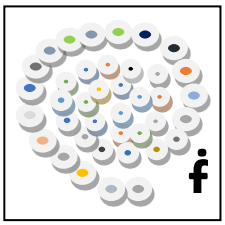

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A two-infection stage model with SIS and SIR dynamics

A.O. Sangotola* and L.J. Sangoyinka†

Abstract

A two-infection stage model is presented in this research work. The dynamics of the model is such that it behaves like a SIS or SIR model depending on the stage treatment is applied. The disease-free equilibrium point and the basic reproduction number are determined. The conditions for the disease-free equilibrium and endemic equilibrium to be globally asymptotically stable are determined. Sensitivity analysis is used to determine the impact of the model parameter on the basic reproduction number. Numerical simulation with suitable approximated parameters using MATLAB is also carried out to give possible dynamics of the model.

Keywords: stability; equilibrium; basic reproduction number; Lyapunov function.

1 Introduction

The dynamic models for infectious disease are mostly based on their compartment structure. The compartment structures for dynamic models are firstly given by Kermack and Mckendrick in 1927 and has been improved over the years [1]. Some of the compartmental models includes: SI, SIS, SIR, SEIR, SEIRS etc. Mathematical models of infectious diseases give insights into disease transmission, progression, stage of infection and helps in mathematical analysis. Blackwood and Childs [3] highlighted several common issues encountered while analyzing basic compartmental models. Melesse and Gumel [9] presented an extensive mathematical analysis of a deterministic model, with a standard incidence function, for the transmission dynamics of a communicable disease with an arbitrary number of distinct infectious stages. The conditions for the global stability of the disease free and endemic equilibrium was determined. Numerical simulation was carried out to illustrate the theoretical results.

* Corresponding Author. Department of Physical Sciences, Bells University of Technology, Ota, Ogun State, Nigeria; E-mail: adekunle4000@hotmail.co.uk , aosangotola@bellsuniversity.edu.ng
†Department of Mathematics and Statistics, The Polytechnic Ibadan, Oyo State, Nigeria; Email: lsangoyinka@gmail.com

Otunuga and Ogunsolu [14] presented a mathematical analysis of the transmission of certain diseases using a stochastic susceptible-exposed-infectious-treated-recovered (SEITR) model with multiple stages of infection and treatment and explore the effects of treatments and external fluctuations in the transmission, treatment and recovery rates. Global stability analysis of the disease free and endemic equilibrium for both the deterministic and stochastic version of the model were presented. Rifanti [16] presented a two-infection stage mathematical method which are chronic stage and acute stage. Both infection stages involve transmissibility. Multistage dynamics of infectious dynamics are also captured in the following literatures: [7, 10, 13, 18].

Here, we consider a two-infection stage model where the first stage is the passive stage and the second stage is the active stage. The model dynamics can be a SIS or SIR dynamics depending on the stage of treatment application. Individuals who recover from the first stage due to early detection and treatment or natural immunity goes back to the susceptible class because the disease has not run its course. Individuals who recover from the second stage moves to the recovered class. This dynamic is explained further under the model formulation.

2 Model formulation

The model is divided into four compartments with the susceptible population denoted by $S(t)$, the first infection stage is denoted by $I_1(t)$, the second infection stage is denoted by $I_2(t)$ while the recovered population denoted by $R(t)$. The susceptible population is increased as a result of migration or birth at rate Λ. The dynamics of the disease is such that there are two infection stages with infectivity in the second stage of infection. There susceptible population is decreased as a result of natural death at rate μ and by interaction with infectious population (I_2) with β as the force of infection. This above interaction causes an increase in the population at the first stage of infection. The first stage of infection is reduced either by natural death, temporary recovery back to the susceptible population at rate σ or allowing the disease to develop into the second stage at rate α. The second infection stage is reduced by natural death, disease induced death at rate δ or by effective treatment at rate γ. The recovered population is increased as a result of recovery from second stage and decreased only by natural death.

The resulting system from the above assumptions is given as

$$\frac{dS}{dt} = \Lambda - \beta S I_2 - \mu S + \sigma I_1 \quad (1)$$
$$\frac{dI_1}{dt} = \beta S I_2 - (\alpha + \mu + \sigma)\, I_1 \quad (2)$$
$$\frac{dI_2}{dt} = \alpha I_1 - (\mu + \delta + \gamma) I_2 \quad (3)$$
$$\frac{dR}{dt} = \gamma I_2 - \mu R \quad (4)$$

Description of parameters in the model $(1)-(4)$:

Parameter	Meaning
Λ	Recruitment rate
β	Transmission rate
μ	Natural death rate
σ	Recovery rate from stage 1
α	Progression rate to second stage
δ	Disease induced death rate
γ	Recovery rate from stage 2

3 Results and discussions

3.1 Invariant region

We obtain the region where the solution of $(1)-(4)$ is epidemiological feasible.

Theorem 3.1: (Invariant region). The feasible region $\mathcal{R}$ defined by $\left\{S(t), I_1(t), I_2(t), R(t) \in R_+^4 : N(0) \leq N(t) \leq \frac{\Lambda}{\mu}\right\}$ with initial conditions $S(0) \geq 0, I_1(0) \geq 0, I_2(0) \geq 0, R(0) \geq 0$ is positive invariant for system $(1)-(4)$.

Proof: The total population size is given by $N(t) = S(t) + I_1(t) + I_2(t) + R(t)$.

$$\frac{dN}{dt} = \Lambda - \mu N - \delta I_2$$
$$\frac{dN_h}{dt} \leq \Lambda - \mu N$$

Solving above, we have

$$0 \leq N(t) \leq \left(N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t})\right)$$

As $t \to \infty, 0 \leq N(t) \leq \frac{\Lambda}{\mu}$, If $N(0) \leq \frac{\Lambda}{\mu}$ *then* $N(t) \leq \frac{\Lambda}{\mu}$. Hence,

$$N(0) \leq N(t) \leq \frac{\Lambda}{\mu}.$$

Thus, $\mathcal{R}$ is a positive invariant set under the model described by $(1)-(4)$.

3.2 Disease-free equilibrium

The disease-free equilibrium is the point where there is no disease in the population. It lies at the point $\pi_o = \left(\frac{\Lambda}{\mu}, 0,0,0\right)$

3.3 Basic reproduction number

The basic reproductive number is the mean number of secondary infections caused by an infectious individual in an entirely susceptible population. The next generation matrix approach by Driessche and Watmough [6] is applied.

From the infectious stages I_1 and I_2, we can create a vector $\mathcal{F}$ that represent new infections and $\mathcal{V}$ that represents outflows from the model equations. Hence,

$$\mathcal{F} = \begin{pmatrix} \beta S I_2 \\ 0 \end{pmatrix} \quad \text{and} \quad \mathcal{V} = \begin{pmatrix} (\alpha+\mu+\sigma) I_1 \\ (\mu+\delta+\gamma) I_2 \; -\alpha I_1 \end{pmatrix} \quad .$$

Next, we compute the Jacobian F from $\mathcal{F}$ and V from $\mathcal{V}$ at the disease-free equilibrium point. They are given by

$$\mathrm{F} = \begin{pmatrix} 0 & \beta\frac{\Lambda}{\mu} \\ 0 & 0 \end{pmatrix} \qquad \text{and} \qquad \mathrm{V} = \begin{pmatrix} (\alpha+\mu+\sigma) & 0 \\ -\alpha & (\mu+\delta+\gamma) \end{pmatrix}$$

The basic reproduction $R_0$is given by $\rho(FV^{-1})$ where ρ is the spectral radius. Thus,

$$R_0 = \frac{\alpha\beta\Lambda}{\mu(\alpha+\mu+\sigma)(\mu+\delta+\gamma)}.$$

3.4 Local stability

Theorem 3.2: (Local stability of disease-free equilibrium). The disease-free equilibrium for the system is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof:
The equilibrium points of model $(1)-(4)$ is locally asymptotically stable if all the eigenvalues of the Jacobian matrix have negative real parts.

The Jacobian matrix evaluated at the disease-free is given by

$$J(\pi_0) = \begin{pmatrix} -\mu & \sigma & -\frac{\beta\Lambda}{\mu} & 0 \\ 0 & -(\alpha+\mu+\sigma) & \frac{\beta\Lambda}{\mu} & 0 \\ 0 & \alpha & -(\mu+\delta+\gamma) & 0 \\ 0 & 0 & \gamma & -\mu \end{pmatrix}$$

There are four roots corresponding to the Jacobian above. Two of the roots are $-\mu$(twice) while the other roots can be obtained from the characteristic equation of the sub matrix given below.

$$J_1(\pi_0) = \begin{pmatrix} -(\alpha+\mu+\sigma) & \frac{\beta\Lambda}{\mu} \\ \alpha & -(\mu+\delta+\gamma) \end{pmatrix}$$

The remaining eigenvalues are negative if trace of $J_1(\pi_0)$ is negative and determinant of $J_1(\pi_0)$ is positive. The trace of $J_1(\pi_0)$ is negative and the determinant is $(\alpha+\mu+\sigma)(\mu+\delta+\gamma) - \frac{\alpha\beta\Lambda}{\mu}$. The determinant is also equivalent to $(\alpha+\mu+\sigma)(\mu+\delta+\gamma)(1-R_0)$ and it is positive provided that $R_0 < 1$.

Theorem 3.3: (Existence of endemic equilibrium). The model $(1)-(4)$ has an endemic equilibrium when $R_0 > 1$.

Proof: Let $E_e^* = (S^*, {I_1}^*, {I_2}^*, R^*)$ be a non-trivial equilibrium of the model. The model at steady state becomes:

$S^* = \frac{(\alpha+\mu+\sigma)(\mu+\delta+\gamma)}{\alpha\beta}$
${I_1}^* = \frac{\Lambda}{R_0(\mu+\alpha)}[\,R_0 - 1]$
$R^* = \frac{\gamma(\alpha+\mu+\sigma)}{\beta(\mu+\alpha)}[\,R_0 - 1]$
${I_2}^* = \frac{\mu(\alpha+\mu+\sigma)}{\beta(\mu+\alpha)}[\,R_0 - 1]$.

3.5 Global stability analysis

Theorem 3.4: (Global stability of disease-free equilibrium). The disease-free equilibrium for the system is globally asymptotically stable if $R_0 < 1$.
Proof: Consider the Lyapunov function:
$L = \alpha I_1 + (\alpha+\mu+\sigma)I_2$
$\dot{L} = \alpha\dot{I}_1 + (\alpha+\mu+\sigma)\dot{I}_2$

Substituting and simplifying the expressions for $\dot{I}_1$ and $\dot{I}_2$ gives
$\dot{L} = \alpha[\beta S I_2 - (\alpha+\mu+\sigma)\,I_1] + (\alpha+\mu+\sigma)[\alpha I_1 - (\mu+\delta+\gamma)I_2]$
$\dot{L} = \alpha\beta S I_2 - (\alpha+\mu+\sigma)(\mu+\delta+\gamma)I_2.$

Since $S = \frac{\Lambda}{\mu}$ it follows that

$\dot{L} = (\alpha+\mu+\sigma)(\mu+\delta+\gamma)I_2[R_0 - 1].$

Thus $\dot{L} \leq 0$ with equality when $I_2 = 0$. Hence by LaSlle's extension to Lyapunov principle, the limit set for each solution is contained in the largest invaraiant set for which $I_2 = 0$.

Theorem 3.5: (Global stability of endemic equilibrium). The endemic equilibrium for the system is globally asymptotically stable if $R_0|_{\sigma=0} > 1$.

Proof: Let the associated endemic equilibrium of model $(1)-(4)$ and $R_0|_{\sigma=0} > 1$ exist. Consider the Lyapunov function:

$$V = S - S^{**} - S^{**}ln\left(\frac{S}{S^{**}}\right) + {I_1}^{**} - {I_1}^{**} - ln\left(\frac{I_1}{{I_1}^{**}}\right) + \frac{(\alpha+\mu)}{\alpha}\left[{I_2}^{**} - {I_2}^{**} - ln\left(\frac{I_2}{{I_2}^{**}}\right)\right]$$

$$\dot{V} = \dot{S} - \frac{S^{**}}{S}\dot{S} + \dot{I}_1 - \frac{{I_1}^{**}}{I_1}\dot{I}_1 + \frac{(\alpha+\mu)}{\alpha}\left[\dot{I}_2 - \frac{{I_2}^{**}}{I_2}\dot{I}_2\right]$$

$$\dot{V} = \Lambda - \beta S I_2 - \mu S - \frac{S^{**}}{S}[\Lambda - \beta S I_2 - \mu S] + \beta S I_2 - (\alpha+\mu) \quad I_1 - \frac{{I_1}^{**}}{I_1}[\beta S I_2 - (\alpha+\mu) I_1]$$

$$+\frac{(\alpha+\mu)}{\alpha}\left[\alpha I_1 - (\mu+\delta+\gamma)I_2 - \frac{{I_2}^{**}}{I_2}\{\alpha I_1 - (\mu+\delta+\gamma)I_2\}\right]$$

$$\dot{V} = \Lambda\left(1 - \frac{S^{**}}{S}\right) - \mu S\left(1 - \frac{S^{**}}{S}\right) + \beta S^{**} I_2 - \beta S I_2 \frac{{I_1}^{**}}{I_1} + (\alpha+\mu){I_1}^{**} - \frac{(\alpha+\mu)(\mu+\delta+\gamma)I_2}{\alpha} - (\alpha+\mu) I_1 \frac{{I_2}^{**}}{I_2} +$$

$$\frac{(\alpha+\mu)(\mu+\delta+\gamma){I_2}^{**}}{\alpha}.$$

At the endemic steady state, the following relations obtained from model $(1)-(4)$ hold:

$$\Lambda = \beta S^{**}{I_2}^{**} + \mu S^{**}$$

$$(\alpha+\mu) = \frac{\beta S^{**}{I_2}^{**}}{{I_1}^{**}}$$

$$(\mu+\delta+\gamma) = \frac{\alpha {I_1}^{**}}{{I_2}^{**}}.$$

Substituting above relations into the Lyapunov function gives:

$$\dot{V} = (\beta S^{**}{I_2}^{**} + \mu S^{**})\left(1 - \frac{S^{**}}{S}\right) - \mu S\left(1 - \frac{S^{**}}{S}\right) + \beta S^{**} I_2 - \beta S I_2 \frac{{I_1}^{**}}{I_1} + \left(\frac{\beta S^{**}{I_2}^{**}}{{I_1}^{**}}\right) {I_1}^{**} -$$

$$\left(\frac{\beta S^{**}{I_2}^{**}}{{I_1}^{**}}\right)\left(\frac{\alpha {I_1}^{**}}{{I_2}^{**}}\right)\left(\frac{I_2}{\alpha}\right) - \left(\frac{\beta S^{**}{I_2}^{**}}{{I_1}^{**}}\right) I_1 \frac{{I_2}^{**}}{I_2} + \left(\frac{\beta S^{**}{I_2}^{**}}{{I_1}^{**}}\right)\left(\frac{\alpha {I_1}^{**}}{{I_2}^{**}}\right)\left(\frac{{I_2}^{**}}{\alpha}\right).$$

Simplifying gives
Further simplification gives

$$\dot{V} = \mu S^{**}\left(2 - \frac{S^{**}}{S} - \frac{S}{S^{**}}\right) + 3\beta S^{**}{I_2}^{**} - \frac{\beta {S^{**}}^2 {I_2}^{**}}{S} - \beta S I_2 \frac{{I_1}^{**}}{I_1} - \frac{\beta S^{**} I_1 {I_2}^{**2}}{{I_1}^{**} I_2}$$

$$\dot{V} = \mu S^{**}\left(2 - \frac{S^{**}}{S} - \frac{S}{S^{**}}\right) + \beta S^{**}{I_2}^{**}\left(3 - \frac{S^{**}}{S} - \frac{S {I_1}^{**} I_2}{S^{**} I_1 {I_2}^{**}} - \frac{I_1 {I_2}^{**}}{{I_1}^{**} I_2}\right).$$

Since arithmetic mean is less than or equal to geometric mean,

$\mu S^{**}\left(2-\frac{S^{**}}{S}-\frac{S}{S^{**}}\right)\leq 0$ and $\left(3-\frac{S^{**}}{S}-\frac{SI_1{}^{**}I_2}{S^{**}I_1I_2{}^{**}}-\frac{I_1I_2{}^{**}}{I_1{}^{**}I_2}\right)\leq 0$.

Thus, $\dot{V}\leq 0$ if and only if $S=S^{**}$, $I_1=I_1{}^{**}$, $I_2=I_2{}^{**}$. Hence, the largest compact invariant subset of the set where $\dot{V}=0$ is the singleton (S, I_1, I_2)= $(S^{**}, I_1{}^{**}, I_2{}^{**})$. It follows by LaSalle's Invariance Principle [8], that every solution to the equations of the model (1) approaches the associated unique endemic equilibria of the model as $t\to\infty$ for $R_0|_{\sigma=0}>1$.

3.6 Sensitivity analysis

Sensitivity analysis is used to determine dependencies between input parameters and results of the model. Sensitivity analysis helps to determine how a small change in parameters affects state variables over time. The normalised forward sensitivity index of a variable,w, that depends on a parameter, q, is defined as: $\Gamma_q^w=\frac{\partial w}{\partial q}\times\frac{q}{w}$.

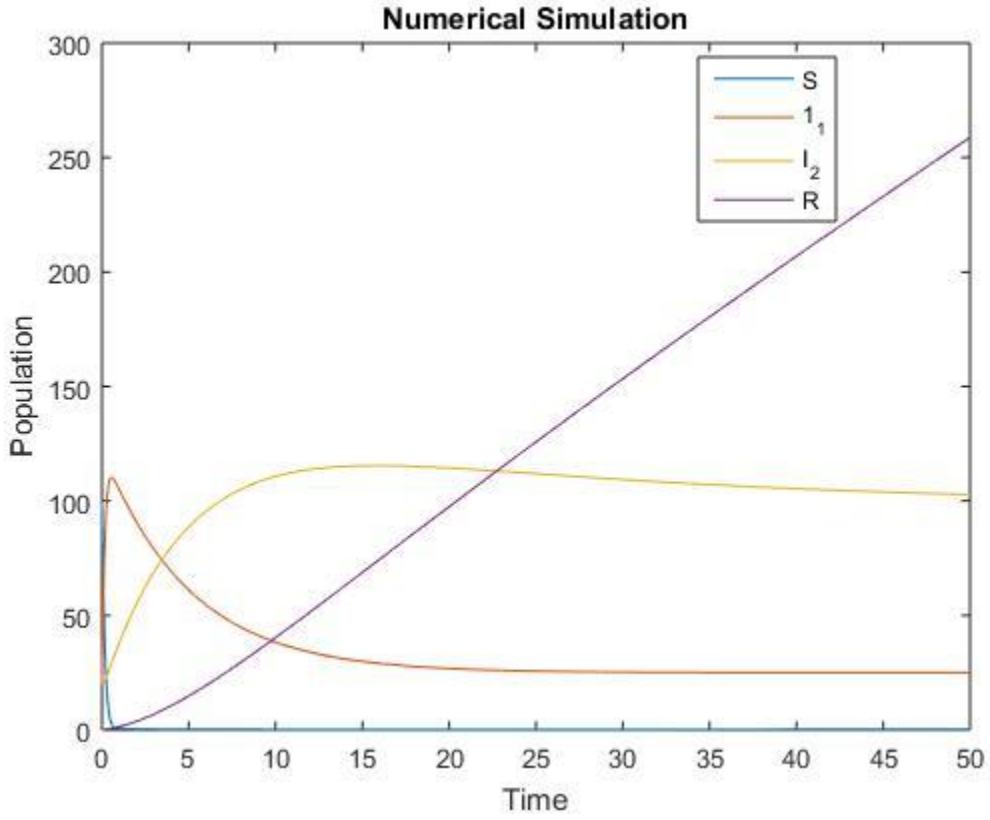
Sensitivity index of the basic reproduction number with respect to the model parameters are computed below:

parameter	$\Gamma_{parameter}^{R_0}$
β	1
Λ	1
α	$\frac{(\mu+\sigma)}{(\alpha+\mu+\sigma)}$
σ	$\frac{-\sigma}{(\alpha+\mu+\sigma)}$
δ	$\frac{-\delta}{(\mu+\delta+\gamma)}$
γ	$\frac{-\gamma}{(\mu+\delta+\gamma)}$
μ	$-\frac{R_0}{\mu}\left[\frac{1}{(\mu+\delta+\gamma)}+\frac{(\alpha+2\mu+\sigma)}{(\alpha+\mu+\sigma)}\right]$

$\Gamma_{R_0}^d=1$ revealed that a 10 percent in transmission rate corresponds to 10 percent increase in the basic reproduction number. Sensitivity analysis gives an insight into the required strategy to control the spread of the disease.

3.7 Numerical simulation

The dynamics of the model depends on the input parameters. The input parameters are approximated from most communicable diseases. $\Lambda = 5, \beta = 0.3,\ \mu = 0.0005, \sigma = 0.01, \delta = 0.0005, 0,\ \alpha = 0.2,\ \gamma$=0.05 with $S(0) = 100, I_1(0) = 20, I_2(0) = 20, R(0) = 0$. The numerical simulation is shown below using MATLAB. The interplay between I_1 and I_2 class will determine whether the susceptible class will have much increase or the recovered class.



4 Conclusion

In this paper, we presented a two-infection stage mathematical model. The basic reproduction number of the model is determined. The disease-free equilibrium point is found to be globally asymptotically stable if $R_0 < 1$. There is an existence of endemic equilibrium provided that $R_0 > 1$. However, the endemic equilibrium is globally asymptotically stable if $R_0|_{\sigma=0} > 1$. Sensitivity analysis shows that the recruitment rate, transmission rate and progression rate from the first infection stage to the second infection stage have a direct proportionality on the basic reproduction number. Numerical simulation with appropriate parameters is carried out to give possible dynamics of the model.

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