International Journal of Engineering, Mathematical and Physical Sciences
ISSN: 2517-9934
Vol:6, No:6, 2012

A simple epidemiological model for typhoid with saturated incidence rate and treatment effect

Steady Mushayabasa

Abstract—Typhoid fever is a communicable disease, found only in man and occurs due to systemic infection mainly by *Salmonella typhi* organism. The disease is endemic in many developing countries and remains a substantial public health problem despite recent progress in water and sanitation coverage. Globally, it is estimated that typhoid causes over 16 million cases of illness each year, resulting in over 600,000 deaths. A mathematical model for assessing the impact of educational campaigns on controlling the transmission dynamics of typhoid in the community, has been formulated and analyzed. The reproductive number has been computed. Stability of the model steady-states has been examined. The impact of educational campaigns on controlling the transmission dynamics of typhoid has been discussed through the basic reproductive number and numerical simulations. At its best the study suggests that targeted education campaigns, which are effective at stopping transmission of typhoid more than 40% of the time, will be highly effective at controlling the disease in the community. The abstract goes here.

Keywords—Mathematical model, Typhoid, saturated incidence rate, treatment, reproductive number, sensitivity analysis.

I. Introduction

TYPHOID fever is a systemic infection caused by *Salmonella enterica* serotype typhi (S *typhi*). A very similar but often less severe disease is caused by S *paratyphi* A, B, and sometimes C. S *typhi*, a highly adapted human-specific pathogen that evolved about 50 000 years ago, [1], [2] has remarkable mechanisms for persistence in its host [2], [3]. It is endemic in most parts of Central America [4]–[6], Southeast Asia [7]–[9], and the Indian subcontinent [10], [11], and recently increasing numbers of cases have been reported in Africa [12], [13]. The disease is estimated to have caused 21.6 million illnesses and 216 500 deaths globally in 2000, affecting all ages [3]. The disease is transmitted by feco-oral route or urine-oral route, either directly through hands soiled with feces or urine of cases or carriers or indirectly by ingestion of contaminated water, milk, food or through flies [14]. It is an acute generalized infection of the reticuloendothelial system, intestinal lymphoid tissue, and the gall bladder. Incubation period usually 10-14 days but it may be as short as 3 days or as long as 21 days depending upon the dose of the inoculums.

A brief survey on previous works provides the context of this paper. Various theoretical studies have been carried out on mathematical modelling of typhoid transmission dynamics, focusing on a number of different issues, see [15]–[19] to mention a few. Motivated by the 2012 typhoid outbreak in Zimbabwe, a simple deterministic mathematical model is developed and analyzed to assess the impact of treatment and educational campaigns on controlling typhoid outbreak. Incidence plays an important role in the modeling of epidemic dynamics. It has been suggested by several authors that the disease transmission process may have a saturation incidence rate (see, for example, [20]–[22]). In many epidemic models , the bilinear incidence rate βSI and the standard incidence rate $\beta SI/N$ are frequently used. The model developed in this study considers a saturated incidence rate $g(I) = \beta I/(1+\alpha I)$, where βI measures the infection force of the disease and $1/(1+\alpha I)$ measures the inhibition effect from the behavioral change of the susceptible individuals when their number increases or from the crowding effect of the infective individuals. This incidence rate seems more reasonable than the bilinear incidence rate βSI, because it includes the behavioral change and crowding effect of the infective individuals and prevents the unboundedness of the contact rate by choosing suitable parameters.

The paper is structured as follows. The typhoid transmission model is formulated and simplified in the next Section. Analytical results of the model are presented in Section III. Simulation results and projection profiles of typhoid are presented in Section IV. Summary and concluding remarks round up the paper.

II. Model formulation

Based on the individual's epidemiological status, the human population denoted by N constitutes the following classes: susceptible S, latently infected individuals E, and infectious individuals I. Thus, $N = S+E+I$. Assuming homogeneous mixing of the population, the model is given by

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \frac{\beta(1-\theta)IS}{1+\alpha I} - \mu S + \omega E + \rho I,\\
\frac{dE}{dt} &= p\frac{\beta(1-\theta)IS}{1+\alpha I} - (\mu+\phi+\omega+d)E, \qquad (1)\\
\frac{dI}{dt} &= (1-p)\frac{\beta(1-\theta)IS}{1+\alpha I} + \phi E - (\mu+\rho+\delta)I,
\end{aligned}$$

where Λ is the recruitment rate of individuals into the community by birth or migration (assumed susceptible), β is the rate of typhoid transmission from infectious individuals to susceptible individuals, μ is the natural mortality rate. Upon

S. Mushayabasa is with the University of Zimbabwe, Department of Mathematics, P.O. Box MP 167, Harare, Zimbabwe, e-mail: steadymushaya@gmail.com.

TABLE I
MODEL PARAMETERS.

Parameter definition	Symbol
Proportion of individuals who join E class	p
Progression from latency to infectious	ϕ
Disease-induced mortality for E class	d
Disease-induced mortality for I class	δ
Treatment rate for E class	ω
Treatment rate for I class	ρ
Educational adjustment	θ
Natural mortality rate	μ
Modification factor	α
Recruitment rate	Λ
Transmissibility	β

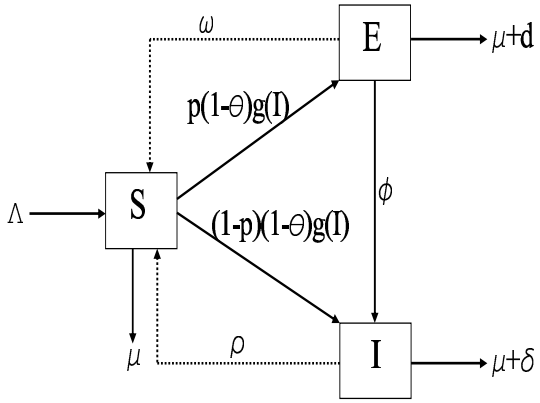

Fig. 1. Model flow diagram

infection with the disease, a fraction p join the latent class, and the complementary fraction $(1-p)$ become infectious. Treatment is offered to individuals in class E and I at rates ω and ρ, respectively. The role of educational campaigns is captured by θ, $1/(1+\alpha I)$ measures the inhibition effect from the behavioral change of the susceptible individuals when their number increases or from the crowding effect of the infective individuals. Furthermore, d and δ represents the disease-induced death rates of individuals in class E and I, respectively.
The structure of the model is presented in Fig. 1.

III. ANALYTICAL RESULTS

A. Basic properties of the model

In this section, we study the basic properties of the solutions of model system (1), which are essential in the proofs of stability.

Lemma 1: The equations preserve positivity of solutions.

Proof: The vector field given by the right hand side of (1) points inward on the boundary of $\Re^3_+ \setminus \{0\}$. For example, if $I=0$, then, $I' = \phi E \geq 0$. In an analogous manner, the same result can be shown for the other model components (variables). ■

Lemma 2: All solutions of system (1) are bounded.

Proof: Using system (1) we have $N' = \Lambda - \mu N - dE - \delta I \leq \Lambda - \mu N$. Assume that $N(t) \leq M$ for all $t \geq 0$ where $M = \dfrac{\Lambda}{\mu} + 1$. Suppose the assumption is not true then there exists a $t_1 > 0$ such that

$$\begin{aligned} &N(t_1) = \frac{\Lambda}{\mu} + 1, \quad N(t) < \frac{\Lambda}{\mu} + 1, \quad t < t_1, \\ &N'(t_1) \geq 0, \quad N'(t_1) \leq \Lambda - \mu N(t_1) = -\mu < 0. \end{aligned} \tag{2}$$

which is a contradiction meaning the assumption is true. This means $N(t) \leq M$ for all $t \geq 0$. ■
Therefore all feasible solutions of system (1) enter the region

$$\Omega = \Big\{ (S, E, I,) \in \Re^3_+ : N \leq \frac{\Lambda}{\mu} \Big\}. \tag{3}$$

Thus, Ω is positively invariant and it is sufficient to consider solutions of system (1) in Ω. Existence, uniqueness and continuation results for system (1) hold in this region and all solutions of system (1) starting in Ω remain in Ω for all $t \geq 0$. All parameters and state variables for model system (1) are assumed to be non-negative (for biological relevance) $\forall t \geq 0$ since it monitors human population.

B. Disease-free Equilibrium and Stability Analysis

Model system (1) has an evident disease-free (DFE), (denoted by $\mathcal{E}_0$), given by

$$\mathcal{E}_0 = \Big(S_0, E_0, I_0 \Big) = \Big(\frac{\Lambda}{\mu}, 0, 0 \Big). \tag{4}$$

The basic reproductive number is defined as the number of secondary cases generated by a primary case when the virus is introduced in a population of fully susceptible individuals at a demographic steady state [23]. Following van den Driessche et al [24], and using the notation defined therein, the matrices F and V for the new infection terms and the remaining transfer terms are, respectively, given by

$$F = \begin{bmatrix} 0 & \dfrac{p\beta(1-\theta)\Lambda}{\mu} \\ 0 & \dfrac{(1-p)\beta(1-\theta)\Lambda}{\mu} \end{bmatrix} \tag{5}$$

and

$$V = \begin{bmatrix} k_1 & 0 \\ -\phi & k_2 \end{bmatrix},$$

with $k_1 = (d + \mu + \phi + \omega)$, and $k_2 = (\mu + \rho + \delta)$. Thus, the reproductive number for system (1) denoted by $\mathcal{R}_0$ is given by

$$\begin{aligned} \mathcal{R}_0 &= \frac{\beta(1-p)(1-\theta)\Lambda}{\mu k_2} + \frac{\beta(1-\theta)p\phi\Lambda}{\mu k_1 k_2} \\ &= \frac{\beta(1-\theta)\Lambda[p\phi + (1-p)k_1]}{\mu k_1 k_2)}. \end{aligned} \tag{6}$$

$\mathcal{R}_0$ measures the average number of new infections generated by a single typhoid infective during his/her entire infectious period when he/she is introduced into a susceptible population in the presence of the aforementioned intervention strategies.

To examine the local stability of DFE ($\mathcal{E}_0$) we evaluate the Jacobian matrix at $\mathcal{E}_0$.

$$J(\mathcal{E}_0) = \begin{bmatrix} -\mu & \omega & -\dfrac{\beta(1-\theta)\Lambda}{\mu} + \rho \\ 0 & -k_1 & \dfrac{p\beta(1-\theta)\Lambda}{\mu} \\ 0 & \phi & \dfrac{\beta(1-p)(1-\theta)\Lambda}{\mu} - k_2 \end{bmatrix}. \quad (7)$$

We have the following stability result that shows $\mathcal{R}_0$ is a sharp threshold.

Theorem 1: $\mathcal{E}_0$ is locally-asymptotically stable (LAS) if $\mathcal{R}_0 < 1$, and unstable otherwise.

Proof: One eigenvalue of $J(\mathcal{E}_0)$ is $\lambda_1 = -\mu < 0$. Thus, system (7) reduces to

$$A = \begin{bmatrix} -k_1 & \dfrac{p\beta(1-\theta)\Lambda}{\mu} \\ \phi & -k_2 + \dfrac{\beta(1-p)(1-\theta)\Lambda}{\mu} \end{bmatrix}. \quad (8)$$

We want to show that, when $\mathcal{R}_0 < 1$, then the Routh-Hurwitz conditions hold, namely $\text{tr}(A) < 0$ and $\det(A) > 0$. Simple calculations show that

$$\text{tr}(A) = k_2 \left[\frac{\beta(1-p)(1-\theta)\Lambda}{\mu k_2} - 1 \right] - k_1.$$

Since $\mathcal{R}_0 < 1$ it follows that

$$\frac{\beta(1-p)(1-\theta)\Lambda}{\mu k_2} + \frac{\beta(1-\theta)p\phi\Lambda}{\mu k_1 k_2} < 1,$$

which implies that

$$\frac{\beta(1-p)(1-\theta)\Lambda}{\mu k_2} < 1, \quad \frac{\beta(1-\theta)p\phi\Lambda}{\mu k_1 k_2} < 1.$$

This shows that, $\text{tr}(A) < 0$. Now we calculate

$$\begin{aligned} \det(A) &= \mu k_1 k_2 \left[1 - \frac{\beta(1-\theta)\Lambda[p\phi + (1-p)k_1]}{\mu k_1 k_2} \right] \\ &= \mu k_1 k_2 \left[1 - \mathcal{R}_0 \right]. \end{aligned} \quad (9)$$

Therefore $\det(A) > 0$ if and only if $\mathcal{R}_0 < 1$. This concludes the proof. ■

Following Castillo-Chavez et al., (2002) [25], we write system (1) in the form

$$\begin{aligned} X'(t) &= F(X, Y), \\ Y'(t) &= G(X, Y),\ G(X, \mathbf{0}) = 0 \end{aligned} \quad (10)$$

where $X = S$ and $Y = (E, I)$. Here $X \in \Re^1_+$ denotes (its components) the number of uninfected individuals and $Y \in \Re^2_+$ denoting (its components) the number of infected individuals. The disease-free equilibrium is now denoted by $\mathcal{E}_0 = (X_0, \mathbf{0})$ where $X_0 = \dfrac{\Lambda}{\mu}$. We have to prove that the two conditions

$$\begin{aligned} &(H1)\ \text{For}\ X'(t) = F(X, \mathbf{0}),\ X \text{ is a globally asymptotically stable,} \\ &(H2)\ \widehat{G}(X, Y) = UY - G(X, Y),\ \widehat{G}(X, Y) \geq 0 \text{ for } (X, Y) \in \Omega, \end{aligned} \quad (11)$$

are satisfied where Ω is a positively invariant attracting domain. Consider

$$F(X, \mathbf{0}) = \begin{bmatrix} \Lambda - \mu S \end{bmatrix}$$

$$U = \begin{bmatrix} -k_1 & \dfrac{p\beta(1-\theta)\Lambda}{\mu} \\ \phi & \dfrac{\beta(1-p)(1-\theta)\Lambda}{\mu} - k_2 \end{bmatrix}$$

Thus,

$$\widehat{G}(X, Y) = \begin{bmatrix} \widehat{G_1}(X, Y) \\ \widehat{G_2}(X, Y) \end{bmatrix} = \begin{bmatrix} p\beta(1-\theta)\left(\dfrac{\Lambda}{\mu} - \dfrac{S}{1+\alpha I}\right) \\ (1-p)\beta(1-\theta)\left(\dfrac{\Lambda}{\mu} - \dfrac{S}{1+\alpha I}\right) \end{bmatrix}. \quad (12)$$

Since, $\frac{\Lambda}{\mu} \geq \frac{S}{1+\alpha I}$ at $\mathcal{E}_0$, it follows that $\hat{G}(X, Z) \geq 0$. We summarize the result in Theorem 2

Theorem 2: The fixed point $\mathcal{E}_0 = (X^*, \mathbf{0})$ is a globally asymptotically stable equilibrium of system (1) provided that $\mathcal{R}_0 \leq 1$, and unstable otherwise

C. Endemic equilibrium: Existence and Stability

Model system (1) has an endemic equilibrium $\mathcal{E}_* = (S_*, E_*, I_*)$ given by,

$$\begin{aligned} S_* &= \frac{\Lambda k_1 k_2}{m_1 + m_2}, \quad E_* = \frac{p(1-\theta)\lambda^* k_2}{m_1 + m_2}, \\ I_* &= \frac{\lambda^* \Lambda (1-\theta)(p\phi + (1-p)k_1)}{m_1 + m_2}, \end{aligned} \quad (13)$$

with,

$\lambda^* = \dfrac{\beta I^*}{1 + \alpha I^*}$,

$m_1 = p\lambda^*(1-\theta)(\rho\phi + \omega k_2)$,

$m_2 = k_1[\lambda^*(1-\theta)(1-p) - (\lambda^*(1-\theta) + \mu)k_2$.

Substituting I^* into λ^* one gets

$$\lambda^*(m_3 + m_4) = 0,$$

where

$$m_3 = p\lambda^*(1-\theta)(\phi(\alpha\Lambda - \rho) + \omega k_2,$$

$$m_4 = k_1(\lambda^*(1-p)(1-\theta)(\alpha\Lambda - \rho) + (\lambda^*(1-\theta) + \mu)k_2), \tag{14}$$

which is a quadratic equation with roots

$$\lambda_1^* = 0, \quad \text{which is the disease-free equlibrium,}$$

$$\lambda_2^* = \frac{\mu k_1 k_2}{m_5 + m_6}(\mathcal{R}_0 - 1),$$

where

$$m_5 = p[\phi(\alpha\Lambda - \rho) + \omega k_2],$$

$$m_6 = (1-\theta)[(\delta + \mu + \alpha\Lambda(1-p) + p\rho)(d + \mu + \phi + \omega)]. \tag{15}$$

λ_2^* denotes the endemic equilibrium point for system (1) which exists for $\mathcal{R}_0 > 1$.

Theorem 3: $\mathcal{E}_*$ of system (1) exists if and only if $\mathcal{R}_0 > 1$.

Since system (1) has a unique equilibrium point for $\mathcal{R}_0 > 1$, we now employ the Centre Manifold Theory [26] to analyze the stability of this equilibrium point as described in Theorem 4.1 [27], to establish the local asymptotic stability of the endemic equilibrium. To apply Centre Manifold Theory, the following simplifications and change of variables are made first. Let $S = x_1$, $E = x_2$, $I = x_3$, and $\lambda = \dfrac{(1-\theta)\beta x_3}{1 + \alpha x_3}$. Further, by using vector notation $\mathbf{x} = (x_1, x_2, x_3)^T$, model system (1) can be written in the form $\dfrac{d\mathbf{x}}{dt} = F(\mathbf{x})$, with $F = (f_1, f_2, f_3)^T$, such that

$$\begin{aligned} x_1' &= f_1 = \Lambda - \lambda x_1 - \mu x_1 + \omega x_2 + \rho x_3, \\ x_2' &= f_2 = p\lambda x_1 - (\mu + \phi + \omega + d)x_2, \\ x_3' &= f_3 = (1-p)\gamma x_1 + \phi x_2 - (\mu + \delta + \rho)x_3. \end{aligned} \tag{16}$$

The Jacobian of (7) is given by

$$J(\mathcal{E}^0) = \begin{bmatrix} -\mu & \omega & -\dfrac{\beta(1-\theta)\Lambda}{\mu} + \rho \\ 0 & -k_1 & \dfrac{p\beta(1-\theta)\Lambda}{\mu} \\ 0 & \phi & -k_2 + \dfrac{\beta(1-p)(1-\theta)\Lambda}{\mu} \end{bmatrix}, \tag{17}$$

with $k_1 = \mu + \phi + \omega + d$ and $k_2 = \mu + \delta + \rho$. It can be shown that the reproductive number is

$$\mathcal{R}_0 = \frac{\beta(1-\theta)\Lambda[p\phi + (1-p)k_1]}{\mu k_1 k_2}. \tag{18}$$

If β is taken as a bifurcation parameter and if we consider the case $\mathcal{R}_0 = 1$ and solve for β, we obtain

$$\beta = \beta^* = \frac{\mu k_1 k_2}{(1-\theta)\Lambda(p\phi + (1-p)k_1)}. \tag{19}$$

Note that the linearized system of the transformed (16) with the bifurcation point β^* has a simple zero eigenvalue. Hence, the Centre Manifold Theory [26] can be used to analyze the dynamics of (16) near $\beta = \beta^*$. It can be shown that the Jacobian of (16) at $\beta = \beta^*$ has a right eigenvector associated with the zero eigenvalue given by $w = [w_1, w_2, w_3]^T$, where

$$\begin{aligned} w_1 &= -\left[\frac{\beta(1-\theta)\Lambda}{\mu}\left(1 - \frac{p}{k_1}\right) - \frac{\rho}{\mu}\right] w_3, \\ w_2 &= \frac{p\beta(1-\theta)\Lambda}{\mu k_1} w_3, \quad w_3 > 0. \end{aligned} \tag{20}$$

The left eigenvector of $J(\mathcal{E}_0)$ associated with the zero eigenvalue at $\beta = \beta^*$ is given by $v = [v_1, v_2, v_3]^T$, where

$$v_1 = 0, \quad v_2 = \frac{\phi}{k_1} v_3, \quad v_3 > 0. \tag{21}$$

Further, we use Theorem 6 from Castillo-Chavez and Song [26], stated below for elucidation.

Theorem 4: Consider the following general system of ordinary differential equations with a parameter ϕ

$$\frac{dx}{dt} = f(x, \phi), \ f : \Re^n \times \Re \to \Re \text{ and } f \in (\Re^n \times \Re), \tag{22}$$

where 0 is an equilibrium of the system that is $f(0, \phi) = 0$ for all ϕ and assume

A1: $A = D_x f(0,0) = \left(\dfrac{\partial f_i}{\partial x_j}(0,0)\right)$ is the linearisation of system (22) around the equilibrium 0 with ϕ evaluated at 0. Zero is a simple eigenvalue of A and other eigenvalues of A have negative real parts;

A2: Matrix A has a right eigenvector u and a left eigenvector v corresponding to the zero eigenvalue.

Let f_k be the k^{th} component of f and

$$\begin{aligned} a &= \sum_{k,i,j=1}^{n} z_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0), \\ b &= \sum_{k,i=1}^{n} z_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0). \end{aligned} \tag{23}$$

The local dynamics of (22) around 0 are totally governed by a and b.

i. $a > 0, \ b > 0$. When $\phi < 0$ with $|\phi| << 1$, 0 is locally asymptotically stable, and there exists a positive unstable equilibrium; when $0 < \phi << 1$, 0 is unstable and there exists a negative and locally asymptotically stable equilibrium;

ii. $a < 0, \ b < 0$. When $\phi < 0$ with $|\phi| << 1$, 0 unstable; when $0 < \phi << 1$, 0 is locally asymptotically stable, and there exists a positive unstable equilibrium;

iii. $a > 0,\ b < 0$. When $\phi < 0$ with $|\phi| << 1$, 0 is unstable, and there exists a locally asymptotically stable negative equilibrium; when $0 < \phi << 1$, 0 is stable, and a positive unstable equilibrium appears;
iv. $a < 0,\ b > 0$. When ϕ changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.

Computations of a and b

For system (7), the associated non-zero partial derivatives of F at the disease-free equilibrium associated with a are given by

$$\frac{\partial^2 f_2}{\partial x_1 \partial x_3} = 2p\beta(1-\theta),\ \frac{\partial^2 f_2}{\partial x_3^2} = -\frac{2p\alpha\beta(1-\theta)\Lambda}{\mu},$$
$$\frac{\partial^2 f_3}{\partial x_1 \partial x_3} = 2\beta(1-p)(1-\theta), \tag{24}$$
$$\frac{\partial^2 f_3}{\partial x_3^2} = -\frac{2\alpha\beta(1-p)(1-\theta)\Lambda}{\mu}.$$

From (24) it follows that

$$a = -\frac{2\beta(1-\theta)(1-p)\alpha\Lambda}{\mu} H w_3^2 v_3 - 2\beta(1-\theta)\left(\frac{\beta(1-\theta)\Lambda}{\mu}\left(1-\frac{p}{k_1}\right) - \frac{\rho}{\mu}\right) H w_3^2 v_3$$
$$\text{with} \quad H = \left[(1-p) + \frac{p\phi}{k_1}\right]. \tag{25}$$

For the sign of b, it is associated with the following non-vanishing partial derivatives of F,

$$\frac{\partial^2 f_2}{\partial x_3 \partial \beta^*} = \frac{p(1-\theta)\Lambda}{\mu},\quad \frac{\partial^2 f_2}{\partial x_4 \partial \beta^*} = \frac{(1-p)(1-\theta)\Lambda}{\mu}. \tag{26}$$

It follows from expressions in (26) that

$$b = \frac{(1-\theta)\Lambda}{\mu}\left[(1-p) + \frac{p\phi}{k_1}\right] w_3 v_3. \tag{27}$$

Since, $a < 0$ and $b > 0$ and using Theorem 4, we have established the following result.

Theorem 5: The unique endemic equilibrium $\mathcal{E}_*$ guaranteed by Theorem 4 is locally asymptotically stable for $\mathcal{R}_0 >$ but close to 1.

IV. Numerical Results

In order to illustrate the results of the foregoing analysis, we have simulated model system (1) using the parameters in Table II.

Fig. 2 demonstrates the impact of p on cumulative latent typhoid cases and infectious cases. Here, we observe that an increase on p may lead to an increase on cumulative typhoid cases, but with a more impact on latent cases.

TABLE II
Model Parameters.

Symbol	Units	Value	Source
p	-	0.5(0.0-1.0)	Assumed
ϕ	/year	0.03(0.03-0.05)	[16]
d	/year	0.013(0.01-0.3)	[16]
δ	/year	0.9(0.1-0.9)	[16]
ω	/year	0.115(0.01-0.25)	[16]
ρ	/year	0.096(0.01-0.3)	[16]
θ	-	0.5(0.0-1.0)	Assumed
μ	/year	0.02(0.01-0.02)	[19]
α	-	6.0	[28]
Λ	People/year	1000000	[15]
β	-	0.0001(0.00001-0.002)	Assumed

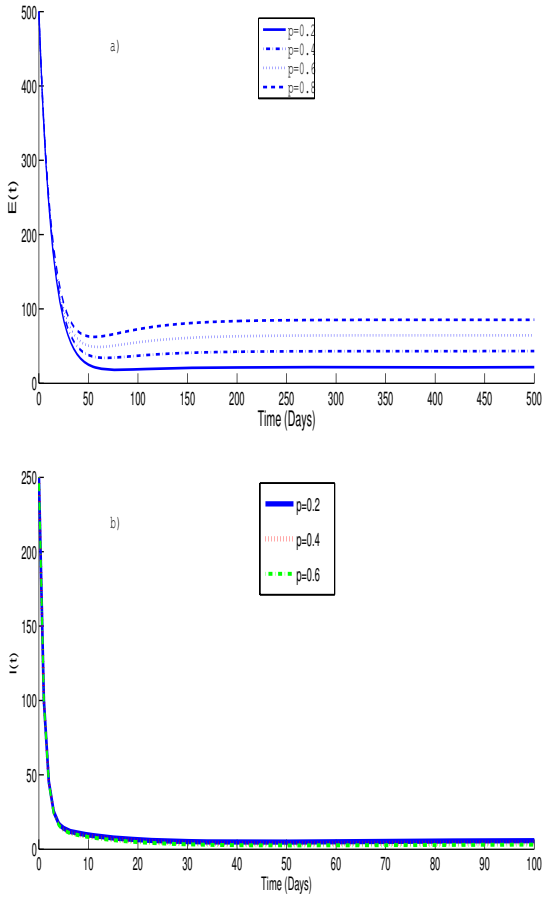

Fig. 2. Effects of p on (a) latent typhoid cases, and (b) infectious cases is demonstrated over time. Parameter values used are in Table II, with the following assumed initial conditions $S = 10000$, $E = 500$ and $I = 250$.

Results on Fig. 3 suggests that increasing educational campaigns may have a significant impact on controlling the transmission dynamics of typhoid (since increasing θ on (a) and (b) reduces cumulative typhoid cases). The impact of treatment on controlling typhoid prevalence has been investigated using numerical simulations depicted on Fig. 4 (effects of early

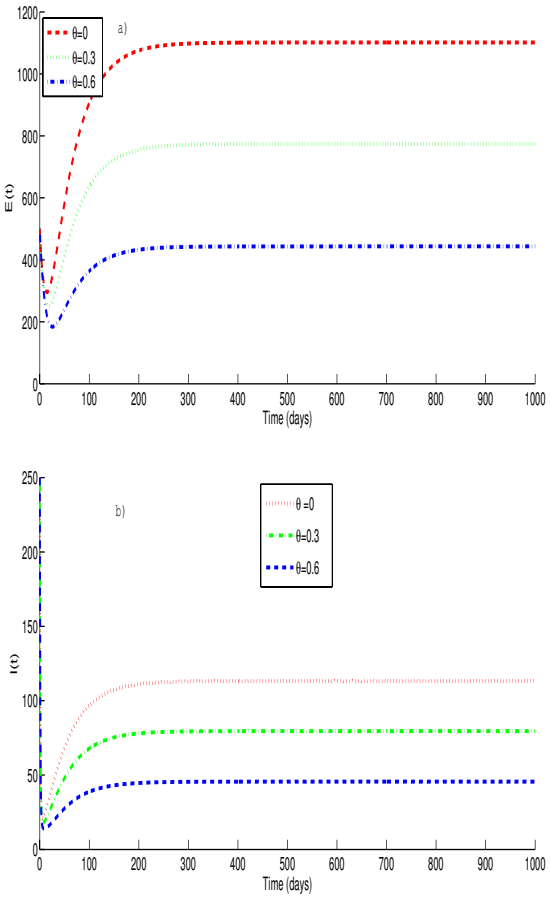

Fig. 3. Simulation results for system (1) showing the effects of educational campaigns on controlling the transmission dynamics of typhoid in the community, parameter values are in Table II, with the following assumed initial conditions $S = 10000$, $E = 500$ and $I = 250$.

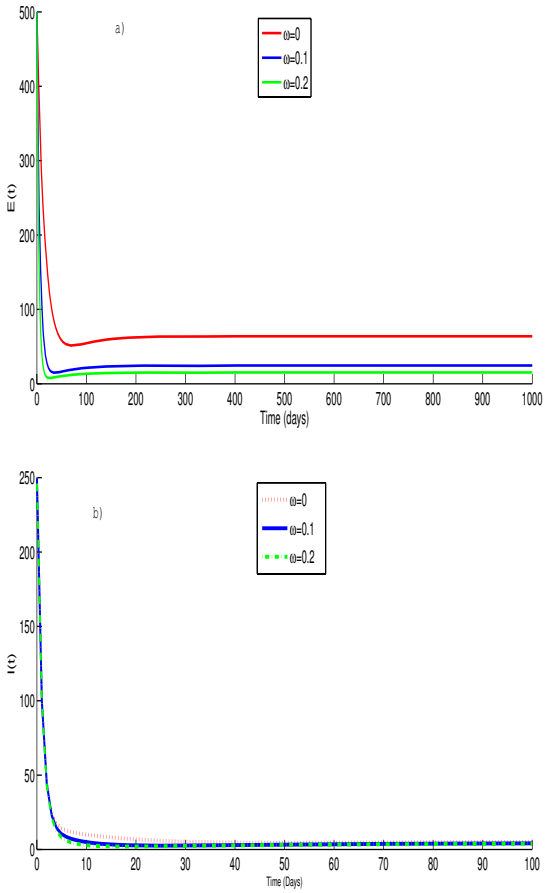

Fig. 4. Simulation results for system (1) showing the effects of early therapy (treatment of latent typhoid cases) on controlling the transmission dynamics of typhoid in the community, parameter values are in Table II, with the following assumed initial conditions $S = 10000$, $E = 500$ and $I = 250$.

therapy, that is treatment administered to latently infected individuals) and Fig. 5 (treatment of infectious individuals), respectively. Comparing the results displayed on Fig. 4 and Fig. 5, we note that early therapy has a more significant impact on reducing new typhoid cases compared to treatment of infectious individuals (since varying ω gives a remarkable change of both, cumulative latent cases and cumulative infectious cases), however, this does not suggests that treating infectious typhoid is not important, but the study may be only stressing the importance of early therapy as a typhoid intervention strategy. We, further examine the impact of the three aforementioned typhoid intervention strategies using sensitivity analysis.

A. Sensitivity analysis

Sensitivity analysis assesses the amount and type of change inherent in the model as captured by the terms that define the reproductive number $(\mathcal{R}_0)$ [29], [30]. If $\mathcal{R}_0$ 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. We begin by estimating the correlation between the reproductive number and the model parameters which define it using Partial Rank Correlation Coefficients (PRCCs).

Fig. 6 illustrates that the reproductive number $\mathcal{R}_0$ is most sensitive to education adjustment (θ). An increase in θ will reduce the magnitude of $\mathcal{R}_0$. It is also worth noting that treatment of infectious individuals has a strong influence on reducing the magnitude of $\mathcal{R}_0$. Since the educational adjustment parameter has a significant effect on the reproductive number, we examined the dependence of the reproductive number in this parameter in more detail (Fig. 7). We used Latin Hypercube Sampling and Monte Carlo simulations to run 1000 simulations, where all parameters were simultaneously drawn from across their ranges.

Fig. 7 illustrates the effect of educational adjustments on controlling typhoid in the community. The results suggests

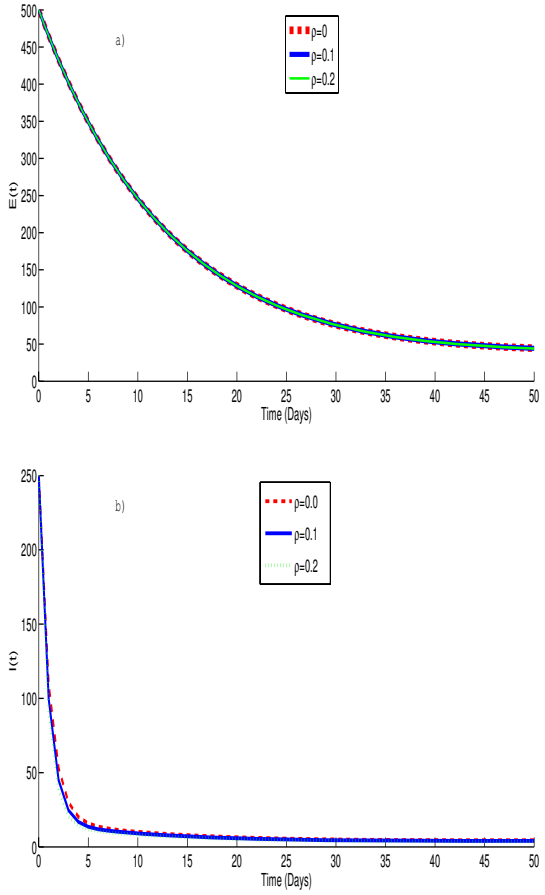

Fig. 5. Simulation results for system (1) showing the impact of treating infectious typhoid infectives on controlling the transmission dynamics of typhoid in the community, parameter values are in Table II, with the following assumed initial conditions $S = 10000$, $E = 500$ and $I = 250$.

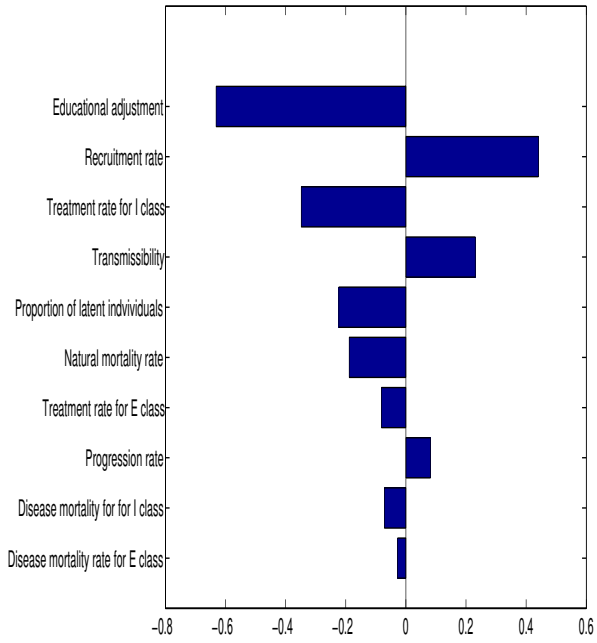

Fig. 6. Partial Rank Correlation Coefficients (PRCCs) showing the effects of parameter variation on, $\mathcal{R}_0$ using ranges in the table. Parameters with positive PRCCs will increase $\mathcal{R}_0$ when they are increased, whereas parameters with negative PRCCs will decrease $\mathcal{R}_0$ when they are increased.

that, in the presence of treatment for latently infected and infectious individuals in the community, an increase in educational campaigns results in a decrease on the reproductive ratio. If educational efforts can be effective 40% of the time or more, then the disease will be controlled.
Fig. 7 illustrates the effect of educational adjustments on controlling typhoid in the community. The results suggests that, in the presence of treatment for latently infected and infectious individuals in the community, an increase in educational campaigns results in a decrease on the reproductive ratio. If educational efforts can be effective 40% of the time or more, then the disease will be controlled.

V. Conclusion

Typhoid fever is an important public-health problem in south-central and southeast Asia, the middle east, Africa, and South America, mainly affecting children and young adults. Motivated by the recent outbreak of typhoid in Zimbabwe, a simple deterministic mathematical model for assessing the impact of educational campaign on controlling the transmission dynamics of typhoid has been formulated and comprehensively analyzed. The reproductive number has been computed. Qualitative analysis of the model reveals the following. The disease-free equilibrium is both locally and globally-asymptotically stable whenever the reproductive number is less than unity. With the aid of robust mathematical techniques it has been shown that the model has a unique endemic equilibrium point which exists if the reproductive number is greater than unity. Center Manifold theory has been used to show that the endemic equilibria is locally asymptotically stable when the reproduction number is greater than unity, but close to unity. Partial rank correlation coefficients (PRCCs) were calculated to estimate the correlation between values of the reproductive numbere and the ten model parameters across 1000 random draws from the empirical distribution of the reproductive number and its associated parameters. From Fig.6, we note that the reproductive number is most sensitive to the educational adjustment parameter. Examining the effects of education more closely, we determined that education was highly likely to control the disease if it can be more than 40% effective (Fig. 7).

The model proposed in this study has limitation(s), which should be acknowledged. The model developed in this study assumes that the disease is transmitted through human

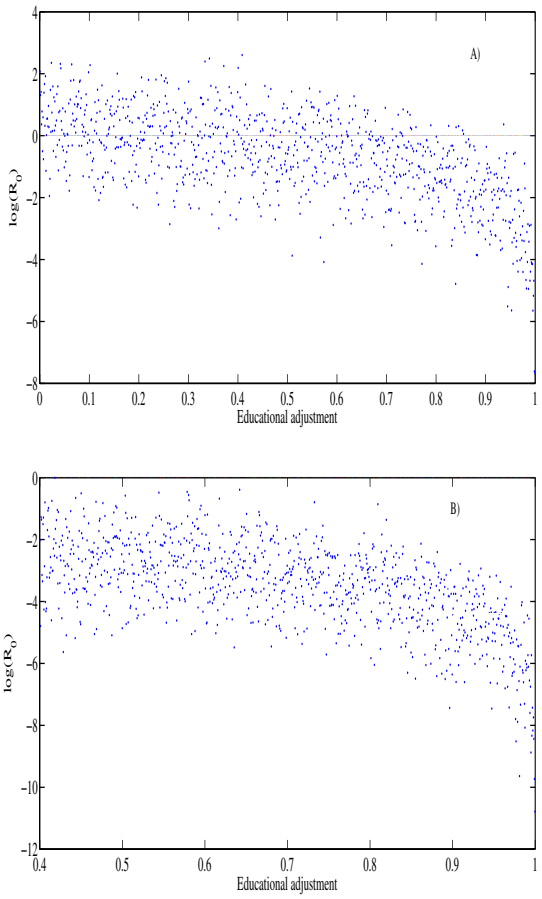

Fig. 7. Latin Hypercube Sampling for varying effectiveness of educational strategies. (A) Varying θ across all possible values. (B) If education is greater than 40% effective, then the disease can be controlled.

contact only, although the disease can be acquired through consumption, mainly of water, but sometimes of food, that has been contaminated by sewage containing the excrement of people suffering from the disease. Furthermore, recruited individuals are assumed to be susceptible which might not be case in some communities.

REFERENCES

[1] C. Kidgell, U. Reichard, and J. Wain J, et al, "Salmonella typhi, the causative agent of typhoid fever, is approximately 50,000 years old," *Infect. Genet. Evol,* vol. 2, pp. 39-45, 2002.

[2] M. K. Bhan, R. Bahl, and ,S. Bhatnagar, "Typhoid and paratyphoid fever," *Lancet*, vol. 366, pp. 749-762, 2005.

[3] D. S. Merrell, and S. Falkow, "Frontal and stealth attack strategies in microbial pathogenesis," *Nature*, vol. 430, pp. 250-26, 2004.

[4] S. Kariuki, G. Revathi, J. Muyodi, J. Mwituria, A. Munyalo, S. Mirza, and C. A. Hart, "Characterization of Multidrug-Resistant Typhoid Outbreaks in Kenya," *J. Clin. Microbiol*, vol. 42(4), pp. 1477-1482, 2004.

[5] A. E. Fica, S. Prat-Miranda, A. Fernandez-Ricci, K. DOttone, and F. C. Cabello, " Epidemic typhoid in Chile: analysis by molecular and conventional methods of Salmonella typhi strain diversity in epidemic (1977 and 1981) and nonepidemic. 1990. years," *J. Clin. Microbiol*, vol. 34, pp. 1701-1707, 1996.

[6] J. Olarte, and E. Galindo, "Salmonella typhi resistant to chloramphenicol, ampicillin and other antimicrobial agents: strains isolated during an extensive typhoid fever epidemic in Mexico," *Antimicrob. Agents Chemother*, vol. 4, pp. 597-601, 1973.

[7] J. M. Ling, N. W. Lo, Y. M. Ho, K. M. Kam, N. T. Hoa, L. T. Phi, and A. F. Cheng, "Molecular methods for the epidemiological typing of Salmonella enterica serotype Typhi from Hong Kong and Vietnam," *J. Clin. Microbiol* vol. 38, pp. 292-300, 2000.

[8] S. H. Mirza, N. J. Beeching, and C. A. Hart, "Multidrug resistant typhoid: a global problem," *J. Med. Microbiol*, vol. 44, pp. 317-319, 1996.

[9] S. Mirza, S. Kariuki, K. Z. Mamun, N. J. Beeching, and C. A. Hart, "Analysis of plasmid and chromosomal DNA of multidrug-resistant Salmonella enterica serovar Typhi from Asia", *J. Clin. Microbiol*, vol. 38, pp. 1449-1452, 2000.

[10] M. Rahman, A. Ahmad, and S. Shoma, "Decline in epidemic of multidrug resistant Salmonella typhi is not associated with increased incidence of antibiotic-susceptible strain in Bangladesh," *Epidemiol. Infect*, vol. 129, pp. 29-34, 2002.

[11] P. M. Shanahan, K. A. Karamat, C. J. Thomson, and S. G. Amyes. "Molecular analysis of and identification of antibiotic resistance genes in clinical isolates of Salmonella typhi from India," *J. Clin. Microbiol*, vol. 36, pp. 1595-1600, 1998.

[12] S. Kariuki, C. Gilks, G. Revathi, and C. A. Hart, "Genotypic analysis of multidrug-resistant Salmonella enterica Serovar Typhi, Kenya", *Emerg. Infect. Dis*, vol. 6, pp. 649-651, 2000.

[13] F. Mills-Robertson, M. E. Addy, P. Mensah, and S. S. Crupper, " Molecular characterization of antibiotic resistance in clinical Salmonella typhi isolated in Ghana," *FEMS Microbiol. Lett*, vol. 215, pp. 249-253, 2002

[14] B. Singh, "Typhoid Fever Epidemiology," *Journal Indian Academy of Clinical Medicine*, vol. 2(1)-(2), pp. 11-12, 2001

[15] D. T. Lauria, B. Maskery, C. Poulos, and D. Whittington, "An optimization model for reducing typhoid cases in developing countries without increasing public spending," *Vaccine* JVAC-8805 (2009).

[16] I. A. Adetunde, "A Mathematical models for the dynamics of typhoid fever in Kassena-Nankana district of upper east region of Ghana," *Journal of Modern Mathematics and statistics*, vol. 2(2), pp. 45-49, 2008.

[17] D. Kalajdzievska, and M. Y. LI, "Modeling the effects of carriers on transmission dynamics of infectious disease", *Math. Biosci. Eng*, vol. 8(3), pp. 711-722, 2011.

[18] S. Mushayabasa, C. P. Bhunu, and E. T. Ngarakana-Gwasira, "Mathematical analysis of a typhoid model with carriers, direct and indirect disease transmission," *IJMSEA*,vol. 7(1), pp. 79-90, 2013.

[19] J. Gonzlez-Guzmn, " An epidemiological model for direct and indirect transmission of typhoid fever," *Math. Biosci*, vol. 96(1), pp. 33-46, 1989.

[20] P. Katri, S. Ruan, "Dynamics of human T-cell lymphototropic virus I (HTLV-I) infection of CD4$^+$ T-cells," *C.R. Biol*, vol. 327, pp. 1009-1016, 2004.

[21] Y. Kuang, Delay differentail equations springer, new York (1997).

[22] S. Buseng, and K. L. Cooke, Vertically transmitted diseases, models and dynamics. Biomathematics, vol. 23. Springer, New York (1993)

[23] H. W. Hethcote, "The mathematics of infectious diseases," *SIAM Rev*, vol. 42, pp. 599-653, 2000.

[24] P. van den Driessche, and J. Watmough, "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission," *Math. Biosci*, vol. 180, pp. 29-48, 2002.

[25] C. Castillo-Chavez, Z. Feng, and W. Huang "On the computation of R0 and its role on global stability. In: Castillo-Chavez, C., et al. (eds.) Mathematical Approaches for Emerging and Reemerging Infectious Diseases: An Introduction," *IMA*, vol. 125, pp. 229-250, 2002.

[26] C. Castillo-Chavez, and B. Song, "Dynamical models of tuberculosis and their applications. *Math. Biosci. Eng*, vol. 1(2), pp. 361-404, 2004.

[27] Carr, J: Applications of Centre Manifold Theory. Springer, New York (1981)

[28] R. Xu, and Z. Ma, "Global stability of a delayed SEIRS epidemic model with saturation incidence rate," *Nonlinera Dyn* vol. 61, pp. 229-239, 2010.

[29] S. Mushayabasa, C. P. Bhunu, and R. J. Smith?, "Assessing the impact of educational campaigns on controlling HCV among women prisoners," *Commun Nonlinear Sci Numeri Simulat*, vol.17, pp. 1714-1724, 2012.

[30] J. C. Helton, "Uncertainty and sensitivity analysis techniques for use in performance assessment for waste disposal," *Reliab. Eng. Syst. Saf*, vol. 42, pp. 42: 327367, 1993.