect the real uptake into treatment. In other words, if the number of patients exceed a fixed large size, then the rate of entering treatment is independent of further changes in the size of the infected individuals' class. Motivated by the recent outbreak of typhoid in Zimbabwe which hit most parts of Zimbabwe by surprise, an explosive surge in the number of typhoid patients was observed in local treatment centers. In that time, the number of patients in need of treatment eventually exceeded the carrying capacities of local treatment centers and patients could not be timely treated because the capacity of local treatment centers had reached a maximum (saturated). Thus, it is important to determine a suitable capacity for the treatment of typhoid patients.

In this paper, we develop a mathematical model that takes into account the possibility of the number of typhoid infected patients in need of treatment exceeding the capacity of public health resources. We make use of the Hill function developed by Hill (1910) to describe the relationship between the space available in treatment and the number of patients in need of treatment to model the effects of limited public health resources on the spread of typhoid. The Hill function has many different properties of great interest in mathematical modelling, pharmacology and biosciences. When related to protein-ligand binding where the Hill function has been used extensively, the formation of a bond between a typhoid patient and a treatment centre is influenced by free space in the treatment centre. The expectation from an effective treatment centre is that a bond formed by a typhoid patient and a treatment centre will lead to some recovered person afterwards. *Reaction kinetics processes*, can be used to describe the mechanism of entering into treatment. One such process is *Cooperativity* which refers to situations where the binding of one (or more) molecules to the receptor enhances (*positive cooperativity*) or weakens (*negative cooperativity*) the binding of additional molecules to that same receptor. In relation to treatment, *positive cooperativity* relates to the presence of other patients being a pull factor for other patients to attend treatment whereas *negative cooperativity* does the opposite. Cooperative binding to a multisite protein was first described in Hill (1910) using the equation

$$\Theta = \frac{[L]^n}{K_d + [L]^n} \tag{1}$$

where Θ is the fraction of the ligand-binding sites on the receptor protein which are occupied by the ligand, $[L]$ is the free (unbound) ligand concentration, K_d is the dissociation constant and n is the Hill coefficient, describing cooperativity (or possibly other biochemical properties, depending on the context in which the Hill equation is being used). In the context of treatment for typhoid patients, the Hill function describes the relationship between the space available in treatment and the number of patients in need of treatment. We define recruitment into treatment by the following expression:

$$H(I) = rf(I)I \tag{2}$$

where $f(I) = \left(\frac{1}{1+\omega I}\right)$. Here, r is the maximum treatment uptake per unit of time and ω measures the extent of the effect of the problem of demand for treatment. Firstly, observe that for small I, $H(I) \approx rI$, that is, when the number of patients in need of treatment is not too large, then the rate of entering treatment is proportional to the

number of patients present. Secondly, observe that for large I, $H(I) \approx r/\omega$, this means that the rate of entering treatment takes a maximum value r/ω. Finally, when $\omega = 0$, we again obtain the result as in the first case, $H(I) = rI$, that is, the function returns to a linear function. It is also important to note that epidemic models including treatment functions of the form (2) are found in Hu et al. (2012), Zhang and Liu (2008), Zhou and Fan (2012) and Zhang et al. (2014). We also include direct and indirect transmission to model the spread of typhoid in a given community. The model developed in this paper fits well in the settings of most developing countries where treatment resources may be limited. Compared to previous models of typhoid (González-Guzmán 1989; Adetunde 2008; Mushayabasa et al. 2013, 2014; Mushayabasa 2014; Omame et al. 2015; Mutua et al. 2015; Nthiiri et al. 2016; Kgosimore and Kelatlhegile 2016), a key novelty of our model is the inclusion of limited public health resources to model the dynamics of typhoid.

The paper is arranged as follows; in Sect. 2, we formulate and establish the basic properties of the model. The model is analysed for stability in Sect. 3. In Sect. 4, we carry out some numerical simulations and sensitivity analysis. Parameter estimation is also presented in this section. The paper is concluded in Sect. 5.

2 Model formulation

The typhoid model classifies the human population at time t, denoted by $N(t)$ into five classes; susceptible individuals (S), infected individuals (I), carrier humans (C), individuals under treatment (T) and recovered individuals (R). The total human population is thus given by

$$N(t) = S(t) + I(t) + C(t) + T(t) + R(t).$$

An additional compartment, $B(t)$, which represents the bacteria in the environment has been incorporated in the model. Many previous models of typhoid dynamics assume direct transmission of typhoid from infected individuals to susceptible individuals (Adetunde 2008; Mushayabasa et al. 2013, 2014; Mushayabasa 2014; Omame et al. 2015; Nthiiri et al. 2016; Kgosimore and Kelatlhegile 2016) and a few have assumed indirect transmission, that is, from environmental bacteria in contaminated water and/or food and drinks to susceptibles (González-guzmán 1988; Mutua et al. 2015). In this paper, we develop a more realistic model for typhoid that takes into account both modes of transmission, that is, direct and indirect transmission. Direct transmission (human-human) is very uncommon as compared to the indirect (environment-human) which occurs by ingesting contaminated food or water (Brachman and Abrutyn 2009). Susceptible individuals acquire typhoid infection either through person-to-person transmission or by ingesting environmental bacteria from contaminated water and/or food and drinks at the rates $\frac{\beta_1(I+\eta C)}{N}$ and $\frac{\beta_2 B}{B+k}$ respectively. Here, we assume that individuals under treatment are infectious but cannot infect susceptible individuals since they will be confined to a certain place and separated from the general population where they will be released upon successful treatment or due to mortality (natural or disease related). The parameter β_1 denotes typhoid transmission rate and is defined as the product of the probability of typhoid transmission per contact and the effective con-

tact rate for typhoid transmission to occur. The modification parameter η, accounts for the relative infectiousness of carriers relative to infected individuals in class I. Here, $\eta = 1$ signifies that the chance of acquiring typhoid infection upon contact with an individual in the infectious class I or upon contact with a carrier is the same, $\eta \in (0, 1)$ signifies a reduced chance of acquiring typhoid infection upon contact with a carrier as compared to an infectious individual in class I and $\eta > 1$ signifies an increased chance of acquiring typhoid infection upon contact with a carrier as compared to an individual in class I. The parameter β_2 denotes the per capita contact rate for humans and the contaminated environment and k denotes the saturation constant. Infected individuals progress to the carrier class C at a rate σ or recover naturally at a rate ϵ_1. Infected individuals experience disease related death at a rate δ_1. Individuals in the carrier state recover naturally at a rate ϵ_2 or experience disease related death at a rate δ_2. Individuals in the infectious state and carrier state excrete bacteria into the environment at rates α_1 and α_2 respectively. Infected individuals enter into treatment at a rate given by $H(I)$. Individuals under treatment can either die (naturally or due to disease related death) or recover successfully. Individuals under treatment experience disease related death at a rate given by δ_3 or recover successfully at a rate given by γ. Individuals in the recovered class are temporarily immune to typhoid infection and immunity to reinfection wanes out at a rate ρ, leading to the individual being susceptible again. The bacteria population is generated at a rate gB and its growth is enhanced by individuals in the infectious and carrier state at rates α_1 and α_2 respectively. We assume that the bacteria in the environment becomes non-infectious at a rate μ_b. The constant recruitment into the susceptible population is represented by Λ, while the natural death rate for the general population is represented by μ. We assume that individuals in each compartment are indistinguishable and there is homogeneous mixing. The schematic diagram below shows the movement of humans as their status with respect to typhoid infection changes (Fig. 1).

Combining the parameters, assumptions and the schematic diagram, we have the following general set of nonlinear ordinary differential equations:

$$\begin{cases} \dfrac{dS}{dt} = \Lambda - \dfrac{\beta_1(I+\eta C)S}{N} - \dfrac{\beta_2 SB}{B+k} - \mu S + \rho R, \\ \dfrac{dI}{dt} = \dfrac{\beta_1(I+\eta C)S}{N} + \dfrac{\beta_2 SB}{B+k} - (\mu+\sigma+\delta_1+\epsilon_1)I - H(I), \\ \dfrac{dC}{dt} = \sigma I - (\mu+\delta_2+\epsilon_2)C, \\ \dfrac{dT}{dt} = H(I) - (\mu+\gamma+\delta_3)T, \\ \dfrac{dR}{dt} = \gamma T + \epsilon_1 I + \epsilon_2 C - (\mu+\rho)R, \\ \dfrac{dB}{dt} = gB + \alpha_1 I + \alpha_2 C - \mu_b B, \end{cases} \tag{3}$$

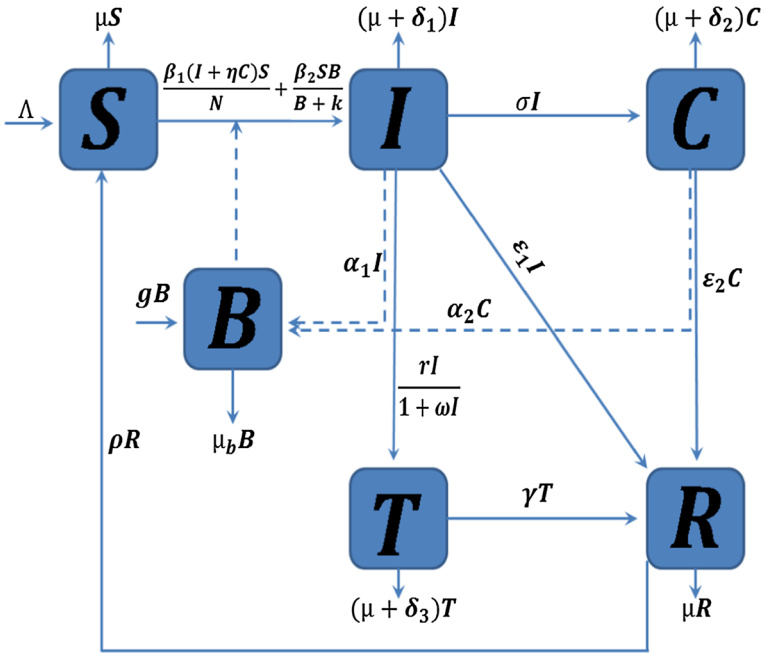

Fig. 1 Model flow diagram

with the initial conditions:

$$S(0) = S_0 > 0,\ I(0) = I_0 \geq 0,\ C(0) = C_0 \geq 0,\ T(0) = T_0 \geq 0,$$
$$R(0) = R_0 \geq 0,\ B(0) = B_0 \geq 0.$$

3 Model analysis

3.1 Positivity of Solutions

We now consider the positivity of model system (3). We prove that all the state variables remain non-negative and the solutions of model system (3) with positive initial conditions will remain positive for all $t > 0$. We thus state the following theorem.

Theorem 1 *Given that the initial conditions of model system* (3) *are* $S(0) > 0$, $I(0) > 0$, $C(0) > 0$, $T(0) > 0$, $R(0) > 0$ *and* $B(0) > 0$. *There exists* $(S(t), I(t), C(t), T(t), R(t), B(t)) : (0, \infty) \to (0, \infty)$ *which solve model system* (3).

Proof Assume that

$$\hat{t} = \sup\{t > 0 :\ S > 0,\ I > 0,\ C > 0,\ T > 0,\ R > 0,\ B > 0\} \in [0, t].$$

Thus $\hat{t} > 0$, and it follows from the first equation of model system (3) that

$$\frac{dS}{dt} = \Lambda - (\lambda + \mu)S + \rho R \text{ where } \lambda = \frac{\beta_1(I + \eta C)}{N} + \frac{\beta_2 B}{B + k}.$$

We thus have

$$\frac{d}{dt}\left[S(t)\exp\left\{\mu t + \int_0^t \lambda(s)\,ds\right\}\right] = (\Lambda + \rho R(t))\exp\left[\mu t + \int_0^t \lambda(s)\,ds\right].$$

So

$$S(\hat{t})\exp\left[\mu\hat{t} + \int_0^{\hat{t}} \lambda(s)\,ds\right] - S(0) = \int_0^{\hat{t}} (\Lambda + \rho R(\hat{t}))\exp\left[\mu\hat{t} + \int_0^{\hat{t}} \lambda(\nu)\,d\nu\right] d\hat{t},$$

giving

$$\begin{aligned} S(\hat{t}) = {} & S(0)\exp\left[-\left(\mu\hat{t} + \int_0^{\hat{t}} \lambda(s)\,ds\right)\right] \\ & + \exp\left[-\left(\mu\hat{t} + \int_0^{\hat{t}} \lambda(s)\,ds\right)\right]\int_0^{\hat{t}} (\Lambda\left[+\rho R(\hat{t})\right)\exp\left[\mu\hat{t} + \int_0^{\hat{t}} \lambda(\nu)\,d\nu\right] d\hat{t}\Bigg] > 0. \end{aligned}$$

From the second equation of model system equations (3), we obtain

$$\begin{aligned} \frac{dI}{dt} &= \lambda S - (\mu + \sigma + \delta_1 + \epsilon_1)I - \frac{rI}{1 + \omega I} \\ &\geq -(\mu + r + \sigma + \delta_1 + \epsilon_1)I, \Rightarrow I(\hat{t}) \\ &\geq I_0 e^{-(\mu + r + \sigma + \delta_1 + \epsilon_1)\hat{t}} > 0. \end{aligned}$$

In a similar fashion it can also be shown that $C(t) > 0$, $T(t) > 0$, $R(t) > 0$ and $B(t) > 0$ for all $t > 0$, and this completes the proof. □

3.2 Invariant region

Theorem 2 *Let* $(S(t), I(t), C(t), T(t), R(t), B(t))$ *be the solution of the system* (3) *with initial conditions* $(S_0, I_0, C_0, T_0, R_0, B_0)$. *The compact set,*

$$\Phi = \left\{(S, I, C, T, R, B) \in \mathbb{R}^6_+, W_H \leq \frac{\Lambda}{\mu}, W_B \leq \frac{(\alpha_1 + \alpha_2)\Lambda}{\mu(\mu_b - g)}\right\}$$

is positively invariant and attracts all solutions in $\mathbb{R}^6_+$.

Proof Consider, $W(t) = (W_H, W_B) = (S + I + C + T + R, B)$. The time derivative of $W(t)$ is given by

$$\begin{aligned}\frac{dW}{dt} &= \left(\frac{W_H}{dt}, \frac{W_B}{dt}\right) = \left(\frac{dS}{dt} + \frac{dI}{dt} + \frac{dC}{dt} + \frac{dT}{dt} + \frac{dR}{dt}, \frac{dB}{dt}\right) \\ &= (\Lambda - \mu W_H - \delta_1 I - \delta_2 C - \delta_3 T, \quad (g - \mu_b)B + \alpha_1 I + \alpha_2 C).\end{aligned}$$

This gives

$$\begin{cases} \frac{dW_H}{dt} = \Lambda - \mu W_H - \delta_1 I - \delta_2 C - \delta_3 T \le \Lambda - \mu W_H \le 0, \quad \text{for } W_H \ge \Lambda/\mu, \\ \frac{dW_B}{dt} = (g - \mu_b)B + \alpha_1 I + \alpha_2 C \le (g - \mu_b)W_B + (\alpha_1 + \alpha_2)W_H \le 0, \quad \text{for } W_B \ge \frac{(\alpha_1 + \alpha_2)\Lambda}{\mu(\mu_b - g)} \\ \text{with } W_H \ge \Lambda/\mu \text{ and } \mu_b > g. \end{cases} \tag{4}$$

From (4) we have $\frac{dW}{dt} \le 0$ which implies that Φ is a positively invariant set. We also note that by solving (4) we have;

$$0 \le (W_H(t), W_B(t)) \le \left(\frac{\Lambda}{\mu} + W_H(0)e^{-\mu t}, \frac{(\alpha_1 + \alpha_2)\Lambda}{\mu(\mu_b - g)} + W_B(0)e^{-(g-\mu_b)t}\right),$$

where $W_H(0)$ and $W_B(0)$ are the initial conditions of $W_H(t)$ and $W_B(t)$ respectively. Thus, $0 \le (W_H(t), W_B(t)) \le \left(\frac{\Lambda}{\mu}, \frac{(\alpha_1+\alpha_2)\Lambda}{\mu(\mu_b-g)}\right)$ as $t \to \infty$ and hence Φ is an attractive set. □

3.3 Disease-free equilibrium and the basic reproduction number

The model has a disease-free equilibrium given by

$$\mathcal{D}_0 = \left(S^0, I^0, C^0, T^0, R^0, B^0\right) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0\right),$$

a scenario depicting a disease-free state in the community or society. The basic reproduction number $\mathcal{R}_0$ of the model measures the average number of new infections generated by a single infected individual in a completely susceptible population. Usually, $\mathcal{R}_0 < 1$ implies that the disease will die out, whereas $\mathcal{R}_0 > 1$ implies that the disease will persist within a community and $\mathcal{R}_0 = 1$ requires further investigation. The determination of $\mathcal{R}_0$ is done using the next generation matrix approach (Driessche and Watmough 2002). This method has been explored in many papers, see for instance (Hsier and Wang 2006; Driessche and Zou 2007; Capistrna et al. 2009; Kodaira et al. 2010; Mastroberardino 2014). Using this method we have

$$F = \begin{pmatrix} \beta_1 & \eta\beta_1 & 0 & 0 & \frac{\Lambda\beta_2}{k\mu} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} g_1 & 0 & 0 & 0 & 0 \\ -\sigma & g_2 & 0 & 0 & 0 \\ -r & 0 & g_3 & 0 & 0 \\ -\epsilon_1 & -\epsilon_2 & -\gamma & \mu+\rho & 0 \\ -\alpha_1 & -\alpha_2 & 0 & 0 & \mu_b - g \end{pmatrix}$$

where

$$g_1 = \mu + r + \sigma + \delta_1 + \epsilon_1, \quad g_2 = \mu + \delta_2 + \epsilon_2, \quad g_3 = \mu + \gamma + \delta_3.$$

Thus, the basic reproduction number of model system (3) is given by

$$\begin{cases} \mathcal{R}_0 = \mathcal{R}_H + \mathcal{R}_E \quad \text{where} \\ \mathcal{R}_H = \dfrac{\beta_1(\eta\sigma + g_2)}{g_1 g_2} \quad \text{and} \quad \mathcal{R}_E = \dfrac{\Lambda\beta_2(\sigma\alpha_2 + g_2\alpha_1)}{k\mu g_1 g_2(\mu_b - g)}. \end{cases} \tag{5}$$

Here, $\mathcal{R}_0$ is the sum of two sub-reproduction numbers $\mathcal{R}_H$ and $\mathcal{R}_E$ representing the contributions of humans and the contaminated environment respectively. We can clearly note that $\mathcal{R}_E$ is non-negative when $\mu_b > g$. Consequently, $\mathcal{R}_0$ is non-negative provided $\mu_b > g$. We now show that typhoid can be eliminated from the community (when $\mathcal{R}_0 < 1$) if the initial sizes of the sub-populations of the model are in the basin of attraction of the disease-free equilibrium. We thus have the following theorem (Theorem 3).

Theorem 3 *The disease-free equilibrium $\mathcal{D}_0$ is locally asymptotically stable when $\mathcal{R}_0 < 1$ and is unstable when $\mathcal{R}_0 > 1$.*

Proof The Jacobian matrix of model system equations (3) at $\mathcal{D}_0$ is given by

$$J(\mathcal{D}_0) = \begin{pmatrix} -\mu & -\beta_1 & -\eta\beta_1 & 0 & \rho & -\frac{\Lambda\beta_2}{k\mu} \\ 0 & \beta_1 - g_1 & \eta\beta_1 & 0 & 0 & \frac{\Lambda\beta_2}{k\mu} \\ 0 & \sigma & -g_2 & 0 & 0 & 0 \\ 0 & r & 0 & -g_3 & 0 & 0 \\ 0 & \epsilon_1 & \epsilon_2 & \gamma & -\mu-\rho & 0 \\ 0 & \alpha_1 & \alpha_2 & 0 & 0 & g - \mu_b \end{pmatrix}$$

where g_1, g_2 and g_3 are defined as before. The local stability of the disease-free equilibrium is determined by the following submatrix of $J(\mathcal{D}_0)$,

$$\bar{J}(\mathcal{D}_0) = \begin{pmatrix} \beta_1 - g_1 & \eta\beta_1 & 0 & 0 & \frac{\Lambda\beta_2}{k\mu} \\ \sigma & -g_2 & 0 & 0 & 0 \\ r & 0 & -g_3 & 0 & 0 \\ \epsilon_1 & \epsilon_2 & \gamma & -\mu-\rho & 0 \\ \alpha_1 & \alpha_2 & 0 & 0 & g - \mu_b \end{pmatrix}.$$

Since all off-diagonal elements are positive, we now consider matrix $-\bar{J}(\mathcal{D}_0)$. We claim that $-\bar{J}(\mathcal{D}_0)$ is an $M-$matrix. Multiplying matrix $-\bar{J}(\mathcal{D}_0)$ by the positive 5×1 matrix

$$W_1 = \begin{pmatrix} g_2 g_3 \\ \sigma g_3 \\ r g_2 \\ (\sigma \epsilon_2 g_3 + r\gamma g_2 + \epsilon_1 g_2 g_3)/(\mu + \rho) \\ (\sigma \alpha_2 g_3 + \alpha_1 g_2 g_3)/(\mu_b - g) \end{pmatrix},$$

we have

$$-\bar{J}(\mathcal{D}_0) \cdot W_1 = (1 - \mathcal{R}_0) \cdot W_2$$

where W_2 is a positive 5×1 matrix given by

$$W_2 = \begin{pmatrix} g_1 g_2 g_3 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}.$$

Then, it follows from $M-$matrix theory that all eigenvalues of $\bar{J}(\mathcal{D}_0)$ have negative real parts, which implies the local asymptotic stability of the disease-free equilibrium if $\mathcal{R}_0 < 1$. On the other hand, it can be shown that the determinant of $\bar{J}(\mathcal{D}_0)$ is given by

$$\det \bar{J}(\mathcal{D}_0) = g_1 g_2 g_3 (\mathcal{R}_0 - 1).$$

Thus, if $\mathcal{R}_0 < 1$, then matrix $\bar{J}(\mathcal{D}_0)$ has eigenvalues with negative real parts, which implies the stability of the disease-free equilibrium. This completes the proof. □

3.4 The endemic equilibrium

The endemic equilibrium $\mathcal{D}^* = (S^*, I^*, C^*, T^*, R^*, B^*)$ always satisfies

$$\begin{cases} 0 = \Lambda - \dfrac{\beta_1 (I^* + \eta C^*) S^*}{N^*} - \dfrac{\beta_2 S^* B^*}{B^* + k} - \mu S^* + \rho R^*, \\ 0 = \dfrac{\beta_1 (I^* + \eta C^*) S^*}{N^*} + \dfrac{\beta_2 S^* B^*}{B^* + k} - (\mu + \sigma + \delta_1 + \epsilon_1) I^* - H(I^*), \\ 0 = \sigma I^* - (\mu + \delta_2 + \epsilon_2) C^*, \\ 0 = H(I^*) - (\mu + \gamma + \delta_3) T^*, \\ 0 = \gamma T^* + \epsilon_1 I^* + \epsilon_2 C^* - (\mu + \rho) R^*, \\ 0 = \alpha_1 I^* + \alpha_2 C^* + (g - \mu_b) B^*. \end{cases} \tag{6}$$

From the third and fourth equations of (6) we have that

$$C^* = \frac{\sigma I^*}{g_2} \text{ and } T_{ip}^* = \frac{r I^*}{(1+\omega I^*)\, g_3}. \tag{7}$$

Substituting expressions (7) into the fifth and sixth equations of (6), we get

$$R^* = \frac{r\gamma I^*}{(\mu+\rho)\,(1+\omega I^*)\, g_3} + \frac{(\epsilon_1 g_2 + \sigma\epsilon_2) I^*}{(\mu+\rho) g_2} \text{ and } B^* = \frac{(\sigma\alpha_2 + \alpha_1 g_2) I^*}{(\mu_b - g) g_2}. \tag{8}$$

From the first equation of (6) we have that

$$\Lambda - \mu S^* + \rho R^* = \frac{\beta_1 (I^* + \eta C^*) S^*}{N^*} + \frac{\beta_2 S^* B^*}{B^* + k}. \tag{9}$$

Substituting (9) into the second equation of (6) gives

$$\Lambda - \mu S^* + \rho R^* - (\mu + \sigma + \delta_1 + \epsilon_1) I^* - H(I^*) = 0. \tag{10}$$

Solving (10) for S^* gives

$$S^* = \frac{-I^*\,(\delta_1+\epsilon_1)\,(I^*\omega+1) - I^*(I^*\omega(\mu+\sigma) - (\Lambda+\rho_1 R^*)\omega + \mu + r + \sigma) + \Lambda + \rho_1 R^*}{I^*\mu\omega + \mu}. \tag{11}$$

Substituting expressions (7), (8) and (11) into the first equation of (6) leads to the following fourth order polynomial equation

$$I^* \left(\chi_3 I^{*3} + \chi_2 I^{*2} + \chi_1 I^* + \chi_0 \right) = 0. \tag{12}$$

Solving (12) gives $I^* = 0$ which corresponds to the disease-free equilibrium or

$$\chi_3 I^{*3} + \chi_2 I^{*2} + \chi_1 I^* + \chi_0 = 0, \tag{13}$$

where the coefficients ξ_i, $1 \le i \le 3$ are in "Appendix 1".

We can clearly note that, $\chi_0 > 0 \Leftrightarrow \mathcal{R}_0 < 1$ and $\chi_0 < 0 \Leftrightarrow \mathcal{R}_0 > 1$. We now determine the number of possible positive real roots of the polynomial (13) using the Descartes Rule of Signs. The possibilities can be tabulated as shown in Table 1 below.

3.5 Backward bifurcation

We show the existence of a backward bifurcation through numerical example by creating bifurcation diagram around $\mathcal{R}_0 = 1$ (Fig. 2). To draw a bifurcation curve

Table 1 Number of positive roots

	$\chi_3 > 0$							
	$\chi_2 > 0$				$\chi_2 < 0$			
	$\chi_1 > 0$		$\chi_1 < 0$		$\chi_1 > 0$		$\chi_1 < 0$	
	$\chi_0 > 0$	$\chi_0 < 0$	$\chi_0 > 0$	$\chi_0 < 0$	$\chi_0 > 0$	$\chi_0 < 0$	$\chi_0 > 0$	$\chi_0 < 0$
i^*	0	1	2	1	2	3	2	1

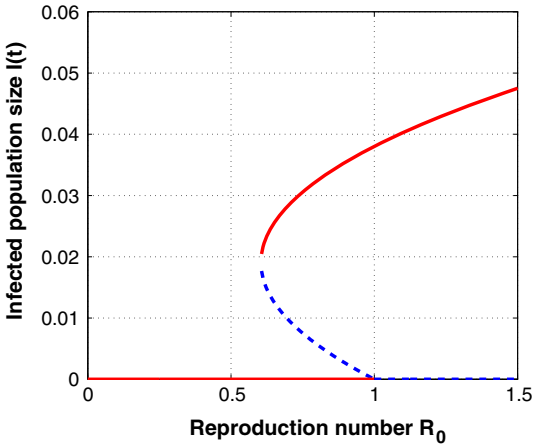

Fig. 2 The figure showing a backward bifurcation. The solid lines denote stable states and the dotted lines denote unstable states

(the graph of I^* as a function of $\mathcal{R}_0$), we fix $\Lambda = 0.25,\ \mu = 0.085,\ \mu_b = 0.9,\ \beta_1 = 0.57,\ \beta_2 = 0.43,\ \eta = 0.7,\ \sigma = 0.03,\ \omega = 0.8,\ k = 0.65,\ r = 0.4,\ \epsilon_1 = 0.06,\ \epsilon_2 = 0.13,\ \alpha_1 = 0.5282,\ \alpha_2 = 0.3201,\ \delta_1 = 0.005,\ \delta_2 = 0.001,\ \delta_3 = 0.0009,\ \gamma = 0.7,\ g = 0.001,\ \rho = 0.02$.

Conditions for the existence of backward bifurcation follow from Theorem 4.1 proven in Castillo-Chavez and Song (2004). We deliberately avoid rewriting the theorem and focus on its application. The theorem has been duplicated by many authors (Garba et al. 2008; Nyabadza and Hove-Musekwa 2010; Buonomo and Lacitignola 2011).

Let us make the following change of variables: $S = x_1,\ I = x_2,\ C = x_3,\ T = x_4,\ R = x_5,\ B = x_6$, so that $\mathrm{N} = \sum_{n=1}^{6} x_n$. We now use the vector notation $X = (x_1, x_2, x_3, x_4, x_5, x_6)^T$. Then, model system (3) can be written in the form $\frac{dX}{dt} = F(t, x(t)) = (f_1, f_2, f_3, f_4, f_5, f_6)^T$, where

$$\begin{cases} \dfrac{dx_1}{dt} = \Lambda - \dfrac{\beta_1(x_2+\eta x_3)x_1}{N} - \dfrac{\beta_2 x_1 x_6}{x_6+k} - \mu x_1 + \rho x_5 = f_1, \\ \dfrac{dx_2}{dt} = \dfrac{\beta_1(x_2+\eta x_3)x_1}{N} + \dfrac{\beta_2 x_1 x_6}{x_6+k} - (\mu+\sigma+\delta_1+\epsilon_1)x_2 - \dfrac{r x_2}{1+\omega x_2} = f_2, \\ \dfrac{dx_3}{dt} = \sigma x_2 - (\mu+\delta_2+\epsilon_2)x_3 = f_3, \\ \dfrac{dx_4}{dt} = \dfrac{r x_2}{1+\omega x_2} - (\mu+\gamma+\delta_3)x_4 = f_4, \\ \dfrac{dx_5}{dt} = \gamma x_4 + \epsilon_1 x_2 + \epsilon_2 x_3 - (\mu+\rho)x_5 = f_5, \\ \dfrac{dx_6}{dt} = \alpha_1 x_2 + \alpha_2 x_3 + (g-\mu_b)x_6 = f_6. \end{cases} \tag{14}$$

We now define

$$\beta_2 = \theta\beta_1 \tag{15}$$

with $\theta = 1$ signifying that the chance of acquiring typhoid infection through person-to-person transmission or by ingesting environmental bacteria is the same, $\theta \in (0, 1)$ signifying a reduced chance of acquiring typhoid infection by ingesting environmental bacteria as compared to infection through person-to-person transmission, $\theta > 1$ signifies an increased rate of acquiring typhoid infection by ingesting environmental bacteria as compared to infection through person-to-person transmission. However, typhoid is largely contracted from environmental bacteria through contaminated water and/or food and drinks as compared to transmission through direct person-to-person contact. Thus, the case $\theta > 1$ is more realistic.

Let β_1 be the bifurcation parameter, $\mathcal{R}_0 = 1$ corresponds to

$$\beta_1 = \beta_1^* = \frac{k\mu(\mu_b - g)g_2 g_2}{\alpha_1\theta\Lambda g_2 + \alpha_2\theta\Lambda\sigma + k\mu(\mu_b - g)\,(\eta\sigma + g_2)}. \tag{16}$$

The Jacobian matrix of model system (3) at $\mathcal{D}_0$ when $\beta_1 = \beta_1^*$ is given by

$$J^*(\mathcal{D}_0) = \begin{pmatrix} -\mu & -\beta_1^* & -\eta\beta_1 & 0 & \rho & -\frac{\theta\Lambda\beta_1^*}{k\mu} \\ 0 & \beta_1 - g_1 & \eta\beta_1^* & 0 & 0 & \frac{\theta\Lambda\beta_1^*}{k\mu} \\ 0 & \sigma & -g_2 & 0 & 0 & 0 \\ 0 & r & 0 & -g_3 & 0 & 0 \\ 0 & \epsilon_1 & \epsilon_2 & \gamma & -\mu-\rho & 0 \\ 0 & \alpha_1 & \alpha_2 & 0 & 0 & g-\mu_b \end{pmatrix}$$

where g_1, g_2 and g_3 are defined as before.

Model system (14), with $\beta_1 = \beta_1^*$ has a simple eigenvalue, hence the center manifold theory can be used to analyse the dynamics of model system (3) near $\beta_1 = \beta_1^*$. It can be shown that $J^*(\mathcal{D}_0)$, has a right eigenvector given by $w = (w_1, w_2, w_3, w_4, w_5, w_6)^T$, where

$$
\begin{aligned}
&w_1 = (g-\mu_b)(-(g_2(g_3(\rho\epsilon_1 - g_1(\mu+\rho)) + \gamma\rho r) + g_3\rho\sigma\epsilon_2)),\\
&w_2 = \mu g_2 g_3(\mu+\rho)(\mu_b - g), \quad w_3 = \mu\sigma g_3(\mu+\rho)(\mu_b - g),\\
&w_4 = \mu r g_2(\mu+\rho)(\mu_b - g), \quad w_5 = \mu(\mu_b - g)(g_2(g_3\epsilon_1 + \gamma r) + g_3\sigma\epsilon_2),\\
&w_6 = g_3\mu(\mu+\rho)\left(\alpha_2\sigma + \alpha_1 g_2\right).
\end{aligned}
$$

Further, the left eigenvector of $J^*(\mathcal{D}_0)$, associated with the zero eigenvalue at $\beta_1 = \beta_1^*$ is given by $v = (v_1, v_2, v_3, v_4, v_5, v_6)^T$, where

$$
\begin{aligned}
&v_1 = v_4 = v_5 = 0, \quad v_2 = \alpha_1\theta\Lambda g_2 + \alpha_2\theta\Lambda\sigma + k\mu(\mu_b - g)\left(\eta\sigma + g_2\right),\\
&v_3 = g_1\left(\alpha_2\theta\Lambda + \eta k\mu(\mu_b - g)\right), \quad v_6 = \theta\Lambda g_1 g_2.
\end{aligned}
$$

The computations of **a** and **b** are necessary in order to apply Theorem 4.1 in Castillo-Chavez and Song (2004). For system (14), the associated non-zero partial derivatives of F at the disease-free equilibrium are in "Appendix 2". It thus follows that

$$
\begin{aligned}
\mathbf{a} &= \sum_{i=2}^{5} v_2 w_2 w_i \frac{\partial^2 f_2}{\partial x_2 \partial x_i} + \sum_{i=2}^{5} v_2 w_3 w_i \frac{\partial^2 f_2}{\partial x_3 \partial x_i} + \sum_{i=2}^{3} v_2 w_4 w_i \frac{\partial^2 f_2}{\partial x_4 \partial x_i}\\
&\quad + \sum_{i=2}^{3} v_2 w_5 w_i \frac{\partial^2 f_2}{\partial x_5 \partial x_i} + v_2 w_6 w_1 \frac{\partial^2 f_2}{\partial x_6 \partial x_1} + v_2 w_6^2 \frac{\partial^2 f_2}{\partial x_6^2}\\
&= \frac{v_2}{k^2\Lambda\mu}\left(2k^2\Lambda\mu r w_2^2\omega - \beta_1\left(2k^2\mu^2\left(w_2 + w_3 + w_4 + w_5\right)\left(\eta w_3 + w_2\right)\right.\right.\\
&\quad \left.\left. - \theta k\Lambda\mu w_1 w_6 + 2\theta\Lambda^2 w_6^2\right)\right)\\
&= \xi_1 - \xi_2 = \xi_2\left(\Delta - 1\right) \quad \left(\frac{\xi_1}{\xi_2} = \Delta\right),
\end{aligned}
$$

where

$$
\begin{aligned}
&\xi_1 = 2k^2 r\Lambda\mu\omega w_2^2 + k\theta\Lambda\mu\beta_1^* w_1 w_6,\\
&\xi_2 = 2\beta_1^* k^2\mu^2(w_2 + \eta w_3)(w_2 + w_3 + w_4 + w_5) + 2\theta\Lambda^2\beta_1^* w_6^2.
\end{aligned}
$$

Note that if $\Delta > 1$, then $\mathbf{a} > 0$ and $\mathbf{a} < 0$ if $\Delta < 1$. Lastly,

$$
\mathbf{b} = \frac{g_3(\mu+\rho)\left(\alpha_1\theta\Lambda g_2 + \alpha_2\theta\Lambda\sigma + k\mu(\mu_b - g)\left(\eta\sigma + g_2\right)\right)^2}{k} > 0.
$$

We thus have the following result

Theorem 4 *If $\Delta > 1$, then model system (3) has a backward bifurcation at $\mathcal{R}_0 = 1$. Otherwise, if $\Delta < 1$ the endemic equilibrium is locally asymptotically stable for $\mathcal{R}_0 > 1$ but close to one.*

Remark When the model exhibits backward bifurcation, reducing $\mathcal{R}_0$ below unit is not sufficient to control the typhoid epidemic.

4 Numerical simulations

Numerical simulations of model system (3) are carried out using matlab together with a set of parameter values given in Table 2 to support our theoretical findings.

4.1 Sensitivity analysis

We examine which model parameter has the greatest effect on the value of the basic reproduction number $\mathcal{R}_0$. Determining these parameters is useful in reducing human mortality and morbidity related to typhoid infection given that $\mathcal{R}_0$ is directly related to typhoid transmission. Following Chitnis et al. (2008), we calculate the sensitivity indices of the basic reproduction number $\mathcal{R}_0$, to the parameters in the model. These indices indicate how sensitive $\mathcal{R}_0$ is to a change in each parameter, in other words, this tells us how crucial each parameter is to typhoid transmission. Since there are usually errors in data collection and presumed parameter values, sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values (Chitnis et al. 2008). Sensitivity indices allow us to measure the relative change in a state variable when a parameter changes. The normalized forward sensitivity index (NFSI) of the basic reproduction number $\mathcal{R}_0$ to a parameter is the relative change in the variable $\mathcal{R}_0$ to the relative change in a given parameter. A directly proportional normalized sensitivity index indicates that an increase/decrease in the parameter value brings about an increase/decrease respectively, in the value of $\mathcal{R}_0$, whereas, an inversely proportional normalized sensitivity index indicates that an increase in the parameter value brings about a decrease in the value of $\mathcal{R}_0$. When $\mathcal{R}_0$ is a differentiable function with respect to each of its parameters, then the sensitivity index may be alternatively defined using partial derivatives as follows;

Definition 1 Let $\mathcal{R}_0 : V \to W$ and $\mathcal{R}_0 \in C^1(V)$, where $V, W \subseteq 1304\mathbb{R}^+$. Then, for every parameter $p \in V$, the NFSI of $\mathcal{R}_0$ is defined as:

$$\Upsilon_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p} \times \frac{p}{\mathcal{R}_0}. \tag{17}$$

Using an explicit formula for $\mathcal{R}_0$ (5) and Definition 1, the sensitivity indices of $\mathcal{R}_0$ with respect to each of the parameters given in Table 2 are calculated and shown in "Appendix 3".

Recall that μ is the natural death rate of the population, δ_1 is the disease-related death rate for individuals in class I and δ_2 is the disease-related death rate for individuals in class C. It is clear that increases in any of these rates is neither ethical nor practical,

thus their sensitivity indices are not evaluated. Parameters Λ, β_1, β_2, α_1, α_2, g and η have a direct proportional relationship with $\mathcal{R}_0$, an increase in any of them results in an increase in $\mathcal{R}_0$ and a decrease in any of them will bring about an equivalent decrease in the value of $\mathcal{R}_0$. Parameters ϵ_1, ϵ_2, r, k and μ_b have an inversely proportional relationship with $\mathcal{R}_0$, an increase in any of them will bring about a decrease in $\mathcal{R}_0$. For almost all parameters, the sign of the sensitivity indices of $\mathcal{R}_0$ agrees with an intuitive expectation. Of interest is the sensitivity index of σ. Here, we note that the parameter σ can have a direct proportional relationship or an inversely proportional relationship with $\mathcal{R}_0$ under certain conditions. These threshold conditions are of great importance to policy makers as they inform what levels of treatment will be helpful in reducing typhoid transmission in a given community. Observe from the sensitivity index of σ that when

$$r > \max\left\{\frac{1}{\eta}\left[\mu(1-\eta)+(\delta_2-\eta\delta_1)+(\epsilon_2-\eta\epsilon_1)\right],\ \frac{1}{\alpha_2}\left[\mu(\alpha_1-\alpha_2)+(\alpha_1\delta_2-\alpha_2\delta_1)+(\alpha_1\epsilon_2-\alpha_2\epsilon_1)\right]\right\} \tag{18}$$

then σ has a direct proportional relationship with $\mathcal{R}_0$. Also, when

$$r < \min\left\{\frac{1}{\eta}\left[\mu(1-\eta)+(\delta_2-\eta\delta_1)+(\epsilon_2-\eta\epsilon_1)\right],\ \frac{1}{\alpha_2}\left[\mu(\alpha_1-\alpha_2)+(\alpha_1\delta_2-\alpha_2\delta_1)+(\alpha_1\epsilon_2-\alpha_2\epsilon_1)\right]\right\} \tag{19}$$

then σ has an inversely proportional relationship with $\mathcal{R}_0$. These results entail that when treatment demand exceed some level given in (18), then due to limited capacity of treatment this will lead to some untreated typhoid cases and thereby increasing the transmission of typhoid. Also, we note that when treatment demand is below some level prescribed in (19), then public health resources will be sufficient enough for the treatment of typhoid patients and thereby reducing transmission of typhoid in a given community.

Sensitivity analysis assesses the amount and type of change inherent in the model as captured by the terms that define the reproductive number. If the reproductive number is very sensitive to a particular parameter, then a perturbation of the conditions that connect the dynamics to such a parameter may prove useful in identifying policies or intervention strategies that reduce epidemic prevalence. Now, we use Latin Hypercube Sampling (LHS) technique to perform sensitivity analysis of the reproductive number $\mathcal{R}_0$. In this section the Partial rank correlation coefficients (PRCCs) were calculated to estimate the correlation between values of the reproductive number and the associated model parameters across 1000 random draws from the empirical distribution of $\mathcal{R}_0$ and its associated parameters.

Figure 3 shows partial rank correlation coefficients (PRCCs), which were calculated to estimate the correlation between $\mathcal{R}_0$ and constituent parameters. The results concur with those from the NFSI.

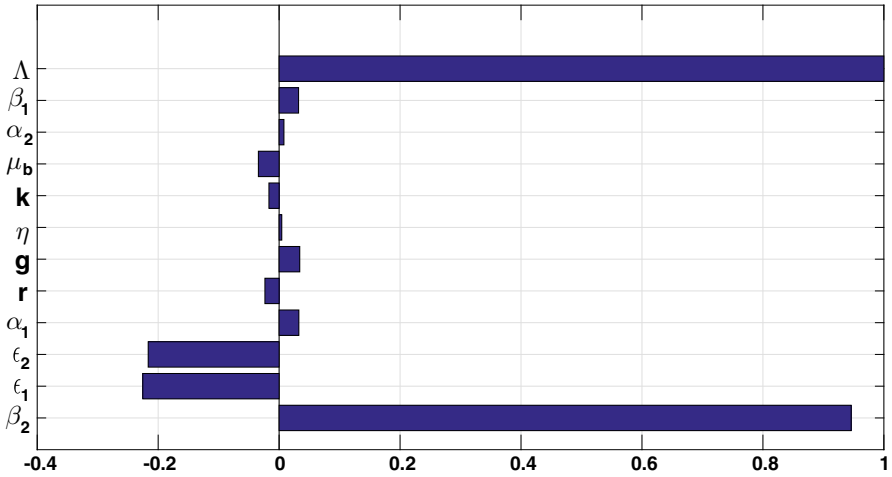

Fig. 3 Partial rank correlation coefficients showing the effects of parameter variation on $\mathcal{R}_0$, using parameter values in Table 2. Parameters with positive PRCCs will increase $\mathcal{R}_0$ when they are increased, whereas parameters with negative PRCCs will decrease $\mathcal{R}_0$ when they are increased

4.2 Numerical results

We carry out detailed numerical simulations using matlab to support our theoretical findings. Numerical solutions of a model depend on the values of all its parameters. The initial conditions used are: $S(0) = 10{,}000$, $I(0) = 10$, $C(0) = 10$, $T(0) = 1$, $R(0) = 0$, $B(0) = 100{,}000$.

4.2.1 Parameter estimation

The average life expectancy in sub-Saharan Africa is 50 years (Jamison et al. 2006) and thus the corresponding mortality rate is postulated to be equal to the inverse of the life expectancy, that is, $\mu = 1/50 = 0.02$. The recruitment rate of the susceptible population, Λ, has been obtained from Song et al. (2002). The per capita rate at which the bacteria in the environment becomes non-infectious is set to be $\mu_b = 0.0345$ (Mutua et al. 2015). The other parameter values used in this study have been extracted from literature as indicated in Table 2. However, not all parameters in literature have exactly the same meaning as the parameters contained in the present study. Therefore, some of the few remaining parameters will be estimated for illustrative purposes. Parameter values used for numerical simulations are given in Table 2.

Figures 4 and 5 illustrate the effect of varying parameters ω, β_1, β_2, r, ϵ_1, ϵ_2, g and ρ on the prevalence of typhoid. An arrow pointing upwards indicates that as the parameter value increases, the prevalence of typhoid infection also increases and an arrow pointing downwards indicates that as the parameter value increases, the prevalence of typhoid infection decreases. We can observe that increasing parameters ω, β_1, β_2, g and ρ results in an increase in the prevalence of typhoid. The percentage increase is especially higher for parameters g and ρ. This is evidence that typhoid

Table 2 Parameter values used in numerical simulations

Parameter	Range	Value	Source
β_1	0–1	0.75	Mushayabasa (2014)
η	0–5	1.2	Mushayabasa (2014)
β_2	0–1	1.97×10^{-11}	Mutua et al. (2015)
k	0–1	0.62	Assumed
ω	0–1	0.62	Assumed
r	0.19–0.8	0.2827	Kgosimore and Kelatlhegile (2016)
δ_1	0.001–1	0.06	Mushayabasa (2014)
δ_2	0–1	0.004	Mushayabasa (2014)
δ_3	0–1	0.0033	Mushayabasa (2014)
σ	0–1	0.04	Adetunde (2008)
ϵ_1	0–1	0.1	Mushayabasa (2014)
ϵ_2	0–1	0.001	Assumed
α_1	0–20	10	Mutua et al. (2015)
α_2	0–10	1	Mutua et al. (2015)
μ_b	0–1	0.0345	Mutua et al. (2015)
γ	0–0.06012	0.002485	Kgosimore and Kelatlhegile (2016)
Λ	0.0028–1	$\mu \times 41$	Song et al. (2002)
μ	0.019–0.021	0.020	Jamison et al. (2006)
ρ	0–1	0.0013	Okosun and Makinde (2011)
g	0–1	0.014	Mutua et al. (2015)

infection is largely spread through contact with environmental bacteria as compared to person-to-person contact. Also, there is need to increase treatment efficacy so as to improve and lengthen the recovery of infected individuals. We also note that increasing the parameter ω results in an increase in the prevalence of typhoid. This is a reflection that saturation in treatment is of great concern in the fight against typhoid. Typhoid patients can be delayed access to treatment, for instance, when there is limited availability of treatment services or when disadvantaged individuals have limited access to treatment facilities due to difficulties in paying for transport to facilities located in urban centres. This will in the long run lead to many untreated individuals who may in turn infect other susceptible individuals. This, thereby will lead to an increase in the prevalence of typhoid. Thus, limited treatment capacity can result in the spread of the typhoid epidemic and is responsible for the disproportionate increase in the prevalence of typhoid. We also observe that increasing parameters r, ϵ_1 and ϵ_2 leads to a decrease in the prevalence of typhoid infection. The percentage decrease is considerably higher for ϵ_2. This indicates that recovery of individuals in the carrier class C can reasonably decrease the prevalence of typhoid infection. In fact, a recovery rate of 20% can result in approximately 40% decrease in the prevalence of typhoid infection.

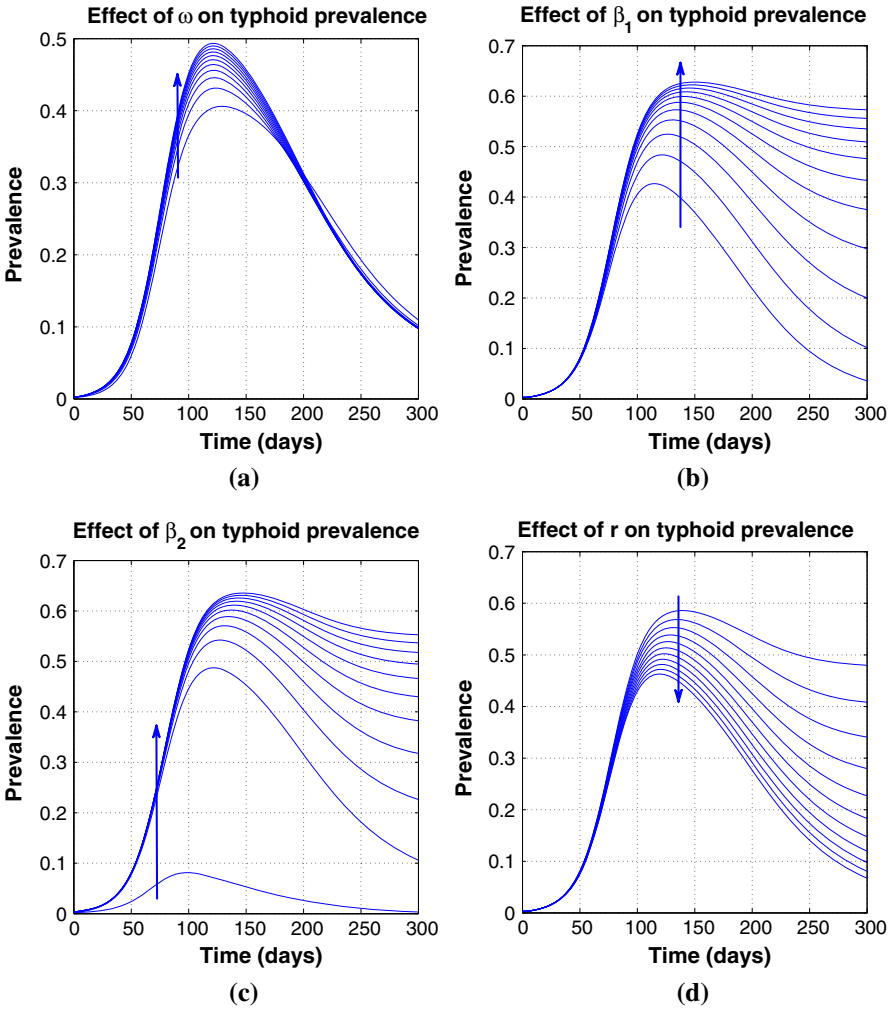

Fig. 4 Effects of varying ω, (**a**), β_1, (**b**), β_2, (**c**) and r, (**d**) on the prevalence of typhoid starting from 0.1 up to 1.0 with a step size of 0.1 across all the parameters

5 Conclusion

A mathematical model that describes the spread of typhoid has been formulated using nonlinear ordinary differential equations. Some treatment function that describes the effect of typhoid patients delayed access to treatment has been incorporated in the model. The model developed in this paper applies mostly to developing countries where there is usually a large shortfall in the provision of treatment services. Inclusion of a treatment function increase the realism of the model and seem to be responsible for interesting dynamical aspects such as the occurrence of a backward bifurcation. Compared with previous typhoid models, the work contained in this study is the first

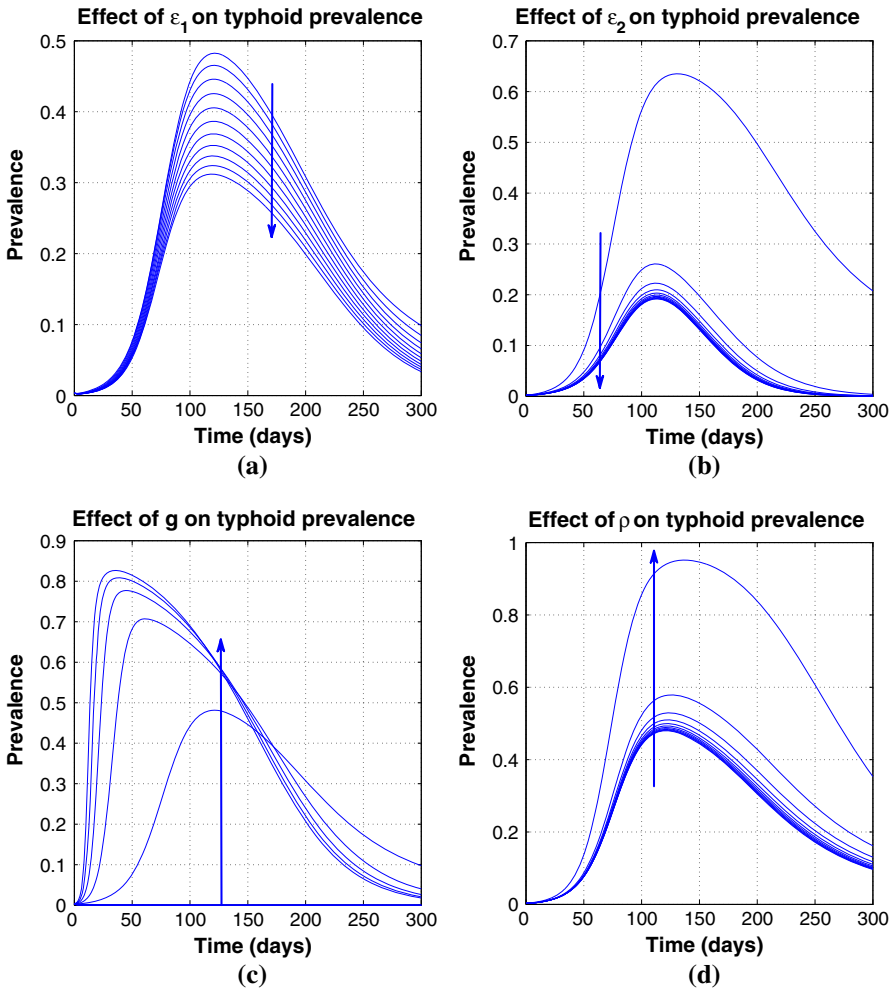

Fig. 5 Effects of varying ϵ_1, (**a**), ϵ_2, (**b**), g, (**c**) and ρ, (**d**) on the prevalence of typhoid starting from 0.1 up to 1.0 with a step size of 0.1 across all the parameters

attempt to model the impact of limited resources of the health care system on the spread of typhoid. The model takes into account both modes of transmission, that is, direct and indirect transmission on the spread of typhoid.

The reproduction number $\mathcal{R}_0$ has been computed. Sensitivity analysis has been performed and results entail that when treatment demand exceed some level, then due to limited capacity of treatment this will lead to some untreated typhoid cases and thereby increasing the transmission of typhoid. Also, it was observed that when treatment demand is below some level, then public health resources will be sufficient enough for the treatment of typhoid patients and thereby reducing transmission of typhoid in a given community. In this study, it has been shown that the classical $\mathcal{R}_0-$threshold is not the key to control typhoid within a population when treatment resources are

limited. In fact typhoid infection may persist in the population even with subthreshold values of $\mathcal{R}_0$. The centre manifold theory has been used to establish conditions for the existence of backward bifurcation. Our results suggest that considerable effort should be directed towards reducing saturation in treatment, this done by increasing the capacity of treatment so as to avoid backward bifurcation. It is advisable that communities should have suitable capacity for the treatment of typhoid patients.

Acknowledgements The authors would like to thank the anonymous referee for their helpful comments and suggestions that greatly improved the manuscript. J. Mushanyu, G. Muchatibaya, G. Nhawu and P. Mafuta authors acknowledge, with thanks, the support of the Department of Mathematics, University of Zimbabwe. F. Nyabadza acknowledges with gratitude the support from National Research Foundation and Stellenbosch University for the production of this manuscript.

Appendix 1: Coefficients of polynomial (13)

$$
\begin{cases}
\chi_0 = k\mu(\mu+\rho)(\mu_b-g)g_1g_3^2\,(1-\mathcal{R}_0)\,,\\
\chi_1 = \dfrac{g_2}{g_3}(-g_3\sigma^2(\alpha_2(\beta_1\eta\Lambda(\mu+\rho)+\beta_2\rho\epsilon_2)+\beta_1\eta k\rho\epsilon_2(\mu_b-g))\\
\quad + g_2\sigma(\gamma\rho r(\beta_1\eta k(g-\mu_b)-\alpha_2\beta_2)+g_3(-\alpha_1\beta_2\rho\epsilon_2\\
\quad + \beta_1(k(\mu_b-g)(\eta(\mu+\rho)(\delta_1-\Lambda\omega+\mu+r+\sigma)\\
\quad + \eta\mu\epsilon_1-\rho\epsilon_2)-\alpha_1\eta\Lambda(\mu+\rho))+\alpha_2(\mu\epsilon_1(\beta_2+\mu+\rho)\\
\quad + (\mu+\rho)(\beta_1(-\Lambda)+\beta_2(\delta_1-\Lambda\omega+\mu+r+\sigma)\\
\quad + \mu(\delta_1+\mu+r+\sigma)))))+g_2^2(\gamma\rho r(\beta_1k(g-\mu_b)-\alpha_1\beta_2)\\
\quad + g_3(\alpha_1(\mu\epsilon_1(\beta_2+\mu+\rho)+(\mu+\rho)(\beta_1(-\Lambda)+\beta_2(\delta_1-\Lambda\omega+\mu+r+\sigma)\\
\quad + \mu(\delta_1+\mu+r+\sigma)))-k(g-\mu_b)(\mu\omega(\mu+\rho)(\delta_1+\mu+\sigma+\epsilon_1)\\
\quad + \beta_1((\mu+\rho)(\delta_1-\Lambda\omega+\mu+r+\sigma)+\mu\epsilon_1)))),\\
\chi_2 = \dfrac{1}{g_3}(g_2\sigma^2(\alpha_2(\beta_1\eta(g_3((\mu+\rho)(\delta_1-\Lambda\omega+\mu+r+\sigma)+\mu\epsilon_1)-\gamma\rho r)\\
\quad - g_3\rho\epsilon_2(\beta_2\omega+\beta_1))-\beta_1\eta g_3\rho\epsilon_2(\alpha_1+k\omega(\mu_b-g)))\\
\quad + g_2^2\sigma(g_3(-\alpha_1\beta_2\rho\omega\epsilon_2+\beta_1(\alpha_1(\eta(\mu+\rho)(\delta_1-\Lambda\omega+\mu+r+\sigma)\\
\quad + \eta\mu\epsilon_1-\rho\epsilon_2)-k\omega(g-\mu_b)(\eta(\mu+\rho)(\delta_1+\mu+\sigma)+\eta\mu\epsilon_1-\rho\epsilon_2))\\
\quad + \alpha_2(\mu\epsilon_1(\omega(\beta_2+\mu+\rho)+\beta_1)+(\mu+\rho)(\omega(\beta_2+\mu)(\delta_1+\mu+\sigma)\\
\quad + \beta_1(\delta_1-\Lambda\omega+\mu+r+\sigma))))-\beta_1\gamma\rho r(\alpha_1\eta+\alpha_2))\\
\quad + g_2^3(g_3(\alpha_1(\mu\epsilon_1(\omega(\beta_2+\mu+\rho)+\beta_1)+(\mu+\rho)(\omega(\beta_2+\mu)(\delta_1+\mu+\sigma)\\
\quad + \beta_1(\delta_1-\Lambda\omega+\mu+r+\sigma)))-\beta_1k\omega(g-\mu_b)((\mu+\rho)(\delta_1+\mu+\sigma)\\
\quad + \mu\epsilon_1))-\alpha_1\beta_1\gamma\rho r)+\alpha_2\beta_1(-\eta)g_3\rho\sigma^3\epsilon_2),\\
\chi_3 = \beta_1\omega(\alpha_2\sigma+\alpha_1g_2)(\eta\sigma+g_2)(g_2(\mu(\delta_1+\mu+\sigma)+\rho(\mu+\delta_1))+\rho\sigma(\mu+\delta_2)).
\end{cases}
\tag{20}
$$

Appendix 2: Associated non-zero partial derivatives of F at the disease-free equilibrium

$$\frac{\partial^2 f_1}{\partial x_1 \partial x_6} = \frac{\partial^2 f_1}{\partial x_6 \partial x_1} = -\frac{\beta_1^* \theta}{k}, \quad \frac{\partial^2 f_1}{\partial x_2^2} = \frac{2\beta_1^* \mu}{\Lambda},$$

$$\frac{\partial^2 f_1}{\partial x_2 \partial x_3} = \frac{\partial^2 f_1}{\partial x_3 \partial x_2} = \frac{\mu \beta_1^* (1+\eta)}{\Lambda}, \quad \frac{\partial^2 f_1}{\partial x_2 \partial x_4} = \frac{\partial^2 f_1}{\partial x_4 \partial x_2} = \frac{\partial^2 f_1}{\partial x_2 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_2} = \frac{\beta_1^* \mu}{\Lambda},$$

$$\frac{\partial^2 f_1}{\partial x_3^2} = \frac{2\beta_1^* \eta \mu}{\Lambda}, \quad \frac{\partial^2 f_1}{\partial x_3 \partial x_4} = \frac{\partial^2 f_1}{\partial x_4 \partial x_3} = \frac{\partial^2 f_1}{\partial x_3 \partial x_5} = \frac{\partial^2 f_1}{\partial x_5 \partial x_3} = \frac{\beta_1^* \eta \mu}{\Lambda},$$

$$\frac{\partial^2 f_2}{\partial x_2^2} = 2r\omega - \frac{2\beta_1 \mu}{\Lambda}, \quad \frac{\partial^2 f_2}{\partial x_2 \partial x_3} = \frac{\partial^2 f_2}{\partial x_3 \partial x_2} = \frac{-\mu \beta_1^* (1+\eta)}{\Lambda},$$

$$\frac{\partial^2 f_2}{\partial x_2 \partial x_4} = \frac{\partial^2 f_2}{\partial x_4 \partial x_2} = \frac{\partial^2 f_2}{\partial x_2 \partial x_5} = \frac{\partial^2 f_2}{\partial x_5 \partial x_2} = -\frac{\beta_1^* \mu}{\Lambda}, \quad \frac{\partial^2 f_2}{\partial x_3^2} = -\frac{2\beta_1^* \eta \mu}{\Lambda}$$

$$\frac{\partial^2 f_2}{\partial x_3 \partial x_4} = \frac{\partial^2 f_2}{\partial x_4 \partial x_3} = \frac{\partial^2 f_2}{\partial x_3 \partial x_5} = \frac{\partial^2 f_2}{\partial x_5 \partial x_3} = -\frac{\beta_1^* \eta \mu}{\Lambda}, \quad \frac{\partial^2 f_2}{\partial x_6^2} = -\frac{2\beta_1^* \theta \Lambda}{k^2 \mu},$$

$$\frac{\partial^2 f_4}{\partial x_2^2} = -2r\omega, \quad \frac{\partial^2 f_1}{\partial x_2 \partial \beta_1^*} = -1, \quad \frac{\partial^2 f_1}{\partial x_3 \partial \beta_1^*} = -\eta,$$

$$\frac{\partial^2 f_1}{\partial x_6 \partial \beta_1^*} = -\frac{\theta \Lambda}{k\mu}, \quad \frac{\partial^2 f_2}{\partial x_6 \partial \beta_1^*} = \frac{\theta \Lambda}{k\mu}, \quad \frac{\partial^2 f_2}{\partial x_2 \partial \beta_1^*} = 1, \quad \frac{\partial^2 f_2}{\partial x_3 \partial \beta_1^*} = \eta.$$

Appendix 3: Sensitivity indices of $\mathcal{R}_0$ with respect to each of the parameters given in Table 2

$$\Upsilon_{\beta_1}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \beta_1} \times \frac{\beta_1}{\mathcal{R}_0} = \frac{\beta_1 k \mu (\mu_b - g)(\eta\sigma + g_2)}{\beta_2 \Lambda (\alpha_1 g_2 + \alpha_2 \sigma) + \beta_1 k \mu (\mu_b - g)(\eta\sigma + g_2)},$$

$$\Upsilon_{\beta_2}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \beta_2} \times \frac{\beta_2}{\mathcal{R}_0} = \frac{\beta_2 \Lambda (\alpha_1 g_2 + \alpha_2 \sigma)}{\beta_2 \Lambda (\alpha_1 g_2 + \alpha_2 \sigma) + \beta_1 k \mu (\mu_b - g)(\eta\sigma + g_2)},$$

$$\Upsilon_{\alpha_1}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \alpha_1} \times \frac{\alpha_1}{\mathcal{R}_0} = \frac{\alpha_1 \beta_2 \Lambda g_2}{\beta_2 \Lambda (\alpha_1 g_2 + \alpha_2 \sigma) + \beta_1 k \mu (\mu_b - g)(\eta\sigma + g_2)},$$

$$\Upsilon_{\alpha_2}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \alpha_2} \times \frac{\alpha_2}{\mathcal{R}_0} = \frac{\alpha_2 \beta_2 \Lambda \sigma}{\beta_2 \Lambda (\alpha_1 g_2 + \alpha_2 \sigma) + \beta_1 k \mu (\mu_b - g)(\eta\sigma + g_2)},$$

$$\Upsilon_{\epsilon_1}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \epsilon_1} \times \frac{\epsilon_1}{\mathcal{R}_0} = -\frac{\epsilon_1}{g_1},$$

$$\Upsilon_{\epsilon_2}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \epsilon_2} \times \frac{\epsilon_2}{\mathcal{R}_0} = -\frac{\sigma \epsilon_2 (\alpha_2 \beta_2 \Lambda + \beta_1 \eta k \mu (\mu_b - g))}{g_2 (\beta_2 \Lambda (\alpha_1 g_2 + \alpha_2 \sigma) + \beta_1 k \mu (\mu_b - g)(\eta\sigma + g_2))},$$

$$\Upsilon_{\sigma}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \sigma} \times \frac{\sigma}{\mathcal{R}_0}$$
$$= \frac{\beta_1 k \mu \sigma (\mu_b - g)\left(\eta\left(\mu + r + \delta_1 + \epsilon_1\right) - g_2\right) + \beta_2 \Lambda \sigma \left(\alpha_2\left(\delta_1 + \mu + r + \epsilon_1\right) - \alpha_1 g_2\right)}{g_1\left(\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) + \beta_1 k \mu (\mu_b - g)\left(\eta\sigma + g_2\right)\right)},$$
$$\Upsilon_{r}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial r} \times \frac{r}{\mathcal{R}_0} = -\frac{r}{g_1},$$
$$\Upsilon_{k}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial k} \times \frac{k}{\mathcal{R}_0} = -\frac{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right)}{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) + \beta_1 k \mu (\mu_b - g)\left(\eta\sigma + g_2\right)},$$
$$\Upsilon_{\mu_b}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \mu_b} \times \frac{\mu_b}{\mathcal{R}_0} = -\frac{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) \mu_b}{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) + \beta_1 k \mu (\mu_b - g)\left(\eta\sigma + g_2\right)(\mu_b - g)},$$
$$\Upsilon_{g}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial g} \times \frac{g}{\mathcal{R}_0} = \frac{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) g}{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) + \beta_1 k \mu (\mu_b - g)\left(\eta\sigma + g_2\right)(\mu_b - g)},$$
$$\Upsilon_{\eta}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \eta} \times \frac{\eta}{\mathcal{R}_0} = \frac{\beta_1 \eta k \mu \sigma (\mu_b - g)}{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) + \beta_1 k \mu (\mu_b - g)\left(\eta\sigma + g_2\right)},$$
$$\Upsilon_{\Lambda}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \Lambda} \times \frac{\Lambda}{\mathcal{R}_0} = \frac{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right)}{\beta_2 \Lambda\left(\alpha_1 g_2 + \alpha_2 \sigma\right) + \beta_1 k \mu (\mu_b - g)\left(\eta\sigma + g_2\right)}.$$

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